Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment of robot-assisted surgery in selected surgical procedures

21 September 2011

Safer Better Care

About the Health Information and Quality Authority

The Health Information and Quality Authority is the independent Authority established to drive continuous improvement in Ireland's health and social care services.

The Authority's mandate extends across the quality and safety of the public, private (within its social care function) and voluntary sectors. Reporting directly to the Minister for Health, the Health Information and Quality Authority has statutory responsibility for:

Setting Standards for Health and Social Services — Developing person-centred standards, based on evidence and best international practice, for health and social care services in Ireland (except mental health services)

Social Services Inspectorate — Registration and inspection of residential homes for children, older people and people with disabilities. Inspecting children detention schools and foster care services.

Monitoring Healthcare Quality — Monitoring standards of quality and safety in our health services and investigating as necessary serious concerns about the health and welfare of service users

Health Technology Assessment — Ensuring the best outcome for the service user by evaluating the clinical and economic effectiveness of drugs, equipment, diagnostic techniques and health promotion activities

Health Information — Advising on the collection and sharing of information across the services, evaluating information and publishing information about the delivery and performance of Ireland's health and social care services

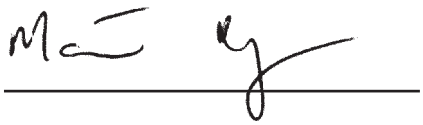
Foreword

Robot-assisted surgery involves the use of an advanced surgical tool to perform minimally invasive surgery for certain procedures. The device includes up to four robotic arms equipped with surgical instruments that are controlled by the surgeon from an operating console a short distance from the patient. It is claimed that this system could result in better outcomes or reduced complications for patients undergoing these procedures. The technique has been used worldwide in a wide range of surgical procedures to date, including diseases in urology, gynaecology, cardiology and diseases of the head and neck.

In January 2011, the Health Information and Quality Authority (the Authority) agreed to undertake a health technology assessment (HTA) of robot-assisted surgery in response to a request from the Health Service Executive (HSE) National Director for Quality and Clinical Care. The purpose of this HTA was to evaluate the available evidence on the safety and efficacy of robot-assisted surgery for selected indications, the costs and cost-effectiveness of a policy of implementing robot-assisted surgery and to advise on other organisational and training issues that may need to be considered prior to a decision regarding the adoption of such technology by the HSE.

Work on the HTA was undertaken by an Evaluation Team from the HTA Directorate of the Authority supported by Dr Siobhan O'Sullivan, Chief Bioethics Officer of the Department of Health, who provided the ethical commentary. A multidisciplinary Expert Advisory Group (EAG) was convened to advise the Authority during the conduct of this assessment.

The Authority would like to thank its Evaluation Team, Dr Siobhan O'Sullivan, the members of the EAG and all who contributed to the preparation of this report.



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The membership of the EAG was as follows:

Dr Máirín Ryan, Director of Health Technology Assessment, Health Information and Quality Authority (Chairperson)

Dr Tammy Clifford, Chief Scientist, Canadian Agency for Drugs and Technologies in Health

Dr Eibhlín Connolly, Deputy Chief Medical Officer, Department of Health

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Ms Deirdre Murphy, Manager, Peer Support Programme, Irish Cancer Society

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Mr Michael Tolan, Consultant Cardiothoracic Surgeon, St James's Hospital, Dublin

Dr Valerie Walshe, Health Economist, Health Service Executive.

Organisations that assisted the Authority in providing information, in writing or through meetings, included:

Department of Health (Ireland)
Health Service Executive (HSE)
Economic and Social Research Institute (ESRI)
The National Cancer Control Programme, HSE
Beaumont Hospital, Dublin
St James's Hospital, Dublin
Cork University Maternity Hospital
The Galway Clinic
Intuitive Surgical Inc.

Members of the Evaluation Team:

Members of the Authority's Evaluation Team included Martin Flattery, Dr Patricia Harrington, Michelle O'Neill, Patrick Moran, Dr Linda Murphy, Dr Conor Teljeur, Dr Máirín Ryan in collaboration with Dr Siobhan O'Sullivan (Chief Bioethics Officer, Department of Health).

Conflicts of Interest:

Cork University Maternity Hospital has been designated an Intuitive Surgical Inc. 'epicentre' for training. Both Dr O'Reilly and Dr Hewitt have declared acting as a proctor in the training of new surgeons, where the payment for the service is made to Cork University Foundation and not directly to the doctors. The Foundation receives payment for visiting surgeons.

Professor Murphy declared being a paid mentor of robotic surgery for Intuitive Surgical Inc. during 2009 and receiving support for travel expenses to attend conferences from Device Technologies Limited in 2010.

Advice to the Health Service Executive

This health technology assessment (HTA) examined the evidence of the effectiveness, safety, costs and budget impact of robot-assisted surgery for a number of procedures. The HTA focussed on the procedures where there is sufficient evidence around the effectiveness of robot-assisted surgery. The organisational and other issues that would need to be considered in order to implement the technology as effectively and efficiently as possible have also been taken into account.

The key findings of this HTA which precede and inform the Authority's advice below were:

- Although robot-assistance is reported for a range of surgeries, prostatectomy and hysterectomy are the two surgical procedures where there is sufficient evidence, albeit of low quality, to inform decision making. Evidence continues to emerge of its use in a broad range of other procedures.
- Robot-assisted prostatectomy is superior to open prostatectomy across a range of outcomes evaluated in this HTA. Improved outcomes include urinary continence, sexual function and surgical margins. Peri-operative improved outcomes include lower risk of transfusion and shorter hospital stays. The benefits of robot-assisted prostatectomy over conventional laparoscopic approaches are minor.
- Robot-assisted hysterectomy, when compared with open surgery, is associated with improved peri-operative outcomes. These include lower risk of transfusion, and shorter hospital stays. Compared to conventional laparoscopic hysterectomy, the benefits of robot-assistance are less pronounced.
- Robot-assisted surgery is more ergonomic than conventional laparoscopic surgery for the operating surgeon, thereby allowing the surgeon to operate more easily.
- The current capital cost of a new surgical robot is €1.45 million, and an annual maintenance fee of €150,000 applies from year 2. This maintenance fee and the amortised capital costs of the robot over its lifetime have been included in the economic models.
- The incremental costs of robot-assisted surgery per procedure range from €2,487 to €3,019 for prostatectomy and hysterectomy respectively based on volumes per robot of 200 prostatectomies or 300 hysterectomies per annum. National demand for robot-assisted prostatectomy could be approximately 300 cases per annum and national demand for robot-assisted hysterectomy would be significantly higher. A single robot may not meet demand in either programme.
- A cost utility analysis of the prostatectomy-only model (based on 200 procedures annually) predicted an incremental cost effectiveness ratio (ICER) of €26,647/quality-adjusted life years (QALY) (95% CI: €14,241 - €61,220/QALY). Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

- The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days for a patient to return to normal activity is significantly shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a societal cost benefit which has not been factored into these models.
- Based on the procedure volumes referred to above, there is a projected reduction in bed days per robot of 360 and 565 annually in the prostatectomy and hysterectomy models, respectively.
- The incremental budget impact over five years for introducing a single robot in the publicly funded system is predicted at €3.1 million to €4.5 million for prostatectomy and hysterectomy procedures respectively. In the first year the incremental cost is estimated at €0.4m and €0.5m respectively.
- There may be additional costs associated with the introduction of a programme, for example in training or in optimising theatre space.
- Robot-assisted surgery has a significant capital and overhead cost. The incremental cost per case is, however, reduced in organisations with a high surgical caseload. A high surgical caseload can be achieved by using the device across a range of specialities, or within organisations with an ability to undertake the volumes of prostatectomy and hysterectomy cases that have been modelled in the economic analysis. Organisations should consider their potential to achieve these.
- There are significant issues to be considered by the HSE prior to the introduction of a new robotic surgery programme. These include arrangements for training, leadership, identification of multidisciplinary robot-assisted surgery teams, coordination of access to the programme for a range of specialities, identification of the optimal theatre space, careful patient selection and a commitment to monitor and report clinical outcomes of the surgeries performed.
- There is existing capacity in the Irish healthcare system in the area of robot-assisted surgery (there is one robot in a public maternity hospital and two private hospitals each have one robot). This capacity could be considered prior to any new investment in the technology in other facilities.
- A decision not to invest may result in ethical issues regarding the equity of access to healthcare, autonomy and justice. However, healthcare budgets are finite and the allocation of resources to this technology may conflict with other values or priorities of decision making, such as the need to benefit the wider community.

Arising from the findings listed above, the Authority's advice to the HSE is that robot-assisted surgery is superior to open surgery for prostatectomy procedures across a range of outcomes, and associated with superior peri-operative outcomes in hysterectomy procedures. As stated throughout the report, however, the methodological quality of research studies that have examined the clinical effectiveness of robot-assisted surgery was poor. This limitation should be taken into account when interpreting the results.

A decision to invest further in a robotic surgery programme in Ireland will, however, have a significant incremental cost per procedure and a significant budget impact. These costs must be taken into account by the decision maker. Best value can only be achieved by ensuring that the programme maximises economies of scale by achieving caseloads of the order of 200 prostatectomy or 300 hysterectomy procedures per annum once the programme is fully established. The HSE should consider the potential of organisations to achieve these.

In relation to the prostatectomy-only cost-utility model, there are varying levels of probability that a robot-assisted programme is cost-effective. Such a programme is less likely to be considered cost-effective as the decision maker's willingness to pay threshold decreases. There is a 20% probability that the technology is cost-effective at a threshold of €20,000 per QALY.

There are significant issues to be considered prior to selecting an organisation as a site for the technology. These are widely discussed in the report. They include ensuring sufficient theatre space for the programme, identifying training requirements and establishing an effective leadership in order that the programme can be successfully implemented.

Executive summary

1. Background

1.1 General information on HTA

The Health Information and Quality Authority (the Authority) is an independent Authority reporting to the Minister for Health, and was established on 15 May 2007. The Authority is the statutory organisation in Ireland with a responsibility to carry out system-wide health technology assessments (HTAs) and to develop guidelines for the preparation of HTAs across our healthcare system.[1]

HTA is a form of health research that generates information about the clinical and cost-effectiveness of health interventions (technologies), as well as information on their wider impact. The term 'technology' includes drugs, medical equipment, diagnostic techniques, surgical procedures, and public health programmes, for example, cancer screening programmes. This information is for use by the public, service providers and health policy makers. The main issues investigated as part of any HTA are:

- Does the technology work?
- For whom does it work?
- What is the benefit to the individual?
- At what cost?
- How does it compare with the alternative options available?

1.2 Background information on this HTA

On 10 December 2010, the Health Service Executive (HSE) National Director for Quality and Clinical Care requested that the Authority undertake a HTA of robot-assisted surgery compared to the alternative surgical approaches (conventional open or laparoscopic techniques) for several indications.

Surgical robots are in use to a limited extent in both public and private healthcare in Ireland. This HTA was requested in order to:

- assess the effectiveness of robot-assisted surgery over the usual standard of care in Ireland (open and conventional laparoscopic surgery)
- assess the costs, cost-effectiveness and budget impact for the publicly funded healthcare service if a decision was taken to develop services further
- assess the service organisational issues to be addressed during the development of a service and
- discuss the ethical issues to be considered by a decision maker prior to investing in the technology.

Surgical robots provide a minimally invasive laparoscopic (or keyhole) approach to performing certain surgical procedures. The surgeon sits at a console with a camera a short distance from the patient, and controls the laparoscopic instruments inside the patient from the console. In contrast, conventional laparoscopic surgery requires the surgeon to manually control the instruments inside the patient at the operating table. The advantages of laparoscopic surgery as a minimally invasive approach for the patient have traditionally been advocated as reduced blood loss, reduced complications post-surgery and potentially shorter length of stays in hospitals or other healthcare settings. Surgical robots were developed to overcome some of the limitations of existing minimally invasive surgery. By allowing for improved three-dimensional (3D) imaging of the surgical area together with a more intuitive manipulation of several surgical arms, it is claimed that improved patient outcomes will result. These include a further reduction in blood loss, reduction in pain and post-operative complications and an overall reduction in duration of hospitalisation. For the surgeon, there is a reduction in fatigue, and potentially complex procedures can be performed more comfortably.

The specific robot-assisted procedures examined in this HTA included a range of urology, gynaecology, cardiac and head and neck procedures. In assessing the clinical effectiveness of robot-assisted surgery over conventional approaches, two procedures were identified that had the best quality and quantity of evidence. These procedures were radical prostatectomy and hysterectomy.

Following completion of this HTA and its submission to the HSE by the Authority, a decision may be made in relation to the further implementation of robot-assisted surgery programmes in Ireland.

2. Objectives

The Terms of Reference of this HTA were to:

a) Describe the epidemiology and clinical burden associated with specified diseases in which robot-assisted surgery may be indicated. These include diseases in urology, gynaecology, cardiology and diseases of the head and neck.

b) Review the evidence of the effectiveness and safety of robot-assisted surgery compared to other surgical interventions for specified indications.

c) Examine the cost-effectiveness of robot-assisted surgery compared to other surgical interventions for indications where there is evidence to show that it is more effective.

d) Estimate the budget impact of implementing robot-assisted surgery for the selected indication(s).

e) Examine the evidence and the research related to training and credentialing requirements to ensure safety and best outcomes.

f) Examine how the health system can be organised in order to implement the technology as effectively and efficiently as possible.

g) Consider any additional evidence that the technology is likely to have wider implications for the health system or for affected patients.

3. Methodology

This HTA was conducted using the general principles of HTA and employing the processes and practices used by the Authority in such projects. In summary:

- The Terms of Reference of the HTA and the specific questions to be addressed were agreed between the Authority and the HSE National Director for Quality and Clinical Care.
- An Expert Advisory Group (EAG) was established. An evaluation team was appointed comprising internal Authority staff. Dr Siobhan O'Sullivan, Chief Bioethics Officer, Department of Health, provided an ethical commentary.
- Systematic literature searches that had been undertaken by two HTA agencies (in Canada and Belgium) were updated by the Evaluation Team in order to inform the evaluation of clinical effectiveness of the technology. Meta-analysis of primary published data was undertaken for the procedures which had sufficient quantity and quality of evidence – prostatectomy and hysterectomy. A review of systematic reviews was carried out for the other indications covered in the Terms of Reference of the evaluation.
- Data were obtained from a range of Irish and international experts where required. This included dossiers submitted by the commercial company manufacturing the da Vinci® Surgical System[†].

[†]At the time of this HTA, Intuitive Surgical Inc. marketed the only commercially available robot-assisted surgical system (da Vinci® system).

- The likely costs, cost-effectiveness and budget impact over five years for the Irish healthcare system were assessed. Three scenarios were modelled: a prostatectomy-only model, a hysterectomy-only model and a combined prostatectomy/hysterectomy model. Derived figures were based on a single robot with a steady state caseload, and based on a predicted lifespan of the robot of seven years.
- Data to support the economic evaluation were obtained from a literature review, published trials, Irish databases and expert opinion. Endorsement of all inputs was sought from the EAG.
- A review of the organisational challenges, including the training requirements, that would need to be addressed in the event of a decision to develop a new programme was also undertaken.

4. Efficacy and safety of robot-assisted surgery

Prostatectomy and hysterectomy were the surgical procedures for which the most evidence existed at time of this HTA. The evidence was considered to be of low quality across the range of studies reviewed. This limitation must be considered when interpreting the results of the meta-analysis of clinical evidence.

Evidence that was available at the time of this HTA indicated that robot-assisted prostatectomy procedures were superior to open procedures across a range of outcomes evaluated. There is a decreased risk of positive surgical margins for pathological stage pT2 tumours (where the tumour is confined to the prostate), superior functional outcomes (urinary continence and sexual function) and a reduction in peri-operative transfusion requirements. Overall lengths of stay are reduced. The robot-assisted procedure is, however, associated with a longer operating time.

The available evidence indicates that the benefits of robot-assisted prostatectomy over conventional laparoscopic approaches are minor. There are comparable oncologic outcomes, marginal improvements in urinary continence and equivocal data on sexual function. Reductions in length of stay are obtained, although these are less pronounced than those reductions obtained by comparison with open surgery. No significant differences were observed for transfusion, operative time or in the rate of conversion to open surgery.

Robot-assisted hysterectomy when compared with open surgery is associated with a reduction in estimated blood loss, lower risk of transfusion or complications and shorter hospital stays. Operating times are, however, longer. Compared to conventional laparoscopic hysterectomy, the difference in the reported results for each of these outcomes is substantially reduced, with no significant difference in operating times. Unlike prostatectomy, however, there is an absence of data in relation to differences in functional and oncological outcomes (where applicable) for robot-assisted hysterectomy compared to alternative approaches.

Evidence to support the use of robot-assistance for a range of other urology, gynaecology, cardiac and head and neck procedures is limited in quantity and quality. Based on the review it is predicted that robot-assisted surgery is safe and feasible for a range of such indications and may provide comparable, but not necessarily superior outcomes to conventional surgical techniques. Additional, higher quality research is required for these indications.
Robot-assisted surgery is more ergonomic than conventional laparoscopic surgery for the operating surgeon. However, this benefit does not apply to the rest of the surgical team, including the assisting surgeon. By comparison with laparoscopic surgery, robot-assistance is considered to be less demanding or technically complex. It has been proposed as an option that will facilitate certain minimally invasive procedures that are otherwise difficult to perform. Mechanical or instrument failure can arise during robot-assisted surgery, which if unrecoverable, can necessitate conversion of the procedure to open surgery in up to 0.6% of cases.

5. Costs and cost-effectiveness

Economic evaluation in HTA involves the comparative analysis of alternative courses of action. In this case, the additional costs and additional health benefits associated with robot-assisted procedures were compared with the usual standard of care (i.e. open and conventional laparoscopic approaches).

Three different scenarios were modelled in this HTA. The first, a prostatectomy-only model, was based on a steady state caseload of approximately 200 cases per annum. As there are differences in outcomes associated with this procedure, a cost-utility analysis was undertaken. The second, a hysterectomy-only model, was based on a steady state caseload of approximately 300 cases per annum. As there are no demonstrable differences in clinical outcomes for this procedure, a cost-minimisation analysis was undertaken. The third scenario, a combined prostatectomy/hysterectomy model, was based on a total caseload of approximately 300 cases per annum. In this model the number of hysterectomy procedures was significantly in excess of the number of prostatectomy procedures, and so a cost-minimisation analysis was carried out.

The perspective of the evaluation is the publicly funded healthcare system. Values for key model parameters were informed primarily by primary data collection and review of the literature and endorsed by the Expert Advisory Group. National Guidelines for the Economic Evaluation of Health Technologies in Ireland, as published by the Authority, were applied.
A seven-year timeframe (lifespan of the robot) was applied with a discount rate of 4% for costs and benefits.

The results of these economic evaluations are shown in Table 1.

Table 1. Summary of economic evaluation

Result	Model 1 (Prostatectomy alone)		Model 2 (Hysterectomy alone)		Model 3 (Combined model)	
	Median	(95% CI)	Median	(95% CI)	Median	(95% CI)
Annual caseload (at steady state)	198	(147 – 250)	297	(222 – 374)	297	(221 – 373)
Incremental cost (€ per case)	2,487	(1,899 – 3,314)	3,019	(2,582 – 3,733)	2,864	(2,384 – 3,587)
5 year budget impact (€ millions)	3.08	(2.50 – 3.76)	4.48	(3. 95 – 5.14)	4.32	(3.77 – 4.99)
Annual reduction in bed days	360	(273 – 472)	565	(422 – 721)	558	(417 – 697)
ICER (€/QALY)	26,647	(14,241 - 61,220)				

The incremental costs associated with robot-assisted procedures in each of the models are indicated above. These are primarily due to the costs associated with surgical equipment, robot purchase and maintenance and the additional cost of theatre staff due to longer operative times. However, based on the steady state volumes used in the models, the use of robot-assisted surgery will reduce the annual number of bed days. Increasing the annual volume of cases would reduce the incremental cost of robot-assisted surgery, as would extending the lifespan of the robot.

The estimated incremental budget impact of robot-assisted procedures on a single robot in the first year is predicted as €0.4 million (prostatectomy), €0.5 million (hysterectomy) and €0.5 million (combination of both). Over five-years, the incremental budget impact of robot-assisted procedures is predicted as €3.1 million, €4.5 million and €4.3 million respectively.

The cost-utility analysis in the prostatectomy-only model, based on an annual steady state caseload of 200 procedures, predicted an incremental cost effectiveness ratio (ICER) of €26,647/quality-adjusted life years (QALY) (95% CI: €14,241 - €61,220/QALY). There is no specified threshold in Ireland below which an ICER is deemed cost-effective. To facilitate comparison, however, economic evaluations of other interventions in an Irish setting which have been adopted include:

- population-based colorectal cancer screening (€1,696/QALY)
- human papillomavirus vaccination programme at €17,383/life year gained (LYG)
- universal infant pneumococcal conjugate vaccination at €5,997/LYG
- universal infant hepatitis B vaccination at €37,018/LYG.

Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days to return to normal activity is significantly shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a societal cost benefit which has not been factored into these models.

6. Organisation and training

The introduction of a new robot-assisted surgery programme in an organisation will introduce new processes and change existing ones. For example, robot-assisted surgery increases theatre time and associated costs per procedure. These increases are higher in the early stages of implementation when staff are new to the technology. Arrangements for leadership, identification of multidisciplinary robot-assisted surgery teams, coordination of access to the programme for a range of specialities, identification of the optimal theatre space, careful patient selection and a commitment to monitor and report clinical outcomes of the surgeries performed are all issues that should be assessed carefully. Additional arrangements may be required to facilitate access by surgeons from other institutions.

There will be significant training requirements for individual surgeons in an organisation if they have not previously been trained in the technique in another institution. It is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of robot-assisted surgery will fall to the various surgical training bodies. Ongoing training to ensure currency of skills and training of other theatre staff and auxiliary staff is required. The use of designated training programmes and a system of mentoring by experienced staff is recommended.

Robot-assisted surgery has a significant capital and overhead cost. The incremental cost per case is, however, reduced in organisations with a high surgical caseload. This could be across a range of specialities, or could be within those organisations which have an ability to undertake, for a given procedure, the volumes that have been envisioned in the economic model. Further, there is existing capacity in the Irish healthcare system in the area of robot-assisted surgery. There is one robot device in a public maternity hospital and one each in two private hospitals. This capacity could be considered prior to any new investment in the technology in other facilities. Any lessons learnt from the experience of the publicly funded hospital should be taken into account when assessing a new investment.

7. Ethical issues

Potential ethical issues arising from a decision to adopt, not to adopt or to adopt in a limited manner are considered as part of this HTA. A decision not to invest may result in ethical issues regarding the equity of access to healthcare, autonomy and justice. However, healthcare budgets are finite and an individual's right to choose certain treatments or services may conflict with other values or priorities of decision making, such as the need to benefit the wider community.

A decision to invest in robot-assisted surgery may have implications for the resource allocation of existing technologies and services for a given finite healthcare budget. Decisions to allocate resources within the publicly-funded healthcare system, or to allocate services to one group rather than another, should be open and transparent. Policy makers should strike a balance between patient expectations and the fair distribution of resources in order to ensure the best medical outcomes for the most people. In the case of robot-assisted surgery, an assessment of the existing capacity in the Irish healthcare system should be explored.

Limited adoption of robot-assisted surgery would raise further issues of equity and justice if a restricted number of patients benefitted from the location of that service. However, improved patient outcomes are associated with hospitals and surgeons performing a higher volume of a given procedure. As such, improving access to central services may be more appropriate.

Informed patient consent is a key ethical principle in the context of robot-assisted surgery. Patients should be advised that the technique is new, and advised of the potential risks and alternative interventions. This should help enhance patient autonomy, patient decision-making, and the promotion of a culture of openness and accountability and ultimately supporting physician-patient trust. It is within a surgeon's rights not to adopt a new technology, but their duty of care is to refer patients to another surgeon if the alternative service is requested.

8. Overall conclusions

Prostatectomy and hysterectomy are the only procedures for which sufficient evidence existed at the time of this HTA to support an economic evaluation of robot-assisted surgery. However, the quality of the evidence to support clinical-effectiveness was poor. This issue should be considered when interpreting the findings of this HTA. Evidence to support the use of robot-assistance for a range of other urology, gynaecology, cardiac and head and neck procedures was limited in quantity and quality. Based on the review it is predicted that robot-assisted surgery is safe and feasible for a range of such indications and may provide comparable but not necessarily superior outcomes to conventional surgical techniques. Additional, higher quality research is required for these indications.

Evidence available at the time of this HTA indicated that robot-assisted prostatectomy procedures were superior to open procedures across a range of outcomes evaluated. There was a decreased risk of positive surgical margins for pathological stage pT2 tumours, superior functional outcomes (urinary continence and sexual function) and a reduction in peri-operative transfusion requirements. Overall lengths of stay are reduced. The procedure is, however, associated with a longer operating time.

The available evidence indicates that the benefits of robot-assisted prostatectomy over conventional laparoscopic approaches are minor. There are comparable oncologic outcomes, marginal improvements in urinary continence and equivocal data on sexual function. Reductions in length of stay are obtained, although these are less pronounced than those reductions obtained by comparison with open surgery. No significant differences were observed for transfusion, operative time or in the rate of conversion to open surgery.

Robot-assisted hysterectomy when compared with open surgery is associated with a reduction in estimated blood loss, lower risk of transfusion or complications and shorter hospital stays. Operating times are, however, longer. Compared to conventional laparoscopic hysterectomy, the difference in the reported results for each of these outcomes is less pronounced, with no significant difference in operating times. Unlike prostatectomy, however, there is an absence of data in relation to functional and oncological outcomes (where applicable) in this procedure.

Robot-assisted surgery is more ergonomic than laparoscopic surgery for the operating surgeon. However, this benefit does not apply to the rest of the surgical team, including the assisting surgeon. Mechanical or instrument failure can arise during robot-assisted surgery, which if unrecoverable, can result in the conversion of the procedure to open surgery in up to 0.6% of cases.

A robot-assisted surgical procedure has an incremental cost over current routine practice (that is a combination of open and laparoscopic surgery). The increased costs associated with the technology (equipment purchase, maintenance, consumables, personnel and theatre time) are partly offset by the reduction in length of stay in hospital. In the economic models developed for this HTA, these incremental procedure costs ranged from €2,487 to €3,019 for prostatectomy and hysterectomy, respectively, at steady state caseloads.

The budget impact for the publicly funded system for introducing a single robot ranged from €3.1 million to €4.5 million, for prostatectomy and hysterectomy procedures, respectively, over a five-year period. There is a projected reduction in bed days of 360 and 565 annually for the prostatectomy and hysterectomy models, respectively.

A cost-utility analysis of robot-assisted prostatectomy was carried out as there is data available to demonstrate improved clinical outcomes for patients. This analysis predicted an incremental cost effectiveness ratio (ICER) of €26,647/QALY (95% CI: €14,241 - €61,220/QALY). There is no specified threshold in Ireland below which an ICER is deemed cost-effective. Economic evaluations of other interventions in an Irish setting which have been adopted include:

- €1,696/QALY, population-based colorectal cancer screening
- €17,383/life year gained (LYG), Human Papillomavirus vaccination programme
- €5,997/LYG, universal infant pneumococcal conjugate vaccination
- €37,018/LYG, universal infant hepatitis B vaccination.

Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days for patients to return to normal activity is significantly shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a societal cost benefit which has not been factored into these models.

There are significant issues to be considered by an organisation prior to the introduction of a new robotic surgery programme. Arrangements for training, leadership, identification of multidisciplinary robot-assisted surgery teams, coordination of access to the programme for a range of specialities, identification of the optimal theatre space, careful patient selection and a commitment to monitor and report clinical outcomes of the surgeries performed are all issues that should be assessed carefully. Additional arrangements may be required to facilitate access by surgeons from other institutions.

Informed patient consent is a key ethical principle in the context of robot-assisted surgery. Patients should be advised that the technique is new, and advised of the potential risks and alternative interventions. Patients should also be advised of the number of such procedures that have been undertaken by the surgeon.

A decision not to invest in this technology could result in ethical issues regarding the equity of access to healthcare, autonomy and justice. However, healthcare budgets are finite and the allocation of resources to this technology may conflict with other values or priorities of decision making, such as the need to benefit the wider community.

List of abbreviations that appear in this report

AR-DRG	Australian Refined Diagnosis Related Groups
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
BIA	Budget impact analysis
BMI	Body mass index
CABG	Coronary artery bypass graft
CADTH	Canadian Agency for Drugs and Technologies in Health
CE mark	Conformité Européene mark
CEAC	Cost-effectiveness analysis curve
CI	Confidence interval
EAG	Expert Advisory Group
ESRI	Economic and Social Research Institute
FDA	Food and Drug Administration
HIPE	Hospital In-Patient Enquiry
HSE	Health Service Executive
HTA	Health technology assessment
ICD-10	International Statistical Classification of Diseases and Related Health Problems (10th revision)
ICER	Incremental cost-effectiveness ration
IIEF-5	International Index of Erectile Function (five-item abridged version)
KCE	Belgian Health Care Knowledge Centre
LAVH	Laparoscopically-assisted vaginal hysterectomy
LH	Laparoscopic hysterectomy
LRP	Laparoscopic radical prostatectomy

MAUDE	Manufacturer and user facility device experience
MIRA	Minimally invasive robotic association
NHMRC	National Health and Medical Research Council
OH	Open hysterectomy
ORP	Open radical prostatectomy
PDE5	Phosphodiesterase type-5 inhibitor
PSA	Prostate specific antigen
PSM	Positive surgical margin
QALY	Quality adjusted life year
RAH	Robot-assisted hysterectomy
RAP	Robot-assisted prostatectomy
RARP	Robot-assisted radical prostatectomy
RCT	Randomised controlled trial
RR	Relative risk
SAGES	Society of American Gastrointestinal and Endoscopic Surgeons
SD	Standard deviation
SHIM	Sexual Health Inventory for Men
US	United States
WMD	Weighted mean difference

Technical Report

Technical Report

1. Introduction and Terms of Reference

1.1 Introduction to Technical Report

On 10 December 2010, the National Director for Quality and Clinical Care (Dr Barry White) in the Health Service Executive (HSE) requested that the Health Information and Quality Authority (the Authority) undertake a health technology assessment (HTA) of robot-assisted laparoscopic surgery as an alternative to conventional open or laparoscopic techniques for a number of surgical indications.

The specific indications to be assessed were urology, gynaecology, cardiology and diseases of the head and neck. Traditional surgical approaches for these conditions involve either open surgery – where an incision is made close to the surgical area to allow direct access to the surgical site – or laparoscopic surgery – a minimally invasive approach requiring smaller incisions through which a laparoscope and laparoscopic instruments are passed. By comparison, robot-assisted laparoscopic surgery allows surgeons to control laparoscopic instruments inside a patient from a console situated a short distance from the operating table. This technique was developed to overcome some of the limitations of minimally invasive surgery and to enable surgeons to perform what are often complex procedures more easily, through improved visualisation, more accurate control of instruments and increased ease-of-use.[2-8] The technical advantages of robot-assisted surgery may result in better clinical outcomes for patients undergoing the procedures. The evidence of the effectiveness and safety of robot-assisted surgery compared to other surgical alternatives is assessed in Chapter 3.

At the time of producing this report, Intuitive Surgical Inc. marketed the only commercially available robot system. The first da Vinci® system received CE-mark approval in January 1999. The Food and Drug Administration (FDA) in the United States approved use of the da Vinci® system for prostatectomy procedures in 2001 and gynaecology procedures in 2005. The system now has regulatory clearance for a wide range of surgical procedures (see Table 1.1). Currently there are four models:

- standard da Vinci® (3 arm, upgradeable to 4)
- da Vinci S® (3 arm, upgradeable to 4)
- da Vinci Si® (4 arm)
- da Vinci Si-e® (3 arm, upgradeable to 4)[9]

The standard da Vinci® system is no longer actively commercialised, but was still being supported by Intuitive Surgical Inc. through its customer service at the time of this HTA. Both the da Vinci S® and Si-e® are upgradeable to the Si® system. The Si-e®, was introduced in 2010 as a cheaper alternative to existing models.[10]

Table 1.1. da Vinci® surgical systems regulatory milestones[10]

Date	Regulator	Clearance
Jan 1999	EU	da Vinci® system received CE-mark approval
Jul 2000	FDA	General laparoscopic procedures
Mar 2001		Non-cardiac thoracoscopic procedures
May 2001		Prostatectomy procedures
Nov 2002		Cardiotomy procedures
Jul 2004		Cardiac revascularisation procedures
Mar 2005		Urologic surgical procedures
Apr 2005		Gynaecologic surgical procedures
Jun 2005		Paediatric surgical procedures
Dec 2009		Transoral otolaryngology surgical procedures

Worldwide, the number of procedures performed using the da Vinci® system is steadily increasing.[11] By April 2011, 1,840 da Vinci® surgical systems were installed in 1,450 hospitals, with the US and Europe accounting for 73% and 18% of this market share, respectively.[11] During 2009, it was estimated that approximately 205,000 robot-assisted surgical procedures were performed worldwide, of which approximately 90,000 were prostatectomies and 69,000 were hysterectomies.[10] It is estimated that over 80% of all radical prostatectomies in the US are now completed using robot assistance.[9;12]

In Ireland at the time of this HTA report, robot-assisted surgery is offered by two private healthcare providers: the Galway Clinic (since 2007)[13] and the Mater Private Hospital, Dublin (since 2010).[14] One robot is available in the publicly-funded healthcare system: the Cork University Maternity Hospital (since 2007) where it is exclusively used for gynaecological surgery, primarily hysterectomies.[15]

The acquisition of a robot to assist in surgical procedures will incur a significant financial cost. The cost-effectiveness and budget impact of a new programme of robot-assisted surgery is assessed in Chapter 4. A new programme of robot-assisted surgery would generate significant training and organisational challenges for the system that would need to be addressed in order to ensure that the efficiency and effectiveness of the technology could be maximised. These are discussed in Chapter 5. Finally, a decision to expand or not expand access to a programme of robot-assisted surgery generates a number of ethical issues that must be considered. These are outlined in Chapter 6.

1.2 Terms of Reference

The HSE may consider, based on the available evidence, if there should be further investment in this technology to facilitate greater access in the publicly-funded healthcare system. The answers to a number of key questions, which were developed in consultation with the HSE, will inform this decision. These questions underpin the Terms of Reference of this HTA.

The Terms of Reference were:

- Describe the epidemiology and clinical burden associated with specified diseases in which robot-assisted surgery may be indicated. These include diseases in urology, gynaecology, cardiology and diseases of the head and neck.
- Review the evidence of the effectiveness and safety of robot-assisted surgery compared to other surgical interventions for specified indications.
- Examine the cost-effectiveness of robot-assisted surgery compared to other surgical interventions for indications where there is evidence to show that it is more effective.
- Estimate the budget impact of implementing robot-assisted surgery for the selected indication(s).
- Examine the evidence and the research related to training and credentialing requirements to ensure safety and best outcomes.
- Examine how the health system can be organised in order to implement the technology as effectively and efficiently as possible.
- Consider any additional evidence that the technology is likely to have wider implications for the health system or for affected patients.

The remit of this HTA was specifically to assess robot-assisted surgery compared to alternative surgical techniques. An assessment of the clinical and cost-effectiveness of robot-assisted surgery compared to other treatment options such as radiotherapy was beyond the scope of this HTA.

Robot-assisted laparoscopic surgery, robot-assisted surgery and robotic surgery are some of the terms used to describe the use of robotic technology in minimally-invasive surgery. In the interest of consistency, the term 'robot-assisted surgery' will be used throughout this report to describe this technology. Additionally, conventional laparoscopic surgery will be referred to as 'laparoscopic surgery'.

2. Methodology

2.1 Overall approach

Following an initial scoping of the technology, the Terms of Reference of this assessment were agreed between the Authority and the Quality and Clinical Care Directorate of the Health Service Executive (HSE).

The Authority convened an expert advisory group (EAG) comprising representation from relevant stakeholders including the Department of Health, the HSE, clinicians with specialist expertise, representatives of patients' organisations and international experts in HTA. The group was chaired by the Authority's Director of Health Technology Assessment. The role of the EAG is to inform and guide the process, provide expert advice and information and to provide access to data where appropriate. A full list of the membership of the EAG is available in the acknowledgements section of this report. The Terms of Reference of the EAG were to:

- contribute to the provision of high quality and considered advice by the Authority to the Health Service Executive
- contribute fully to the work, debate and decision-making processes of the group by providing expert guidance, as appropriate
- be prepared to provide expert advice on relevant issues outside of group meetings, as requested
- provide advice to the Authority regarding the scope of the analysis
- support the Evaluation Team led by the Authority during the assessment process by providing expert opinion and access to pertinent data, as appropriate
- review the project plan outline and advise on priorities, as required
- review the draft report from the Evaluation Team and recommend amendments, as appropriate
- contribute to the Authority's development of its approach to HTA by participating in an evaluation of the process on the conclusion of the assessment.

The Authority appointed an Evaluation Team comprised of internal staff from the HTA Directorate to carry out the assessment. Dr Siobhan O'Sullivan, Chief Bioethics Officer of the Department of Health and Lecturer in Healthcare Ethics and Law, Royal College of Surgeons in Ireland, provided an ethical commentary and wrote this section of the report.

The Terms of Reference of the HTA were agreed by the EAG at the initial meeting of the group. Interim findings from the assessment and issues to be addressed, including the parameters for the cost-effectiveness model, were discussed at subsequent meetings. A final draft report was reviewed by the EAG and subsequently presented to the Board of the Authority for approval prior to submission to the HSE.

2.2 Literature review

Robot-assisted surgery is an emerging technology that has gained considerable attention in recent years. An initial scoping search identified several recent HTAs and systematic reviews. A core value of most individual HTA organisations is to share information and avoid duplication of work.[16;17] In consultation with the EAG, it was agreed that the information published by other agencies on robot-assisted surgery should be used as a basis to support this evaluation.

An initial review of published HTAs retrieved as part of the project scoping exercise indicated that the highest quantity and quality of safety and effectiveness evidence existed for robot-assisted prostatectomy and hysterectomy. A HTA[18] by the Canadian Agency for Drugs and Technologies in Health (CADTH), published in September 2011, examined the evidence base for clinical and cost-effectiveness of robot-assisted surgery in these indications. The aims of the CADTH HTA are closely aligned to the aims of this evaluation. The information up to May 2010 collated in the CADTH HTA was therefore updated by the Evaluation Team (using the same search strategy). The data extracted from all selected studies was used to inform an updated meta-analysis of the clinical effectiveness of robot-assisted surgery in prostatectomy and hysterectomy.

The initial scoping exercise for the evaluation indicated that the quantity and quality of evidence for robot-assisted surgery for the other indications included in the Terms of Reference of this evaluation was poor. These conditions were: urology (excluding prostatectomy), gynaecology (excluding hysterectomy), cardiology and diseases of the head and neck. A HTA by the Belgian Health Care Knowledge Centre (KCE) in February 2009 reviewed the evidence for robot-assisted surgery in a range of indications. As these indications closely matched those included in the Terms of Reference for this project, the information up to 2008 collated in the KCE HTA was updated by the Evaluation Team (using the same search strategies). A narrative report on these indications was produced.

2.2.1 Comparative clinical effectiveness of robot-assisted surgery for prostatectomy and hysterectomy

Four recently published and relevant HTA reports of robot-assisted surgery for prostatectomy and hysterectomy were identified. These reports were completed by CADTH (Canada) in 2011,[18] the Medical Advisory Secretariat (Ontario) in 2010,[19] ASERNIP-S (Australia) in 2009[20] and KCE (Belgium) in 2009.[8]

As previously outlined, the systematic review performed by the Canadian agency was updated with appropriate analysis of the data and expert support provided by the CADTH team.

The CADTH search, which included studies published up to May 2010, retrieved 66 studies of which 33 related to prostatectomy and 19 to hysterectomy. Reported outcomes included operative time, length of hospital stay, estimated blood loss, transfusion requirements and complication rates.[18] The Canadian report details the clinical and cost-effectiveness of robot-assisted surgery versus open surgery and conventional laparoscopic surgery.

A systematic literature search using the CADTH HTA approach was carried out to update the review to January 2011. Study quality was assessed using an appraisal form that took into account both study design and study performance (modified from Hailey et al.[21]) that was used in the CADTH HTA. A detailed search strategy, exclusion criteria and a flow chart of the search findings are included in Appendix 1.

Meta-analysis was conducted using the results from all relevant studies. Details of the studies included in the meta-analysis and their characteristics are presented in Appendix 2. Random effects meta-analysis was used to generate summary measures of the reported outcomes. Meta-analyses are conducted for each effect of interest. For length of hospital stay, the sub-group of non-US studies is also analysed. Details of the meta-analyses are included in Appendix 3.

2.2.2 Comparative clinical effectiveness of robot-assisted procedures in other urological and gynaecological indications, cardiac procedures and head and neck surgery

As outlined in Section 2.2.1, four recently published HTAs were retrieved for robot-assisted surgery in a range of indications. The KCE report (Belgium) included the remaining procedures included in the Terms of Reference of this evaluation.

The KCE search was conducted in 2008 and included articles published between 2002 and October 2008. The search retrieved 234 studies for inclusion and a review was completed on the most recent systematic reviews and technology assessments retrieved. The findings were presented in a narrative format. Outcomes included operative time, length of hospital stay, estimated blood loss, transfusion requirements and complication rates.[8]

The systematic literature search performed in the KCE HTA was updated to January 2011. The detailed search strategy, exclusion criteria and a flow chart of the search findings are included in Appendix 1. Included studies were graded according to the National Health and Medical Research Council (NHMRC) hierarchy of evidence.[22] A narrative of the results of included studies is provided in Chapter 3.

2.3 Documentation and data review

In addition to the systematic literature searches referred to above, data to inform the HTA was sourced from a number of organisations. These included:

- Department of Health
- Health Service Executive
- Economic and Social Research Institute
- The National Cancer Control Programme
- St James's Hospital, Dublin
- Galway Clinic
- Cork University Maternity Hospital
- Beaumont Hospital, Dublin
- Intuitive Surgical Inc.

One commercially available, CE marked and FDA approved robot was identified at the time this HTA was conducted – namely the da Vinci® Surgical System. The company that manufactures and supplies this device and its associated accessories (Intuitive Surgical Inc.) was invited to submit price quotations, dossiers in support of the safety, efficacy and use of their products and training, and credentialing information to the Evaluation Team.

2.4 Cost-effectiveness and budget impact analysis

To assess the cost-effectiveness of robot-assisted surgery, future costs and outcomes must be predicted using an economic modelling approach. Data were obtained from literature review, published trials and Irish databases. Expert opinion was sought when published data were unavailable, or where the data were conflicting. All data inputs were endorsed by the EAG. Results were presented in terms of the most likely outcome along with confidence bounds indicating the range of probable outcomes. The confidence bounds indicate possible best and worst case scenarios given the selected parameter ranges. Details of the model and the parameter inputs are provided in Chapter 4 and Appendix 4.

A budget impact analysis (BIA) was also performed as part of this HTA. Data were obtained from a number of sources to inform this analysis, including the Department of Health, HSE, hospitals and Intuitive Surgical Inc. Details of the BIA model and parameter inputs are provided in Chapter 4.

2.5 Organisational issues

A review of organisational and training considerations relating to the provision of robot-assisted surgery was conducted by the Evaluation Team. This review is presented in Chapter 5.

2.6 Ethical considerations

A review of the ethical considerations surrounding the further adoption, or non-adoption, of robot-assisted surgery in Ireland was conducted by Dr Siobhan O'Sullivan, Chief Bioethics Officer, Department of Health. This review is presented in Chapter 6.

3. Clinical effectiveness

3.1 Introduction

The purpose of this section is to:

- examine the quality and quantity of the available evidence in robot-assisted surgeries
- examine the evidence comparing the clinical effectiveness and safety of robot-assisted to open and laparoscopic prostatectomy
- examine the evidence comparing the clinical effectiveness and safety of robot-assisted to open and laparoscopic hysterectomy
- examine the evidence comparing the clinical effectiveness and safety of robot-assisted surgery to other surgical interventions for indications other than prostatectomy and hysterectomy
- review specific issues related to the use of this surgical device
- discuss the relevance of the clinical effectiveness data that has been presented.

The quality of the available evidence is a key consideration in determining to what extent valid conclusions can be drawn about the relative effectiveness of robot-assisted surgery compared with open or laparoscopic surgery. The limitations that exist in this regard have been discussed in a number of published reports,[8;18-20] and many of these issues are applicable to the evidence base used in this HTA, including:

- Low quality of evidence. The vast majority of the evidence is derived from observational studies with either concurrent or historical controls. The risk of bias in these study designs is high because of the lack of randomised allocation and the use of some historical control groups that may not be adequately matched to the intervention group. Using the criteria developed by the GRADE working group[23] these observational studies would be considered low quality evidence. Biases that need to be considered in observational study designs in surgery include patient selection bias, where there may be baseline differences in the control and intervention groups, as well as confounding bias, where the true effect may not be caused solely by the factor under investigation. This could potentially occur in situations where it is difficult to separate the effect of the skill of the surgeon from that of the surgical device for one or more outcomes.
- High degree of heterogeneity in pooled estimates. There is a high degree of heterogeneity observed for many of the pooled results, as indicated by the I^2 values given for each estimate of effect. This indicates that there is a high degree of inconsistency between the reported results and they should be interpreted with due consideration of this.
- Inconsistent reporting of outcomes. Many of the outcomes analysed are not consistently reported across studies. Some studies do not explicitly define some outcomes or use different criteria to those used in other included studies. Some examples of this include different methods of calculating operative time, using different validated questionnaires or self-reported assessment of erectile function and differing definitions of urinary continence ranging from no leakage to the use of one incontinence pad per day.

- Lack of long-term oncological and quality of life outcomes. There is a lack of long-term functional and oncological outcome data associated with robot-assisted surgery and its effect on patients' quality of life. This is evidenced by the use of surrogate oncological outcomes such as positive margin rates and a relative shortage of longer term follow up for outcomes related to sexual function and urinary continence.

A more detailed description of the evidence base for each individual indication is provided in the relevant section in this chapter.

The limitations on the quality and quantity of evidence available for a range of individual procedures are as described above. Despite this, there is a greater quantity of higher quality data available for robot-assisted prostatectomy and hysterectomy than for the other surgeries which allows for a systematic analysis of the data for these two procedures.

The lay-out of the remainder of this chapter is:

- Section 3.2 – systematic analysis of the data available in robot-assisted prostatectomy procedures
- Section 3.3 – systematic analysis of the data available in robot-assisted hysterectomy procedures
- Section 3.4 – review of currently available evidence of robot-assisted procedures in other urological indications
- Section 3.5 – review of currently available evidence in robot-assisted procedures in other gynaecological indications
- Section 3.6 – review of currently available evidence in robot-assisted procedures in cardiac disease
- Section 3.7 – review of currently available evidence in robot-assisted procedures in diseases of the head and neck.

The methods used in the selection of evidence to support these reviews are described in Chapter 2.

Section 3.8 of this chapter reviews specific issues relating to the actual use of the device itself, while section 3.9 provides an overview of the relevance of the clinical-effectiveness data that has been generated through provision of a summary of the information and 'key messages'.

3.2 Prostatectomy

3.2.1 Background

Apart from non-melanoma skin cancer, prostate cancer is the most commonly diagnosed cancer in men in Ireland, accounting for 29% of all cancer diagnoses.[24] An average of 2,462 new cases were diagnosed each year in Ireland between 2005 and 2007,[24] with an average number of 524 deaths each year during the same time period.[25-27]

The National Cancer Control Programme (NCCP) of the HSE established rapid access clinics in 2010 for the assessment of patients with suspected prostate cancer. These clinics provide rapid access to a prostate clinic where patients are assessed by a urologist and have access to a urology nurse. The clinics have been established in an effort to speed up the process of referring men with a possible prostate cancer, to bypass waiting times for outpatient clinics and to provide access to prostate biopsy more quickly for those who need it.[28] It is believed that this service will result in an increase in annual numbers of prostate cancer patients being successfully diagnosed.[29]

Radical prostatectomy is a surgical procedure in men with prostate cancer, intended to remove all of the prostate gland and some of the tissue around it.[30] The number of operations performed in the Irish public health system between 2005 and 2009 has fluctuated between 275 and 310 each year.[31] An additional 60 to 140 cases per year are performed in the private sector.[32] Data from the National Cancer Registry Ireland indicates that the percentage of prostate cancer patients treated surgically was 27% in 2007 (the most recent year for which data was available). The number of prostatectomy procedures being performed may increase year on year, however, in line with the development of the rapid access clinics referred to above and with the ageing population demographic.

There are three main types of radical prostatectomy:

- Open radical prostatectomy (ORP) – this involves making an incision in the lower abdomen (radical retropubic prostatectomy) or groin (radical perineal prostatectomy) to facilitate removal of the prostate.
- Laparoscopic radical prostatectomy (LRP) – this is a minimally invasive approach requiring several small incisions to allow access for surgical instruments that are directly manipulated by the surgeon.
- Robot-assisted radical prostatectomy (RARP) – this is another minimally invasive technique that also requires several small incisions; the surgical instruments passed through the incisions are controlled by the surgeon via the robotic system.

The goals of radical prostatectomy are to cure cancer, maintain urinary continence, maintain erectile function, and minimise complications and peri-operative suffering.[33] In order to measure the extent to which these goals are achieved, a number of outcomes (Table 3.1) are frequently reported by surgeons following prostatectomy procedures and can be used to assess the relative clinical effectiveness of the different types of procedure considered in this section.

Table 3.1. Clinical effectiveness outcomes for radical prostatectomy

Outcomes reported	Description
Oncological outcomes	
Positive surgical margin	A positive surgical margin (PSM) refers to the pathologic finding of cancer cells on the outer edge of the tissue removed during surgery. Positive margins are associated with a higher risk of recurrence of prostate cancer[34] and are commonly used as a pathologic surrogate for oncologic efficacy.[35]
Pathological tumour stage: pT2 pT3 pT2 and pT3	When considering PSM rates, it is important to consider the pathological tumour staging. This describes the extent of the disease based on tumour size and the local and distant spread. The two pathological tumour stages analysed in this HTA are: pT2 - tumour is confined to the prostate pT3 - tumour extends through the prostate capsule.[36] Results of the meta-analysis of data from included studies are provided for each of these stages individually and for pT2 and pT3 combined.
Functional outcomes	
Sexual function	Reduced sexual function can be a side effect of radical prostatectomy. There are a range of methods used to assess the degree of post-operative sexual function. In this analysis, return of sexual function was reported as the ability to maintain an erection sufficient for intercourse with or without the help of phosphodiesterase type 5 inhibitors (PDE5 inhibitors), or as a score of >17 using the SHIM or IIEF-5 validated questionnaires for erectile dysfunction.
Urinary function (3, 6 and 12 months)	Radical prostatectomy can result in incontinence. Data on continence provided at intervals of 3, 6 and 12 months post-operatively is analysed in this report. Urinary function is defined as the use of one or no (incontinence) pads per day.
Peri-operative outcomes	
Estimated Blood loss	Blood loss is an expected outcome from prostatectomy procedures. In this HTA, estimated blood loss (ml) during each type of surgery is included in the meta-analysis. However, due to the use of different methods of estimating surgical blood loss, including subjective measures like visual estimation, there is a high level of inconsistency in the measurement of this outcome.
Transfusion	Blood transfusion rates associated with each type of surgery are examined, in order to identify any significant differences in the risk of transfusion between different surgical approaches.

Complications	Reported complications associated with each type of surgery can be used to assess the safety profile of the different surgical approaches. Some studies used a standardised approach to complications reporting (e.g. Clavien-Dindo), others categorised complications as major or minor or provided a list of the complications recorded; complication rates could be based on the absolute number of complications or the number of patients who experienced complications. Complications could include intra-operative, peri-operative or post-operative complications, or combinations thereof. In this HTA, it was assumed that the complication count represented the number of patients who experienced any reported complications.
Operative time	This is the length of time needed to perform the prostatectomy procedure. This is most commonly defined as skin-to-skin time, which is the time from the first incision to skin closure. Other definitions used have included the total operating theatre time, and, for robot-assisted surgery, the docking and console times.
Hospital stay	Length of hospital stay is defined as the number of days spent in hospital before being discharged.

Note: PDE5 inhibitors – Phosphodiesterase type 5 inhibitors; PSM – Positive surgical margin; SHIM – Sexual Health Inventory for Men; IIEF-5 - International Index of Erectile Function Questionnaire

3.2.2 Summary of included studies

Identification of studies concerning the clinical effectiveness of robot-assisted surgery for radical prostatectomy was carried out as described in Chapter 2. A total of 50 studies were selected for inclusion. A table of included studies and their characteristics is included in Appendix 2.

One randomised single-surgeon study[37] and 49 observational studies were identified from the literature search. Of the observational studies included, 26 are retrospective comparisons or studies using historical comparison groups and 23 are prospective observational studies (Appendix 2). Limitations of the quality of the evidence can be observed from the high percentage of observational studies (98%), retrospective comparisons (52%) and studies involving multiple surgeons (60% used more than one surgeon or failed to report how many surgeons were involved).

Thirty-six studies compare robot-assisted and open surgery, nine compare robot-assisted versus laparoscopic surgery and five provide comparative data for robot-assisted, open and laparoscopic surgery in the same study. Over half (32/50, 64%) of the included studies originated in the USA, with the remaining studies (18/50, 36%) being carried out in a range of countries, including France (4), Italy (4), South Korea (3), Sweden (3) and one study each from Australia , Switzerland, Hong Kong and Taiwan.

The total sample size in the included studies ranged from 40[38] to 1,904,[39] with patient numbers in the robot-assisted arms ranging from 20[38] to 1,413.[39] The mean sample size in studies comparing robot-assisted to open surgery was 512 (SD: 487); for robot-assisted versus laparoscopic surgery it was 241 (SD: 183); and for studies that compared robot-assisted surgery to both, the mean sample size was 390 (SD: 247). Reported patient characteristics between treatment groups were broadly similar. Average age was reported in 26/36 robot-assisted versus open studies (pooled averages of 60.5 vs 61.8 years, respectively); mean body mass index (BMI) was reported in 11/36 studies (26.4 vs 26.3 kg/m^2); and pre-operative prostate-specific antigen (PSA) levels were reported in 21/36 studies (7.6 vs 9.6 ng/ml). In the robot-assisted versus laparoscopic study group, average age was reported in all nine studies (60.5 vs 61.2 years); BMI was reported in 6/9 studies (26.8 vs 26.7 kg/m^2); and pre-operative PSA levels were reported in 8/9 studies (7.4 vs 7.1 ng/ml). For studies that compared robot-assisted surgery to both open and laparoscopic surgery, average age was reported in 3/5 (60.9 vs 61.5 years); only 1/5 studies reported mean BMI (22.6 vs 23.2 kg/m^2); and 3/5 studies reported mean pre-operative PSA levels (6.9 vs 8.2 ng/ml).

The number of different surgeons performing robot-assisted surgery was reported in 76% of studies (38/50). Of these, 20 were single-surgeon studies, with the remaining studies involving between two and seven surgeons in the robot-assisted arm. In the 78% (39/50) of studies that provided any information on surgeon experience, there were differences in how that experience was reported. The degree of surgeons' experience in robot-assisted prostatectomy in the included studies ranged from surgeons performing their first series of cases,[40-47] to surgeons who had performed over 300 procedures[37] using the device. Therefore the influence of the training curve for inexperienced surgeons is included in the overall estimate of effect calculated in the meta-analysis.

Differences between how various intra-operative and post-operative outcomes were reported in the included studies were noted. Twelve studies reported how operation time was defined (24%). The most common definition for operative time was skin-to-skin time (7/12),[40;44;45;47-51] with other studies using total operating time[52-54] or alternative definitions.[41;42] Continence was defined in 15/50 studies, with 12[38;40;42;47-52;55-57] using a definition of either no leakage or the use of 0 to 1 pads per day, while three studies[37;58;59] used continence questionnaires. A definition of what was considered the regaining of sexual function was defined in 12/50 studies.[37;40;42;47;49;50;52;55;57-60] This was most commonly defined as the ability to maintain an erection sufficient for intercourse with or without the help of phosphodiesterase type 5 inhibitors. Reporting of complications also varied widely, with most of the studies that provided this data including a list of intra-operative and post-operative complications recorded as part of the individual study. Some studies used a standardised approach to complications reporting (e.g. Clavien-Dindo), others categorised complications as major or minor or provided a list of the complications recorded; complication rates could be based on the absolute number of complications or the number of patients who experienced complications.

3.2.3 Data analysis and synthesis

Comparison of robot-assisted prostatectomy with open and laparoscopic prostatectomy was performed separately. The results of the meta-analysis comparing robot-assisted to open surgery are presented first followed by the comparison of robot-assisted versus laparoscopic prostatectomy.

Robot–assisted prostatectomy versus open radical prostatectomy

Combined results for all the outcomes for which data was extracted is presented in Table 3.2, along with the total number of studies that reported on each individual outcome, the 95% confidence intervals (95% CI) for the estimate of effect and the I^2 value indicating the level of inconsistency across the findings of the included studies. Forest plots displaying the spread of effect estimates from included studies as well as the combined estimate are provided for each outcome.

Meta-analysis of the data from included studies was carried out. A summary of the results of the analysis comparing robot-assisted and open radical prostatectomy are provided below, followed by a description of the sensitivity and sub-groups analyses carried out and the impact this had on the estimate of the effect on relevant outcomes.

Table 3.2 Clinical effectiveness outcomes for robot-assisted radical prostatectomy (RARP) compared to open radical prostatectomy (ORP)

Outcome	Studies (n)	Patients (n)	RARP (mean)	ORP (mean)	Estimate of effect*	Range (95% CI)*	I^2 (%)	p-value
Oncological outcomes								
Positive surgical margin	14	2,190	11%	18%	RR 0.67	0.51 - 0.88	25.6	0.0037
pT2	14	940	50%	45%	RR 1.11	0.86 - 1.42	53.3	0.4224
pT3	22	8,525	20%	23%	RR 0.89	0.74 - 1.07	74.6	0.2218
pT2+pT3 combined								
Functional outcomes								
Sexual function	7	1550	70%	46%	RR 1.56	1.27 - 1.92	70.7	<0.0001
Urinary function								
@ 3 months	6	1,193	76%	67%	RR 1.14	1.02 - 1.29	32.0	0.0271
@ 6 months	4	737	91%	81%	RR 1.13	1.06 - 1.20	0.0	0.0001
@12 months	7	1,812	95%	89%	RR 1.06	1.01 - 1.12	58.8	0.0273
Peri-operative outcomes								
Estimated blood loss (ml)	20	6,247	245ml	765ml	-516 ml	-596 - -437 ml	99.0	<0.0001
Transfusion rate	19	8,246	7%	30%	RR 0.21	0.15 - 0.30	23.7	<0.0001
Complication rate	15	5,738	15%	20%	RR 0.72	0.52 - 1.00	73.0	0.0490
Operative time (mins)	18	4,415	236mins	195mins	36 mins	18 – 54 mins	97.0	0.0001
Length of hospital stay (days)	18	5,746	3.0	4.6	-1.5 days	-2.1 - -0.9 days	99.3	<0.0001

CI – Confidence interval; ORP – Open radical prostatectomy; RARP – Robot-assisted radical prostatectomy; RR – Relative risk; pT2 - tumour is confined to the prostate; pT3 - tumour extends beyond the prostate

** Estimate of effect (and associated 95% CI) is presented as the relative risk (RR) of achieving the specified outcome using robot-assisted surgery compared to open surgery, except where absolute values are provided, as indicated by the use of units of measurement (ml/mins/days).*

Meta-analysis of oncological outcomes

There was no statistically significant difference in the rate of overall positive surgical margins (PSM) for robot-assisted compared to open prostatectomy (RR 0.89; 95% CI: 0.74 to 1.07) using data from 22 studies (see Figure 3.1). When PSM rates were stratified according to the pathological tumour stage, pT2 (14 studies) and pT3 (14 studies), robot-assisted prostatectomy appears to be associated with a decreased risk of PSM for pT2 patients (RR 0.67; 95% CI: 0.51 to 0.88) (Figure 3.2). No significant difference in pT3 PSM rates was observed (RR 1.11; 95% CI: 0.86 to 1.42) (Figure 3.3).

Figure 3.1 Overall relative risks of positive surgical margin (PSM) rates for robot-assisted radical prostatectomy versus open radical prostatectomy

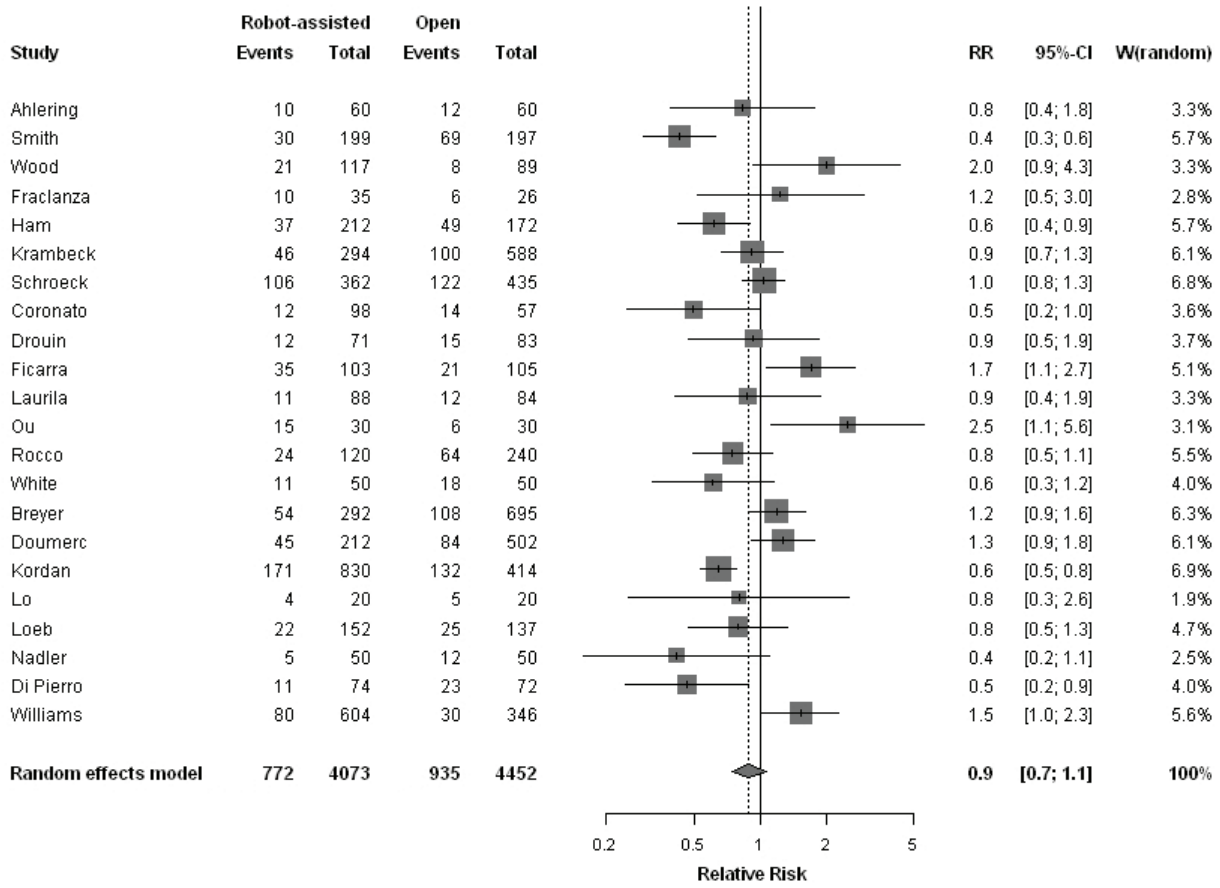


Figure 3.2 Relative risks of positive surgical margin (PSM) rates for tumour stage pT2 for robot-assisted radical prostatectomy versus open radical prostatectomy

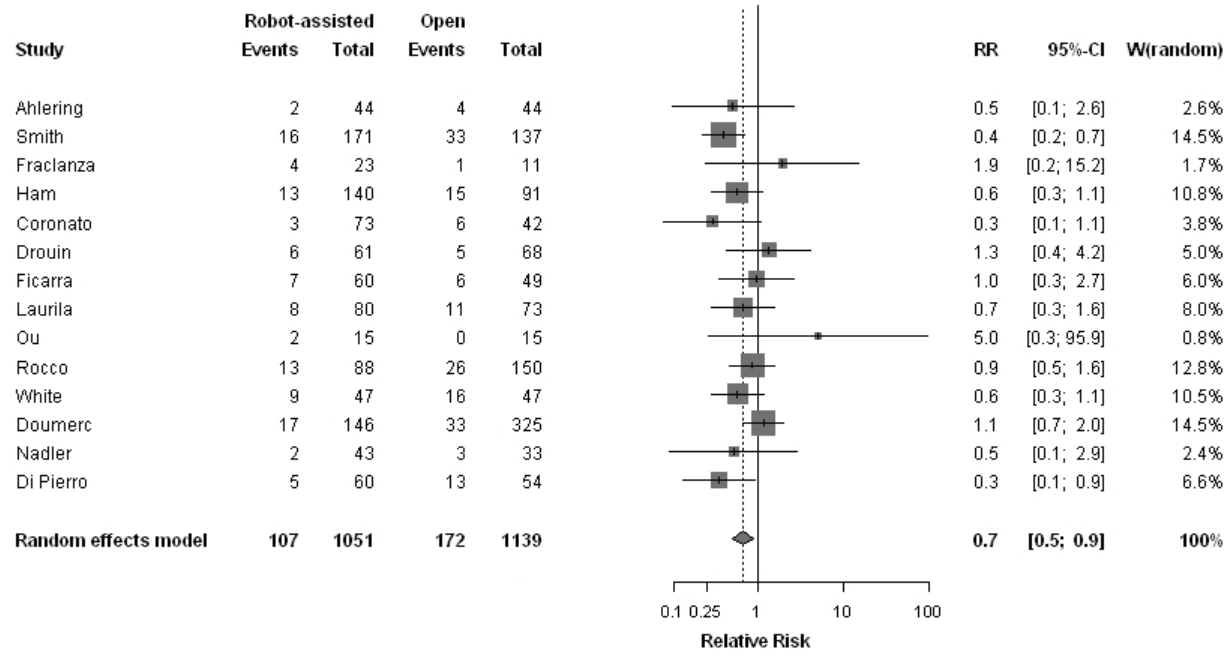
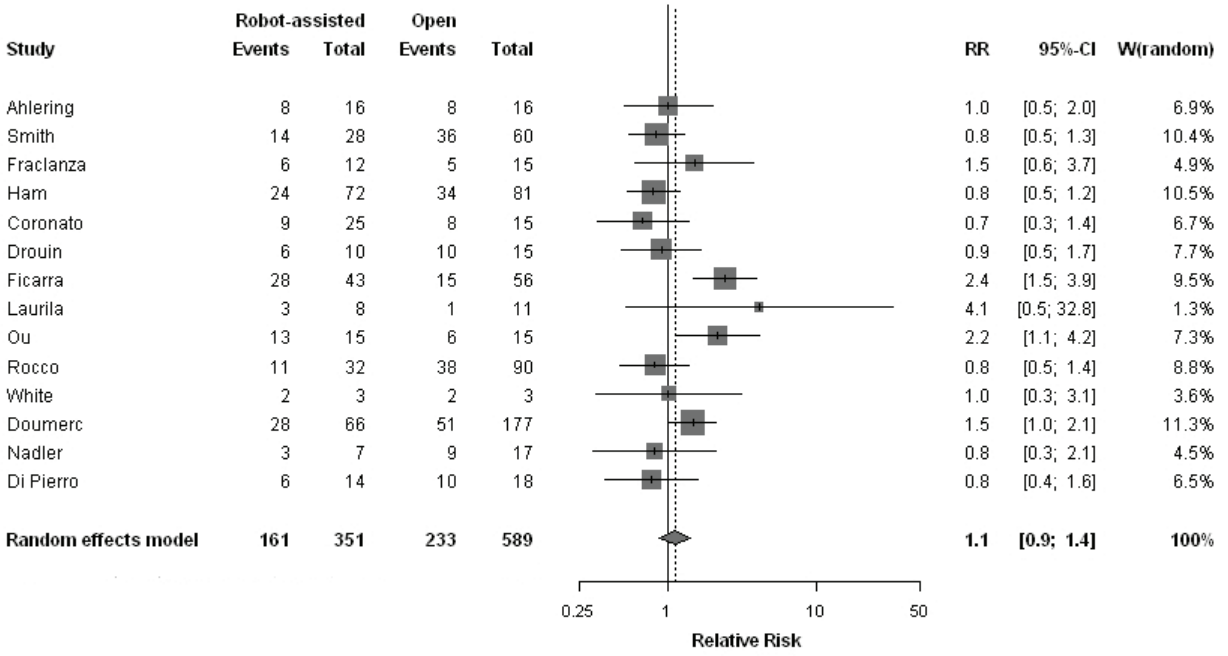


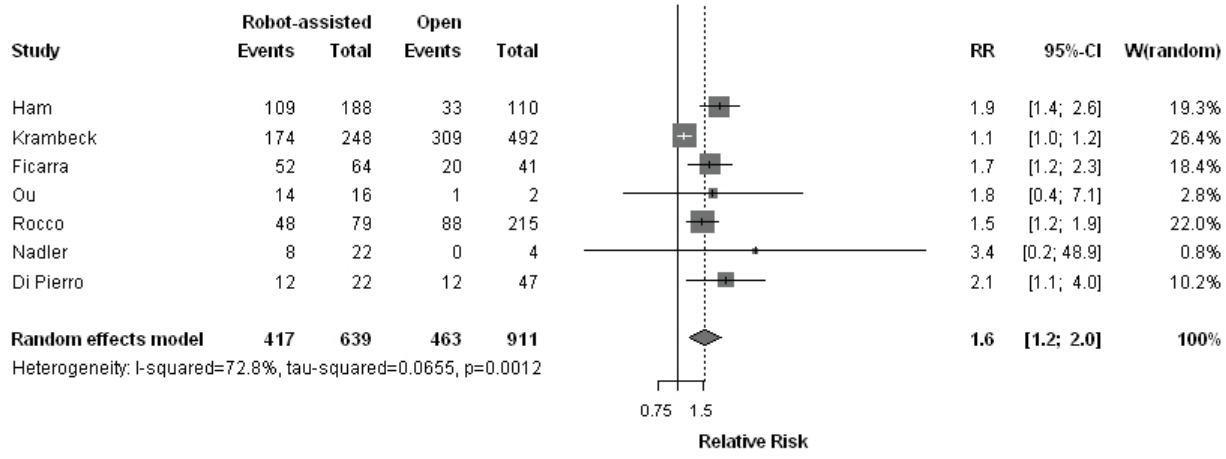
Figure 3.3 Relative risks of positive surgical margin (PSM) rates for tumour stage pT3 for robot-assisted radical prostatectomy versus open radical prostatectomy



Meta-analysis of functional outcomes

Based on the results of eight included studies, robot-assisted radical prostatectomy is associated with improved post-operative sexual function compared to open surgery (RR 1.56, 95% CI 1.27 to 1.92). However, the level of heterogeneity between results of individual studies is high (I^2 70.7%) (Figure 3.4).

Figure 3.4 Relative risk of post-operative sexual function for robot-assisted radical prostatectomy versus open radical prostatectomy



Robot-assisted surgery was associated with slight, but statistically significant improvements in urinary function at three months (RR 1.14; 95% CI: 1.02 to 1.29) (Figure 3.5); six months (RR: 1.13; 95% CI: 1.06 to 1.20) (Figure 3.6); and 12 months (RR 1.06; 95% CI: 1.01 to 1.12) (Figure 3.7) compared to open radical prostatectomy.

Figure 3.5 Relative risk of post-operative urinary continence at three months for robot-assisted radical prostatectomy versus open radical prostatectomy

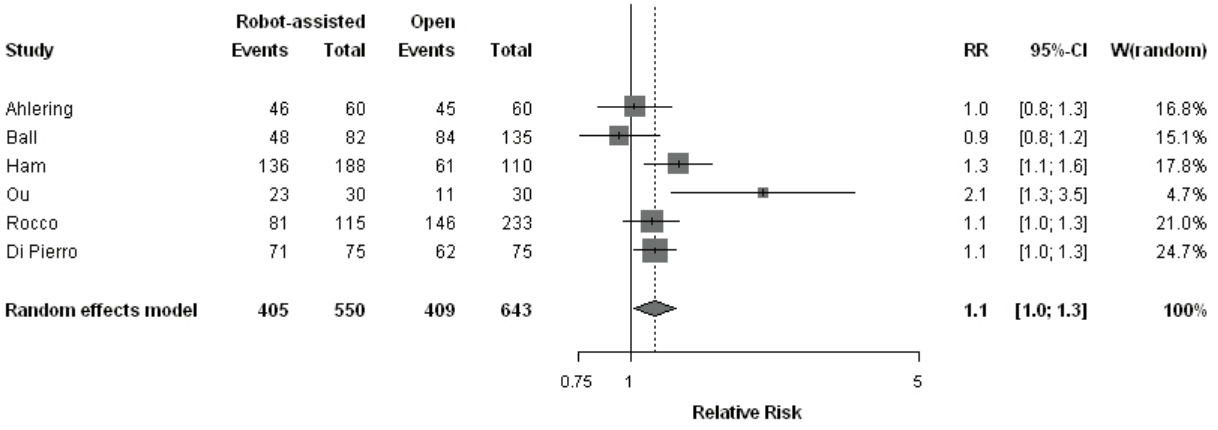


Figure 3.6 Relative risk of post-operative urinary continence at six months for robot-assisted radical prostatectomy versus open radical prostatectomy

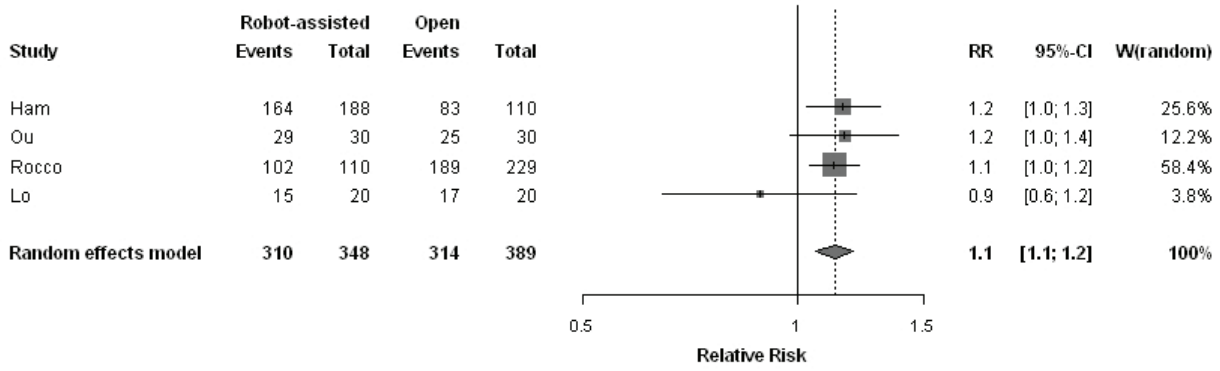
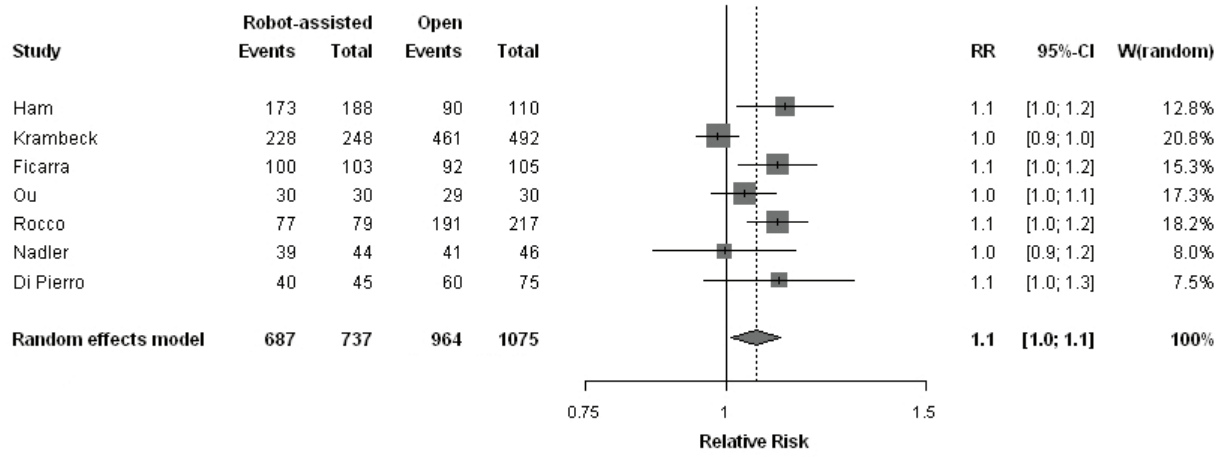


Figure 3.7 Relative risk of post-operative urinary continence at 12 months for robot-assisted radical prostatectomy versus open radical prostatectomy



Meta-analysis of peri-operative outcomes and length of stay

Robot-assisted surgery is associated with decreased blood loss compared to open surgery (516ml less per procedure; 95% CI: 596ml to 437ml) (Figure 3.8). However, there is a high degree of heterogeneity between the 20 studies which reported this outcome (I^2 99%). This reduction in blood loss is consistent with a lower risk of transfusion in the robot-assisted group, an outcome which was separately reported in 19 studies (RR 0.21, 95% CI 0.15 – 0.30) (Figure 3.9).

Figure 3.8 Estimated blood loss (ml) for robot-assisted radical prostatectomy versus open radical prostatectomy

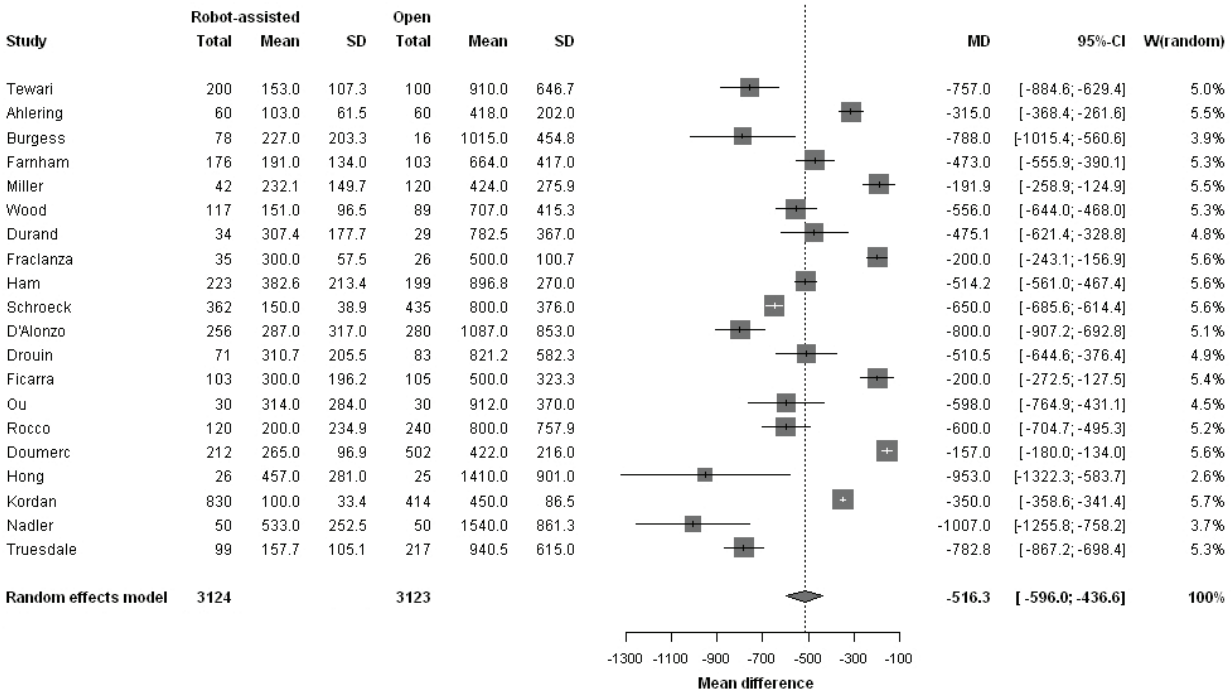
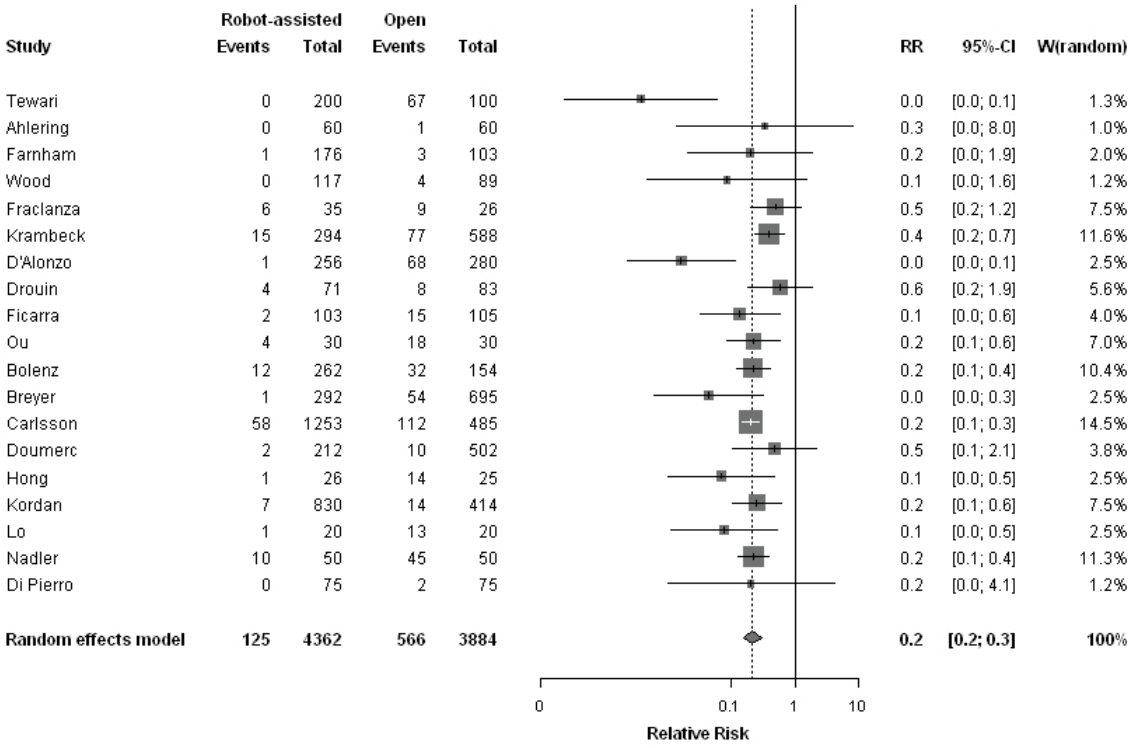


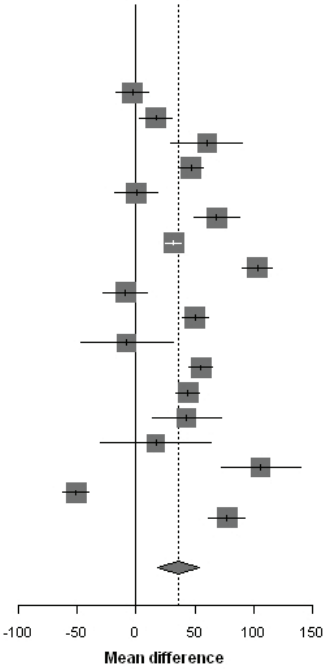
Figure 3.9 Relative risk of blood transfusion for robot-assisted radical prostatectomy versus open radical prostatectomy



Robot-assisted radical prostatectomy is associated with longer operating times than open prostatectomy (36 minutes more per procedure; 95% CI: 18 to 54 minutes) (Figure 3.10). The level of heterogeneity between the results of different studies is high (I^2 97%).

Figure 3.10 Mean differences in operating time (minutes) for robot-assisted radical prostatectomy versus open radical prostatectomy

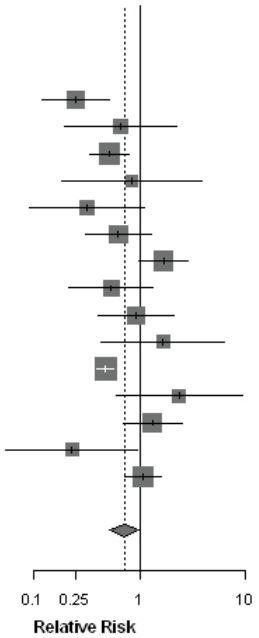
Study	Robot-assisted Total	Mean	SD	Open Total	Mean	SD	MD	95%-CI	W(random)
Tewari	200	160.0	58.8	100	163.0	59.7	-3.0	[-17.3; 11.3]	5.8%
Ahlering	60	231.0	47.2	60	214.0	26.7	17.0	[3.3; 30.7]	5.8%
Burgess	78	262.0	97.5	16	202.0	43.8	60.0	[29.5; 90.5]	5.1%
Wood	117	210.0	41.3	89	163.0	29.0	47.0	[37.4; 56.6]	5.9%
Durand	34	186.3	28.0	29	186.0	41.7	0.3	[-17.6; 18.2]	5.7%
Fraclanza	35	195.6	45.0	26	127.2	31.7	68.4	[49.1; 87.7]	5.6%
Krambeck	294	236.0	46.6	588	204.0	52.0	32.0	[25.2; 38.8]	6.0%
D'Alonzo	256	296.0	76.0	280	193.0	69.0	103.0	[90.7; 115.3]	5.9%
Drouin	71	199.6	36.6	83	208.5	76.0	-8.9	[-27.3; 9.5]	5.7%
Ficarra	103	185.0	45.6	105	135.0	34.7	50.0	[39.0; 61.0]	5.9%
Ou	30	205.2	102.6	30	213.0	37.2	-7.8	[-46.9; 31.3]	4.7%
Rocco	120	215.0	46.4	240	160.0	41.8	55.0	[45.2; 64.8]	5.9%
Doumerc	212	192.0	66.5	502	148.0	53.3	44.0	[33.9; 54.1]	5.9%
Hong	26	279.6	34.2	25	236.5	67.3	43.1	[13.6; 72.6]	5.2%
Lo	20	306.0	85.0	20	289.0	64.0	17.0	[-29.6; 63.6]	4.3%
Nadler	50	341.0	109.7	50	235.0	53.0	106.0	[72.2; 139.8]	5.0%
Truesdale	99	153.4	51.3	217	204.0	32.9	-50.6	[-61.6; -39.6]	5.9%
Di Pierro	75	330.0	54.0	75	253.0	41.0	77.0	[61.7; 92.3]	5.8%
Random effects model	**1880**			**2535**			**36.1**	**[18.1; 54.1]**	**100%**



The rate of complications was reported in 15 studies. The risk of complications was lower in the robot-assisted group, however, this finding was not statistically significant (RR 0.72; 95% CI: 0.55 to 1.00) (Figure 3.11).

Figure 3.11 Relative risk of complications for robot-assisted radical prostatectomy versus open radical prostatectomy

Study	Robot-assisted Events	Total	Open Events	Total	RR	95%-CI	W(random)
Tewari	10	200	20	100	0.2	[0.1; 0.5]	7.5%
Ahlering	4	60	6	60	0.7	[0.2; 2.2]	4.5%
Wood	25	117	37	89	0.5	[0.3; 0.8]	9.9%
Durand	3	34	3	29	0.9	[0.2; 3.9]	3.3%
Fraclanza	3	35	7	26	0.3	[0.1; 1.1]	4.3%
Ham	12	223	17	199	0.6	[0.3; 1.3]	7.6%
Krambeck	23	286	27	564	1.7	[1.0; 2.9]	9.0%
Drouin	6	71	13	83	0.5	[0.2; 1.3]	6.1%
Ficarra	10	103	11	105	0.9	[0.4; 2.1]	6.8%
Ou	5	30	3	30	1.7	[0.4; 6.4]	4.0%
Carlsson	197	1253	159	485	0.5	[0.4; 0.6]	11.4%
Doumerc	4	212	4	502	2.4	[0.6; 9.4]	3.8%
Nadler	16	50	12	50	1.3	[0.7; 2.5]	8.2%
Yi	2	153	25	439	0.2	[0.1; 1.0]	3.6%
Di Pierro	30	75	28	75	1.1	[0.7; 1.6]	10.0%
Random effects model	**350**	**2902**	**372**	**2836**	**0.7**	**[0.5; 1.0]**	**100%**

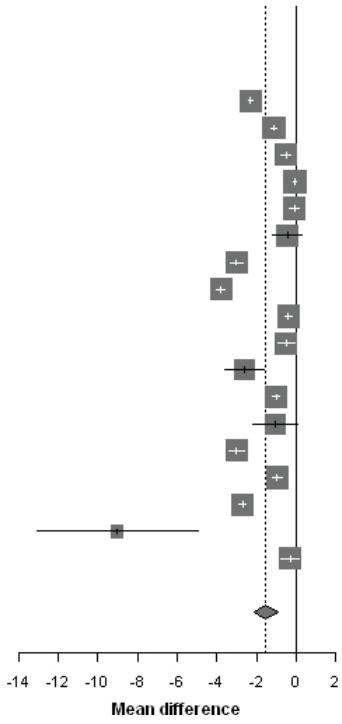


Robot-assisted prostatectomy was associated with a reduction in the length of hospital stay following prostatectomy (1.5 fewer days; 95% CI: 0.9 to 2.1 days), (Figure 3.12). There was a high degree of heterogeneity between the 18 studies that reported this outcome (I^2 99.3%).

Sub-group analysis was carried out by limiting the analysis to non-US studies and European studies only to investigate the influence of differing types of health system on outcomes. Anecdotal evidence suggest that patients undergoing prostatectomy operations in Europe and Australia tend to remain in hospital for longer than US patients.[61] Results of a sub-group analysis of 10 non-US studies found a greater reduction in hospital stay associated with robot-assisted prostatectomy compared to open radical prostatectomy, that is, a mean difference of 2.5 days (95% CI: 1.6 – 3.3) between the procedures compared to 1.53 days (95% CI: 0.9 – 2.1) when all studies were included. When only European studies were used (US and Asian studies excluded), the mean reduction in length of stay for robot-assisted versus open surgery was two days (95% CI: 1.2 – 2.8).

Figure 3.12 Mean differences in length of hospital stay (days) for robot-assisted radical prostatectomy versus open radical prostatectomy

Study	Robot-assisted Total	Mean	SD	Open Total	Mean	SD	MD	95%-CI	W(random)
Tewari	200	1.20	0.61	100	3.50	0.49	-2.3	[-2.4; -2.2]	6.0%
Ahlering	60	1.08	0.37	60	2.20	0.54	-1.1	[-1.3; -1.0]	5.9%
Burgess	78	1.20	0.32	16	1.70	0.49	-0.5	[-0.8; -0.2]	5.9%
Nelson	629	1.17	0.81	374	1.23	0.41	-0.1	[-0.1; 0.0]	6.0%
Wood	117	1.20	0.84	89	1.30	0.95	-0.1	[-0.3; 0.1]	5.9%
Durand	34	4.41	1.81	29	4.85	1.17	-0.4	[-1.2; 0.3]	5.5%
Fraclanza	35	5.00	0.19	26	8.00	0.78	-3.0	[-3.3; -2.7]	5.9%
Ham	223	3.85	0.63	199	7.63	1.35	-3.8	[-4.0; -3.6]	5.9%
Krambeck	294	1.86	1.05	588	2.25	1.47	-0.4	[-0.6; -0.2]	5.9%
D'Alonzo	256	1.83	3.21	280	2.33	1.08	-0.5	[-0.9; -0.1]	5.8%
Drouin	71	4.40	2.45	83	7.00	3.71	-2.6	[-3.6; -1.6]	5.2%
Ficarra	103	6.00	0.70	105	7.00	0.71	-1.0	[-1.2; -0.8]	5.9%
Ou	30	7.33	2.32	30	8.37	2.22	-1.0	[-2.2; 0.1]	5.0%
Rocco	120	3.00	1.44	240	6.00	2.60	-3.0	[-3.4; -2.6]	5.8%
Bolenz	262	1.56	1.53	161	2.51	1.37	-0.9	[-1.2; -0.7]	5.9%
Doumerc	212	2.80	0.70	502	5.50	1.65	-2.7	[-2.9; -2.5]	5.9%
Lo	20	8.00	6.00	20	17.00	7.00	-9.0	[-13.0; -5.0]	1.7%
Nadler	50	2.50	1.52	50	2.80	0.66	-0.3	[-0.8; 0.2]	5.8%
Random effects model	**2794**			**2952**			**-1.5**	**[-2.1; -0.9]**	**100%**



Sensitivity analysis

Sensitivity analysis was carried out to determine the effect of removing any outliers. Results from prospective and retrospective studies were pooled separately to investigate the effect of study design on various outcomes. Forest plots for each outcome were inspected visually to look for distributions of results which may indicate systematic variations. Outliers were observed for the following outcomes: hospital stay,[38] operative time,[62] pT3 PSM rate[57] and transfusion rate.[45;50] The change in the estimate of the effect caused by removing outliers was minimal, and resulted in no changes to the significance of any of the results.

Separate analysis of the results from prospective study designs resulted in a lower average reduction in blood loss associated with robot-assisted radical prostatectomy (-392ml vs -516ml) along with a wider 95% confidence interval (-482ml to -302ml). No significant change in the relative risk of transfusion was observed. The full set of results of the sensitivity analysis is provided in Appendix 3. Visual inspection of the degree of asymmetry of funnel plots was inspected to assess for potential publication bias for each of the outcomes. Estimated blood loss was the single outcome for which a degree of asymmetry suggestive of publication bias was observed.

Robot-assisted radical prostatectomy versus laparoscopic radical prostatectomy

Meta-analysis of data from studies comparing robot-assisted and laparoscopic radical prostatectomy was also carried out. Results are provided in Table 3.3, along with the total number of studies that reported on each individual outcome, the 95% confidence intervals for the estimate of effect and the I^2 value indicating the level of inconsistency across the findings of the included studies. Forest plots displaying the spread of effect estimates from included studies as well as the combined estimate are provided for each outcome.

A summary of the main observations from this meta-analysis are provided below, followed by a description of the sensitivity and sub-group analyses conducted and any impact these had on the estimate of the effect on relevant outcomes.

Table 3.3 Clinical effectiveness outcomes for robot-assisted radical prostatectomy (RARP) compared to laparoscopic radical prostatectomy (LRP)

Outcome	Studies (n)	Patients (n)	RARP (mean)	LRP (mean)	Estimate of effect*	Range (95% CI)*	I^2 (%)	p-value
Oncological outcomes								
Positive surgical margin								
pT2	5	772	14%	15%	RR 0.92	0.63 - 1.34	0.5	0.6769
pT3	5	162	46%	41%	RR 1.09	0.69 - 1.72	0	0.7111
pT2+pT3 combined	7	1,114	16%	18%	RR 0.93	0.70 - 1.22	0	0.5838
Functional outcomes								
Sexual function	2	262	67%	40%	RR 1.68	0.84 - 3.37	86.9	0.1424
Urinary function								
@ 3 months	5	818	76%	70%	RR 1.09	0.98-1.21	31.4	0.1232
@ 6 months	3	512	86%	71%	RR 1.20	1.08 - 1.34	0	0.0011
@12 months	3	512	94%	86%	RR 1.09	1.02 - 1.17	0	0.0127
Peri-operative outcomes								
Estimated blood loss (ml)	9	2,027	316ml	387ml	-72ml	-148 - 5ml	98.2	0.0656
Transfusion rate	7	1634	3%	5%	RR 0.66	0.32 - 1.36	38.7	0.2604
Complication rate	8	1,911	12%	14%	RR 0.96	0.53 - 1.73	63.4	0.8985
Operative time (mins)	9	2,027	209mins	233mins	-24 mins	-51 - 3 mins	97.0	0.0795
Length of hospital stay (days)	7	1,649	3.3	3.9	-0.6 days	- 1.2 - -0.1 days	91.2	0.0217
Conversion rate to open surgery	7	1,694	1%	3%	RR 0.51	0.11 - 2.31	45.0	0.3816

CI – Confidence interval; RARP – Robot-assisted radical prostatectomy; RR – Relative risk.
** Estimate of effect (and associated 95% CI) is presented as the relative risk (RR) of achieving the specified outcome using robot-assisted surgery compared to laparoscopic surgery, except where absolute values are provided, as indicated by the use of units of measurement (ml/mins/days).*

Meta-analysis of oncological outcomes

There was no statistically significant difference in the positive surgical margin (PSM) rates between robot-assisted and laparoscopic radical prostatectomy when analysed as an overall PSM rate (RR 0.93; 95% CI: 0.70-1.22) (Figure 3.13) or when PSM rates were stratified according to the tumour stage for pT2 (RR 0.92; 95% CI: 0.63-1.34) (Figure 3.14) and pT3 (RR 1.09; 95% CI: 0.69-1.72) (Figure 3.15). The pooled estimate effect for PSM rates obtained from combining the results of all included studies is in general agreement with the results of the single randomised controlled trial (RCT) identified in the literature search,[37] which also found no statistically significant differences in PSM rates.

Figure 3.13 Relative risk for overall positive surgical margin (PSM) rates for robot-assisted versus laparoscopic radical prostatectomy

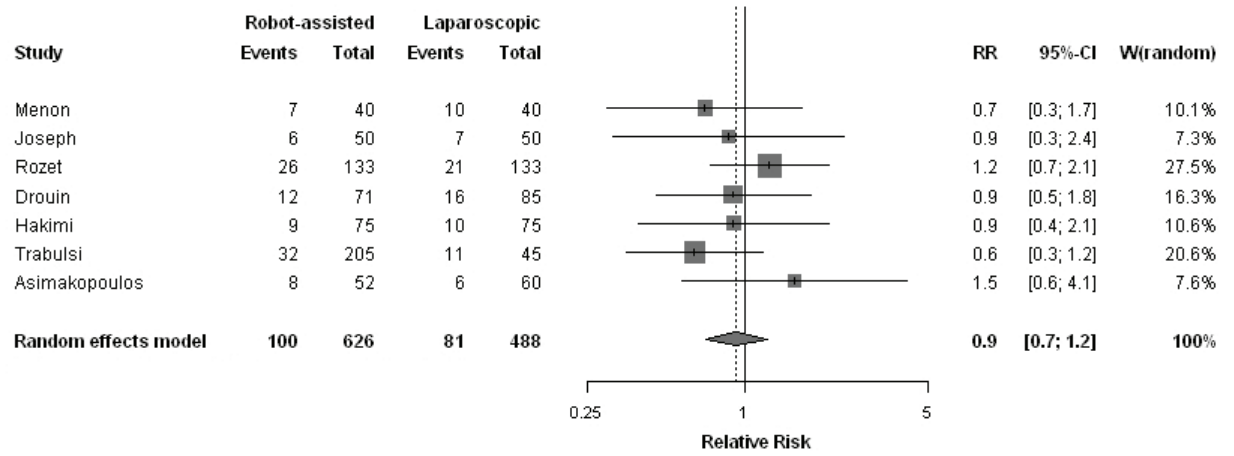


Figure 3.14 Relative risk of positive surgical margin (PSM) rates for tumour stage pT2 for robot-assisted versus laparoscopic radical prostatectomy

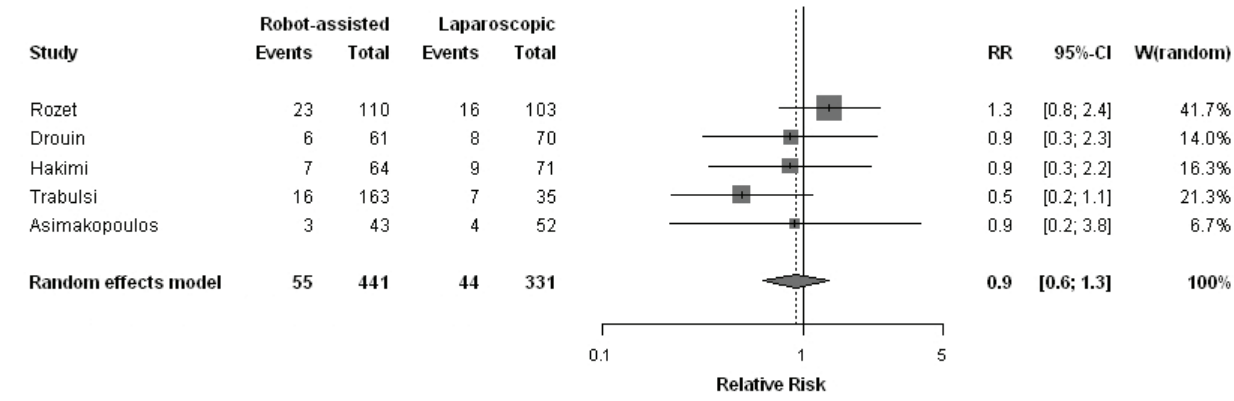
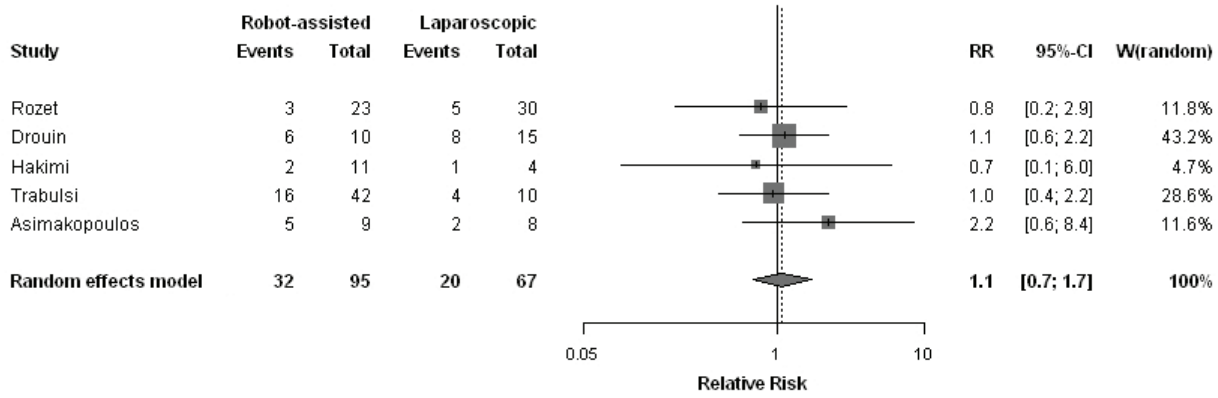


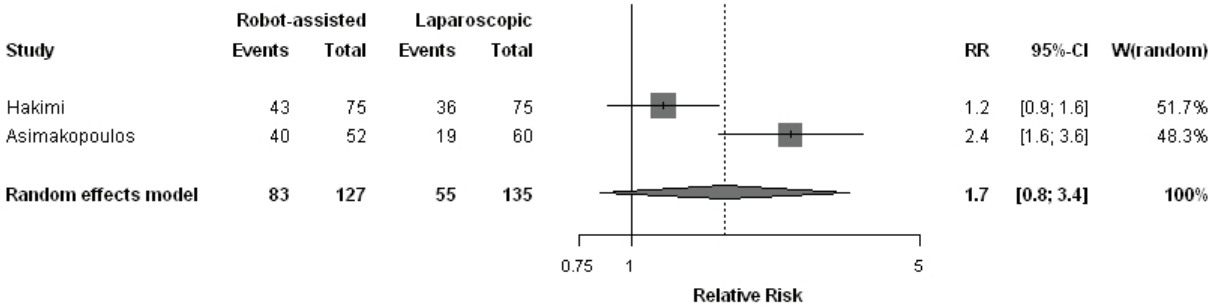
Figure 3.15 Relative risk of positive surgical margin (PSM) rates for tumour stage pT3 for robot-assisted versus laparoscopic radical prostatectomy



Meta-analysis of functional outcomes

Two studies providing data on sexual function following robot-assisted and laparoscopic radical prostatectomy produced a pooled estimate of effect favouring the robot-assisted approach (Figure 3.16). This result was not statistically significant (RR 1.68; 95% CI: 0.84–3.37). The results of the single RCT differed from the meta-analysis, which included only one additional study of lower quality. No statistically significant difference in function was found in the meta-analysis in contrast with the clearly superior results reported for robot-assisted surgery in the RCT.[37] At 12-months follow up, sexual function (as defined by capability of intercourse with or without the help of phosphodiesterase type 5 inhibitors) was 32% in the laparoscopic surgical group compared to 77% in the robot-assisted surgical group ($p<0.0001$). This is equivalent to a relative risk of 2.43 (95% CI: 1.63 to 3.63) for return to sexual function following robot-assisted compared to laparoscopic radical prostatectomy.

Figure 3.16 Relative risk of post-operative sexual function for robot-assisted versus laparoscopic radical prostatectomy



Results for urinary function at 3, 6 and 12 months were similar between both surgical approaches, with robot-assisted prostatectomy associated with marginally better outcomes. (RR 1.09, 1.2, 1.09; 95% CI 0.98 – 1.21, 1.08 – 1.34 and 1.02 – 1.17, respectively. Figures 3.17 – 3.19.) However, the results for urinary function at three months did not achieve statistical significance. The results of the single randomised controlled trial (RCT) identified in the literature search[37] shows similar results for continence at three months, but also failed to find statistically significant differences in continence outcomes at 6 or 12 months.

Figure 3.17 Relative risk of post-operative urinary continence at three months for robot-assisted versus laparoscopic radical prostatectomy

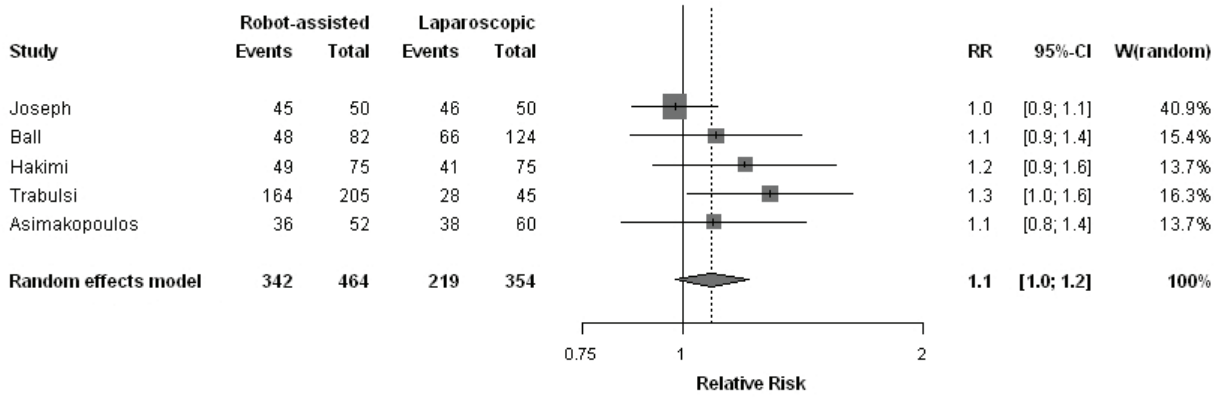


Figure 3.18 Relative risk of post-operative urinary continence at six months for robot-assisted versus laparoscopic radical prostatectomy

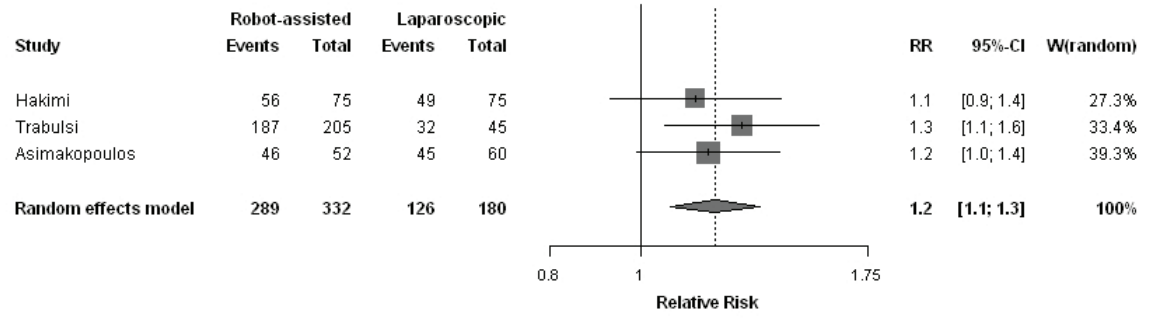
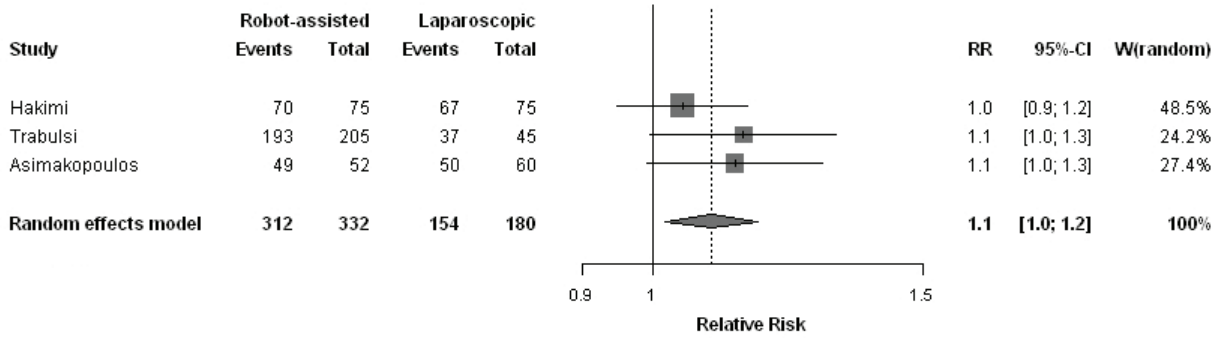


Figure 3.19 Relative risk of post-operative urinary continence at 12 months for robot-assisted versus laparoscopic radical prostatectomy



Meta-analysis of peri-operative outcomes and length of stay

Pooled data from nine separate studies indicate that robot-assisted surgery is associated with a non-statistically significant reduction in estimated blood loss compared to laparoscopic surgery (72ml less per procedure, 95% CI -148ml to 5ml) (Figure 3.20). However, there was a high degree of heterogeneity between studies reporting this outcome (I^2 98.2%). The relative risk of transfusion was reported in seven studies and shows no significant differences in the risk of transfusion (RR 0.66; 95% CI: 0.32 to 1.36) (Figure 3.21).

Figure 3.20 Mean difference in blood loss (ml) for robot-assisted versus laparoscopic radical prostatectomy

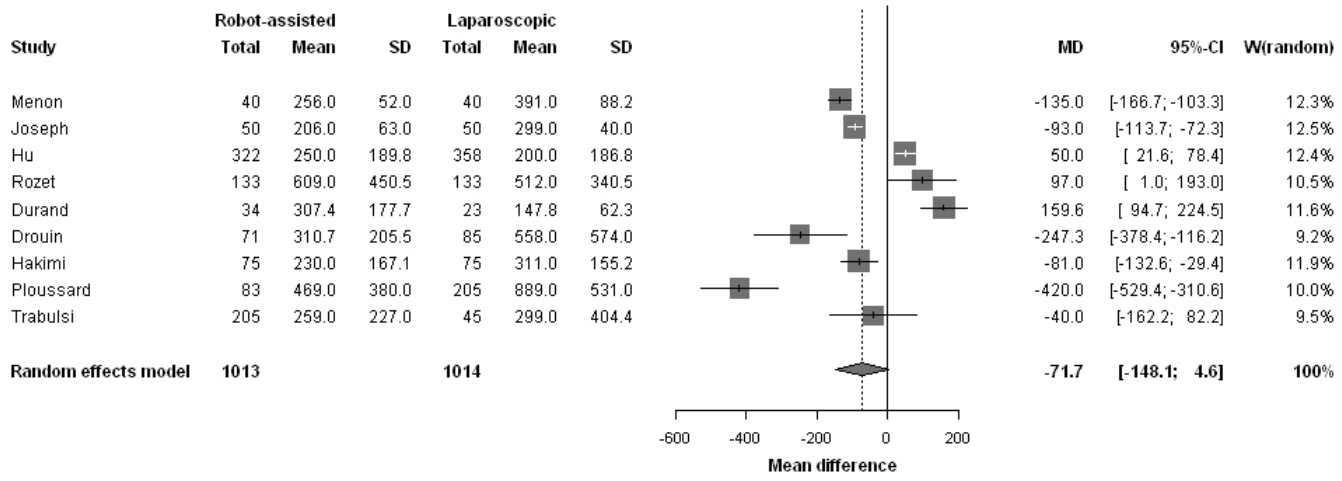
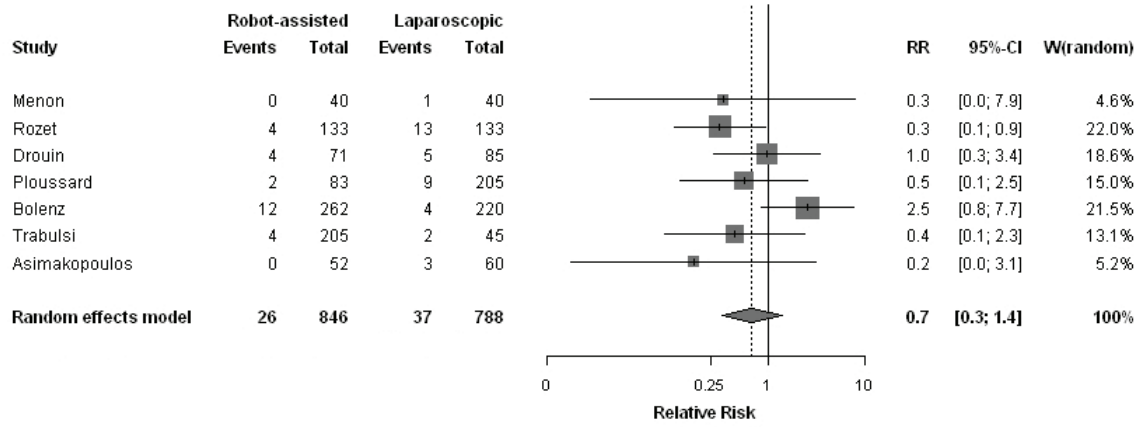
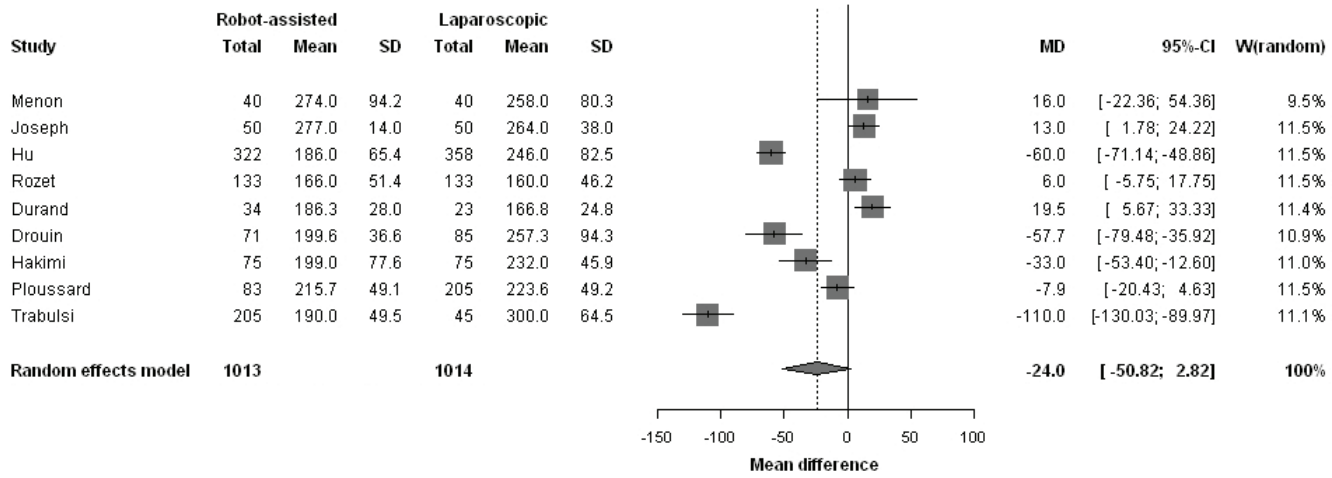


Figure 3.21 Relative risk of blood transfusion for robot-assisted versus laparoscopic radical prostatectomy



The pooled estimate of the difference in operative time between robot-assisted and laparoscopic radical prostatectomy was not found to be statistically significant. The level of heterogeneity between the results of different studies was high (I^2 97%). The pooled mean operative time was shorter in the robot-assisted group (24 minutes less per procedure, 95% CI: 51 minutes shorter to 3 minutes longer) (Figure 3.22).

Figure 3.22 Mean difference in operating time (minutes) for robot-assisted versus laparoscopic radical prostatectomy



Pooled results from eight studies indicate no significant difference in complication rates between robot-assisted and laparoscopic radical prostatectomy (RR 0.96; 95% CI: 0.53 – 1.73), (Figure 3.23). A reduction in the rate of conversion to open surgery associated with robot-assisted prostatectomy was not statistically significant (RR 0.51; 95% CI: 0.11 to 2.31), (Figure 3.24).

Figure 3.23 Relative risk of complications for robot-assisted versus laparoscopic radical prostatectomy

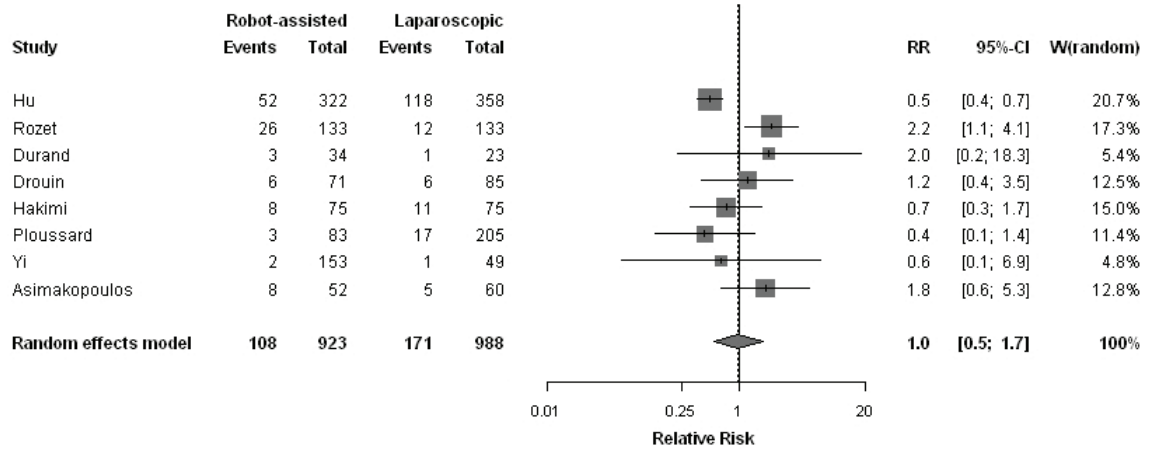
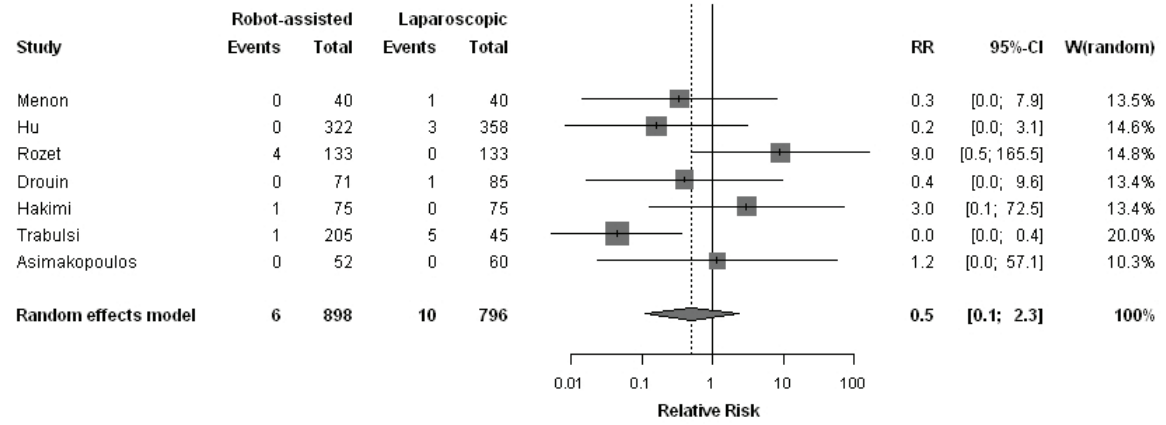
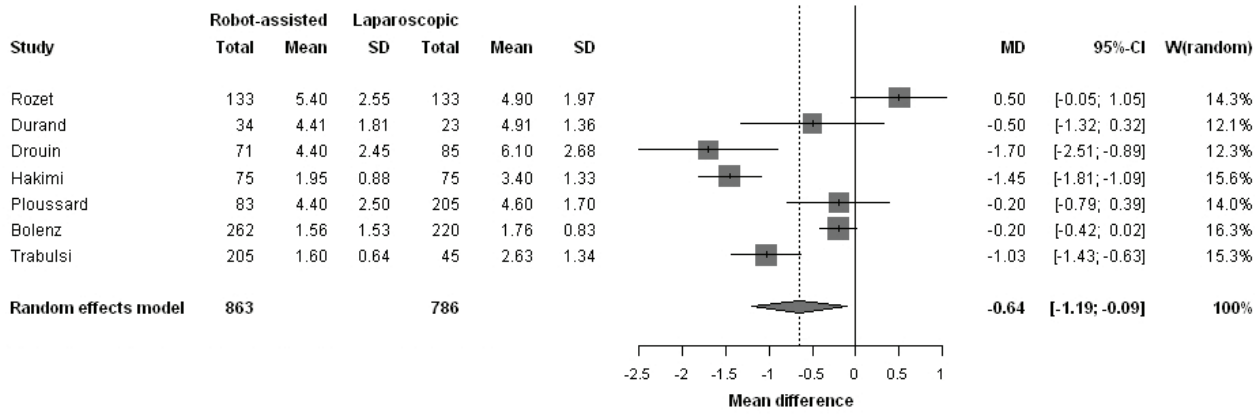


Figure 3.24 Relative risk of conversion to open surgery for robot-assisted versus laparoscopic radical prostatectomy



Robot-assisted radical prostatectomy was associated with a reduction in the average length of hospital stay (0.6 days less; 95% CI: 0.1 – 1.2 days), compared to laparoscopic surgery (Figure 3.25). The level of heterogeneity between studies reporting this outcome was high (I^2 91.2%). Sub-group analysis of differences in the duration of hospital stays for robot-assisted versus laparoscopic radical prostatectomy failed to achieve statistical significance when US studies were omitted (0.4 fewer days, 95% CI: 1.3 days less to 0.4 days more).

Figure 3.25 Mean differences in length of hospital stay for robot-assisted versus laparoscopic radical prostatectomy



Sensitivity analysis

Sensitivity analysis was carried out to determine the effect of removing outliers in the reported results for each outcome. Results from prospective and retrospective studies were pooled separately to investigate the effect of study design. Funnel plots for each outcome were inspected visually to identify distributions of results which may indicate systematic variations. Outliers were identified for estimated blood loss[53] and operative time.[51] Removal of these had the effect of reducing the difference in mean operating time from 24 minutes to 13 minutes in favour of robot-assisted surgery (95% CI: 37 minutes shorter to 10 minutes longer) and reducing the mean estimated blood loss from 72ml to 33ml, still favouring robot-assisted surgery (95% CI: -105ml to 40ml). However, both of these results remained statistically insignificant. Separate analysis of the results from prospective study designs resulted in low reliability of effect estimates due to smaller number of studies (≤ 3) for each outcome. However, this analysis showed a large, but still not statistically significant increase in the average reduction in estimated blood loss associated with robot-assisted surgery (-273ml, 95% CI:-552ml to 7ml). The asymmetry of funnel plots was tested using Egger's regression test and showed some evidence of publication bias associated with urinary outcomes at three months (z=1.9, p=0.057). There was no evidence of publication bias for any other outcome.

3.2.4 Summary

A meta-analysis was conducted comparing robot-assisted radical prostatectomy to both open radical prostatectomy and to laparoscopic radical prostatectomy for a range of oncological, functional and peri-operative outcomes as well as complication rate and length of stay.

There is no published data demonstrating the long-term efficacy of robot-assisted radical prostatectomy in reducing morbidity and mortality from prostate cancer. Using PSM rates as a surrogate marker of oncological efficacy, robot-assisted surgery has comparable efficacy to open and laparoscopic radical prostatectomy and may be superior to open radical prostatectomy for patients with tumour grade pT2.

Functional outcomes assessed included post-operative urinary continence and sexual function. Robot-assisted surgery is associated with a small, but statistically significant increase in the percentage of patients reporting continence compared to open (at 3, 6 and 12 months) and laparoscopic (at 6 and 12 months) radical prostatectomy. Robot-assisted surgery is associated with comparable or improved post-operative sexual function compared to open or laparoscopic radical prostatectomy. These outcomes were variably defined and reported, with a high level of heterogeneity between the results of individual studies.

A range of peri-operative outcomes were assessed. Robot-assisted surgery is associated with a significant reduction in estimated blood loss and a corresponding reduction in transfusion rates compared to open radical prostatectomy. Although also statistically superior to laparoscopic surgery in terms of estimated blood loss, the benefit is less marked; there is no statistically significant difference in transfusion rates between these procedures.

Average length of stay is significantly shorter for patients undergoing robot-assisted compared to laparoscopic (-0.6 days) or open (-1.5 days) radical prostatectomy. This benefit is more marked when the analysis is limited to non-US studies. Mean operative times are approximately 36 minutes longer for robot-assisted surgery compared to open radical prostatectomy, but do not differ significantly from those reported for laparoscopic radical prostatectomy.

These results are consistent with those reported in published review articles[33;63;64] and other recent HTA studies,[8;18-20] which have found evidence of reduced blood loss, shorter length of stay and longer operating times but limited data on the superiority of robot-assisted prostatectomy in functional and oncological outcomes. The difference between length of stay in US and non-US studies is also highlighted by Coelho et al.[63] who reported a range of 3 to 5.4 days for non-US and 1 to 1.2 days for US patients undergoing robot-assisted prostatectomy. Inclusion of RCT data from Asimakopoulos et al.[37] resulted in a significant improvement in the sexual function outcomes associated with robot-assisted compared to laparoscopic radical prostatectomy, and provides a higher estimate of effect for this outcome than was previously reported.

The limitations that exist with regard to the evidence are apparent from the scarcity of RCTs with high numbers of participants.[65] All comparative data for robot-assisted versus open radical prostatectomy are derived from observational studies, with only a single study involving random allocation being identified for robot-assisted versus laparoscopic radical prostatectomy. The quality of the evidence base is further diminished by the fact that approximately half of the observational studies are retrospective or use historical controls and the inconsistent manner in which some outcomes were reported across studies. Excluding retrospective studies or studies that used historical controls generally decreased the statistical significance of the estimate due to a decrease in the number of studies included.

The results of this meta-analysis need to be interpreted in the context of the general low quality of the evidence base at the time of this HTA and with due consideration of the high level of heterogeneity associated with the estimated effect of robot-assisted prostatectomy on some of the clinical outcomes measured.

3.3 Hysterectomy

3.3.1 Background

A hysterectomy is an operation to remove the uterus. Total hysterectomy is removal of the entire uterus while partial hysterectomy involves removal of the uterine body while leaving the cervix intact. Radical hysterectomy, which is mostly carried out when cancer is present, is the removal of the uterus, the tissue on both sides of the cervix (parametrium), and the upper part of the vagina.[66] Hysterectomy can be performed to treat a number of different conditions, both benign (including uterine fibroids, endometriosis, female genital prolapse) and malignant (including cancer of the uterus, cervix or ovaries). There are approximately 2,800 hysterectomies carried out in Ireland annually.[67] The main diagnoses associated with the procedure are genital prolapse (25%), uterine fibroids (17%), excessive, frequent or irregular menstruation (14%) and uterine cancer (8%). When combined, diseases of the genitourinary system (ICD-10 N00-N99, including prolapse, endometriosis, excessive menstruation) account for 55% of hysterectomies. Benign, in-situ and neoplasms of uncertain behaviour (ICD-10 D00-D48, including fibroids) account for 25%, and malignant neoplasms (ICD-10 C00-C97, including uterine, ovarian and cervical cancer) account for 17%.[67] Laparoscopic assisted vaginal hysterectomy may be an alternative to conventional laparoscopic surgery in some benign conditions. Where possible, the procedures included in the meta-analysis include only those where a direct comparison between a robot-assisted approach and a conventional open or laparoscopic approach is valid.

A hysterectomy can be performed using a number of different surgical approaches as follows:

- Abdominal hysterectomy involves making an incision in the lower abdomen to facilitate removal of the uterus.
- Vaginal hysterectomy is where the uterus is removed through an incision made in the vagina rather than the abdomen.
- Laparoscopic hysterectomy is a minimally invasive technique where instead of one large incision, several smaller incisions are made to allow access to laparoscopic instruments used in the removal of the uterus. This technique can be used in both abdominal and vaginal hysterectomy.
- Laparoscopic-assisted vaginal hysterectomy (LAVH) is a surgical procedure using a laparoscope inserted through small incisions in the abdomen to guide the removal of the uterus and/or Fallopian tubes and ovaries through the vagina.
- Robot-assisted hysterectomy is another minimally invasive technique that also requires several small incisions, but the surgical instruments passed through these are controlled remotely by the surgeon via the robotic system.

The clinical outcomes associated with hysterectomy that are reported in the literature and that are analysed in this report are listed in Table 3.4. These are generally limited to peri-operative complications and length-of-stay issues.

Table 3.4 Peri-operative clinical effectiveness outcomes for hysterectomy procedures

Outcomes reported	Description
Estimated blood loss	Estimated blood loss during each type of surgery is included in the meta-analysis. Varying methods were used to capture this outcome in the different studies, resulting in a high level of inconsistency in the measurement of this outcome.
Transfusion	Transfusion rates associated with each type of surgery are examined, in order to identify any significant differences in the risk of transfusion between different surgical approaches.
Complications	Complications associated with each type of surgery can be used to assess the safety profile of different surgical approaches. Some studies used a standardised approach to complications reporting (e.g. Clavien-Dindo), others categorised complications as major or minor or provided a list of the complications recorded; complication rates could be based on the absolute number of complications or the number of patients who experienced complications. Complications could include intra-operative, peri-operative or post-operative complications, or combinations thereof. In this HTA, it was assumed that the complication count represented the number of patients who experienced any reported complications.
Operative time	The length of time needed to perform the hysterectomy operation. This is most commonly defined as skin-to-skin time, which is the time from the first incision to skin closure.
Hospital stay	Length of hospital stay is defined as the number of days spent in hospital before being discharged.

3.3.2 Summary of included studies

Identification of studies concerning the clinical effectiveness of robot-assisted surgery in hysterectomy was carried out as described in Chapter 2. A total of 33 studies were selected for inclusion (see Appendix 1). A table of included studies and their characteristics is included in Appendix 2.

All of the 33 studies identified are observational, 30 are retrospective comparisons or use historical comparison groups, while three are prospective observational studies. Sixteen studies compare robot-assisted surgery to open surgery, 12 compare robotic and laparoscopic surgery and five studies provide comparative data for robot-assisted, laparoscopic and open surgery in the same study. The majority of studies (24/33, 73%) were carried out in the USA, with two studies from Turkey and two from South Korea; and one study each from Canada, Italy, Netherlands, Norway and Switzerland (see Appendix 2 for details).

Total sample size for included studies ranged from 14[68] to 502,[69] with patient numbers in the robot-assisted arms ranging from 7[68] to 237.[69] The mean sample size in studies comparing robot-assisted to open hysterectomy was 89 (SD: 74), for robot-assisted versus laparoscopic surgery it was 181 (SD: 155) and for studies that compared robot-assisted surgery to both open and laparoscopic surgery the mean sample size was 190 (SD: 133). Age and BMI characteristics were similar between intervention and comparison groups. Average patient age and BMI was reported for 11/16 robot-assisted versus open surgery studies (52 vs 53 years; 31.1 vs 30 kg/m^2, respectively) and in 11/12 studies comparing robot-assisted and laparoscopic surgery (52 vs 52 years; 30.5 vs 30 kg/m^2, respectively). For studies comparing robot-assisted surgery to both open and laparoscopic surgery, average patient age was reported in 5/5 (57 vs 55 years) and mean BMI was reported in 4/5 (29.8 vs 29.5 kg/m^2).

The number of surgeons who performed robot-assisted surgery was reported in 67% of the included studies (22/33). Eleven studies[68;70-79] involved a single surgeon performing all robot-assisted surgeries, nine studies[69;80-87] used two surgeons and two studies[88;89] used four surgeons in the robot-assisted group. Surgeons' experience using the robot was poorly reported overall, with 55% (18/33) providing some description on the experience of the surgeon or the length of time a robot-assisted surgery had been available in the study setting, although the way this was reported varied widely. In 15 out of 18 studies[68;69;76;77;79;83-85;87-93] that did provide some information, either the surgeon had little experience using the device or the robotic system was new to the setting in which the study was carried out. Therefore the influence of the training curve for inexperienced surgeons is included in the overall estimate of effect calculated in the meta-analysis.

Reporting of outcomes differed across many of the included studies. Twenty-three studies provided a definition of operative time,[68-73;76-79;82;83;85-87;90-97] with the most commonly reported operative time (17/23) being the time from skin incision to skin closure. Criteria for blood transfusion were not explicitly reported in any of the included studies. Reporting of complications also varied, with most of the studies that provided this data including a list of intra-operative and post-operative complications recorded as part of the individual study.

3.3.3 Data analysis and synthesis

Comparison of robot-assisted hysterectomy with open and laparoscopic hysterectomy was performed separately. The results of the meta-analysis comparing robot-assisted to open surgery are presented first followed by the comparison of robot-assisted versus laparoscopic hysterectomy.

3.3.4 Robot–assisted hysterectomy compared to open hysterectomy

Meta-analysis of data extracted from studies comparing robot-assisted and traditional open surgical approaches to hysterectomy was carried out as described in Chapter 2 and Appendix 3. The outcomes analysed were estimated blood loss, transfusion rate, operative time, complication rate and duration of hospital stay. The overall results of this meta-analysis are provided in Table 3.5, along with the number of studies containing data on each outcome, total sample size and a measure of the heterogeneity of the data for a particular outcome. Forest plots showing the spread of results for each outcome are also provided.

A summary of the main observations is provided below, followed by a description of the sensitivity and sub-groups analyses carried out and their impact on the estimate of the effect for relevant outcomes.

Table 3.5 Clinical effectiveness outcomes for robot-assisted hysterectomy (RAH) compared to open hysterectomy (OH)

Outcome	Studies (n)	Patients (n)	RAH (mean)	OH (mean)	Estimate of effect*	Range	I^2 (%) (95% CI)*	p-value
Estimated blood loss (ml)	20	2,014	110ml	378ml	-267ml	-320 - -214	98.8	<0.0001
Transfusion rate	17	1,743	6%	27%	RR 0.23	0.15 - 0.37	0.0	<0.0001
Complication rate	20	2,053	18%	36%	RR 0.40	0.27 - 0.60	56.4	<0.0001
Operative time (mins)	20	1,826	231mins	181mins	49 mins	29 – 69	98.1	<0.0001
Length of hospital stay (days)	22	2,113	1.9	4.4	-2.6 days	-2.9 - -2.2	91.2	<0.0001

CI – Confidence interval; OH– Open hysterectomy; RAH – Robot-assisted hysterectomy; RR – Relative risk.
** Estimate of effect (and associated 95% CI) is presented as the relative risk (RR) of achieving the specified outcome using robot-assisted surgery compared to open surgery, except where absolute values are provided, as indicated by the use of units of measurement (ml/mins/days).*

Table 3.6 Clinical effectiveness outcomes for robot-assisted hysterectomy (RAH) compared to laparoscopic hysterectomy (LH)**

Outcome	Studies (n)	Patients (n)	RAH (mean)	LH (mean)	Estimate of effect*	Range (95% CI)*	I^2 (%)	p-value
Estimated blood loss (ml)	16	2,151	92ml	165ml	-84ml	-117 - -52	92.4	<0.0001
Transfusion rate	9	1,226	6%	10%	RR 0.53	0.28 - 0.99	17.2	0.0482
Complication rate	14	2,055	18%	26%	RR 0.73	0.57 - 0.94	0.0	0.0163
Conversion rate	12	1,971	7%	17%	RR 0.44	0.28 - 0.69	0.0	0.0003
Operative time (mins)	15	2,077	173mins	161mins	5 mins	-14 - 24	95.4	0.6003
Length of hospital stay (days)	17	2,204	1.5	1.9	-0.4 days	-0.6 - -0.2	90.9	<0.0001

CI – Confidence interval; LH– Laparoscopic hysterectomy; RAH – Robot-assisted hysterectomy; RR – Relative risk.
** Estimate of effect (and associated 95% CI) is presented as the relative risk (RR) of achieving the specified outcome using robot-assisted surgery compared to laparoscopic surgery, except where absolute values are provided, as indicated by the use of units of measurement (ml/mins/days).*

*** This table is discussed in Section 3.3.5*

Meta-analysis of estimated blood loss and transfusion rates

Pooled results from 20 studies indicate that robot-assisted hysterectomy is associated with a reduction in average blood loss of 267ml (95% CI: 214 ml to 320ml) compared to open surgery (Figure 3.26). However, there is a high degree of heterogeneity between the results of included studies (I^2 98.8%). A corresponding decrease in the relative risk of transfusion associated with robot-assisted surgery is also observed (RR 0.23; 95% CI: 0.15 to 0.37) (Figure 3.27).

Subgroup analysis by type of hysterectomy was performed for radical and simple total hysterectomy with node staging. Results from 10[68;72;76;80;81;91;93;94;96;98] studies comparing open radical hysterectomy to robot-assisted radical hysterectomy indicate that there is a mean reduction in estimated blood loss of 417ml (95% CI -533ml to -302ml, I^2 = 91.8%, individual pooled means of 121ml versus 538ml) in favour of robot-assisted surgery. The corresponding relative risk (RR) of transfusion using data from eight [68;76;80;81;91;94;96;97] studies is 0.17 (95% CI 0.08 – 0.35, I^2 = 0%). Results from seven [71;75;77;87;88;90;92] studies comparing open simple total hysterectomy with node staging versus robot-assisted simple total hysterectomy with node staging indicate that there is a mean reduction in estimated blood loss of 159ml (95% CI -210ml to -109ml, I^2 =92.9%, individual pooled means of 120ml versus 279ml) in favour of robot-assisted surgery. The corresponding relative risk (RR) of transfusion using data from seven [71;75;77;82;87;90;92] studies is 0.34 (95% CI 0.18 – 0.62, I^2 = 0%). Insufficient data were available to compare any other types of hysterectomy.

Figure 3.26 Mean differences in estimated blood loss (ml) for robot-assisted versus open hysterectomy

Study	Robot-assisted Total	Mean	SD	Open Total	Mean	SD	MD	95%-CI	W(random)
Bell	40	166.0	225.9	40	316.8	282.10	-150.8	[-262.8; -38.8]	5.0%
Boggess	103	74.5	101.2	138	266.0	184.50	-191.5	[-228.0; -155.0]	6.2%
Boggess2	51	96.5	85.8	49	416.8	188.10	-320.3	[-378.0; -262.6]	5.9%
DeNardis	56	105.0	77.0	106	241.0	115.00	-136.0	[-165.8; -106.2]	6.2%
Ko	16	81.9	53.5	32	665.6	474.40	-583.7	[-750.1; -417.3]	3.9%
Veljovich	25	66.6	44.8	131	197.6	129.40	-131.0	[-159.3; -102.7]	6.3%
Estape	32	130.0	119.4	14	621.4	294.00	-491.4	[-650.9; -331.9]	4.0%
Lowe	7	75.0	53.4	7	700.0	483.60	-625.0	[-985.4; -264.6]	1.6%
Maggioni	40	78.0	94.8	40	221.8	132.40	-143.8	[-194.3; -93.3]	6.0%
Seamon2	92	109.0	98.0	162	394.0	311.70	-285.0	[-337.0; -233.0]	6.0%
Cantrell	63	50.0	37.9	64	400.0	225.80	-350.0	[-406.1; -293.9]	5.9%
Geisler	30	165.0	117.3	30	323.0	229.80	-158.0	[-250.3; -65.7]	5.3%
Göçmen	10	95.0	48.8	12	255.0	98.10	-160.0	[-223.2; -96.8]	5.8%
Goel	59	231.7	47.9	38	307.9	34.07	-76.2	[-92.5; -59.9]	6.3%
Halliday	16	106.0	113.0	24	546.0	570.00	-440.0	[-674.7; -205.3]	2.8%
Matthews(p1)	5	51.3	34.0	104	374.0	310.00	-322.7	[-389.3; -256.1]	5.8%
Matthews(p2)	65	82.3	106.0	113	430.0	417.00	-347.7	[-428.8; -266.6]	5.5%
Nam	32	220.9	134.7	32	531.5	435.50	-310.6	[-468.5; -152.7]	4.1%
Nevadunsky	66	83.0	59.9	43	193.0	172.90	-110.0	[-163.7; -56.3]	6.0%
Schreuder	13	300.0	183.7	14	2000.0	796.60	-1700.0	[-2129.1; -1270.9]	1.2%
Random effects model	**821**			**1193**			**-267.2**	**[-320.0; -214.3]**	**100%**

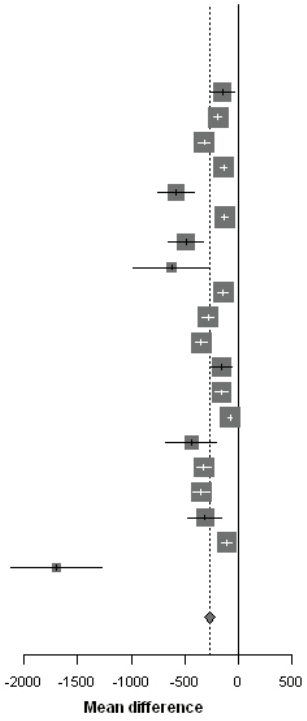
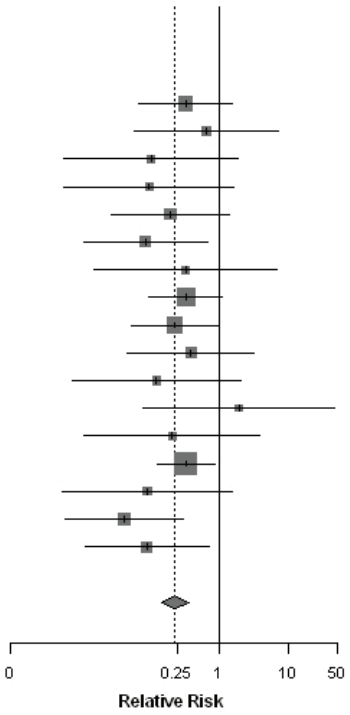


Figure 3.27 Relative risk of blood transfusion with robot-assisted versus open hysterectomy

Study	Robot-assisted Events	Total	Open Events	Total	RR	95%-CI	W(random)
Bell	2	40	6	40	0.3	[0.1; 1.6]	8.7%
Boggess	1	103	2	138	0.7	[0.1; 7.3]	3.6%
Boggess2	0	51	4	49	0.1	[0.0; 1.9]	2.4%
DeNardis	0	56	9	106	0.1	[0.0; 1.7]	2.6%
Ko	1	16	10	32	0.2	[0.0; 1.4]	5.3%
Estape	1	32	5	14	0.1	[0.0; 0.7]	4.9%
Lowe	0	7	1	7	0.3	[0.0; 6.9]	2.2%
Maggioni	3	40	9	40	0.3	[0.1; 1.1]	13.5%
Seamon2	2	92	15	162	0.2	[0.1; 1.0]	9.7%
Göçmen	1	10	3	12	0.4	[0.0; 3.3]	4.6%
Göçmen2	0	8	3	7	0.1	[0.0; 2.1]	2.6%
Goel	1	59	0	38	1.9	[0.1; 46.4]	2.0%
Halliday	0	16	3	24	0.2	[0.0; 3.8]	2.4%
Jung	4	28	24	56	0.3	[0.1; 0.9]	22.4%
Matthews	0	70	16	217	0.1	[0.0; 1.5]	2.6%
Nam	1	32	23	32	0.0	[0.0; 0.3]	5.4%
Nevadunsky	1	66	7	43	0.1	[0.0; 0.7]	4.8%
Random effects model	**18**	**726**	**140**	**1017**	**0.2**	**[0.1; 0.4]**	**100%**

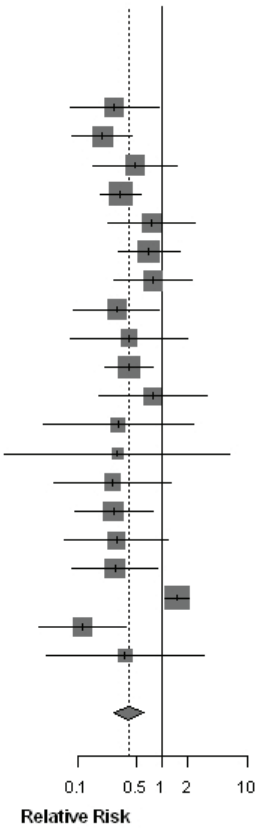


Complication rates

Complication rates are significantly lower for robot-assisted than traditional open hysterectomy using pooled results from 20 studies (RR 0.4; 95% CI: 0.27 to 0.60 (Figure 3.28). There is a moderate degree of heterogeneity between studies (I^2 56.4%) as well as considerable differences in how complications were reported in individual studies. Subgroup analysis by type of hysterectomy was performed for radical and simple total hysterectomy with node staging. Results from 10[68;72;76;80;81;91;93;94;96;97] studies indicate that there is a non-statistically significant reduction in the risk of complications in robot-assisted radical hysterectomy compared to open radical hysterectomy (RR = 0.58, 95% CI 0.33 – 1.01, I^2 = 66.9%). Results from eight studies [71;75;77;82;87;88;90;92] comparing robot-assisted simple total hysterectomy with node staging to open simple total hysterectomy with node staging show a statistically significant reduction in the risk of complications associated with use of the robot (RR = 0.34, 95% CI 0.25 – 0.46, I^2 = 0%). Insufficient data was available to compare the risk of complications for any other types of hysterectomy.

Figure 3.28 Relative risk of complications with robot-assisted versus open hysterectomy

Study	Robot-assisted Events	Total	Open Events	Total	RR	95%-CI	W(random)
Bell	3	40	11	40	0.3	[0.1; 0.9]	5.0%
Boggess	6	103	41	138	0.2	[0.1; 0.4]	6.4%
Boggess2	4	51	8	49	0.5	[0.2; 1.5]	5.2%
DeNardis	11	56	65	106	0.3	[0.2; 0.6]	7.4%
Ko	3	16	8	32	0.8	[0.2; 2.4]	5.0%
Veljovich	5	25	38	131	0.7	[0.3; 1.6]	6.4%
Estape	7	32	4	14	0.8	[0.3; 2.2]	5.5%
Lowe	2	7	7	7	0.3	[0.1; 0.9]	5.1%
Maggioni	2	40	5	40	0.4	[0.1; 1.9]	3.8%
Seamon2	10	92	44	162	0.4	[0.2; 0.8]	7.1%
Cantrell	3	63	4	64	0.8	[0.2; 3.3]	4.2%
Göçmen	1	10	4	12	0.3	[0.0; 2.3]	2.8%
Göçmen2	0	8	1	7	0.3	[0.0; 6.2]	1.5%
Goel	2	59	5	38	0.3	[0.1; 1.3]	3.8%
Halliday	3	16	17	24	0.3	[0.1; 0.8]	5.5%
Jung	2	28	14	56	0.3	[0.1; 1.2]	4.3%
Matthews	3	70	34	217	0.3	[0.1; 0.9]	5.2%
Nam	28	32	19	32	1.5	[1.1; 2.0]	8.2%
Nevadunsky	3	66	17	43	0.1	[0.0; 0.4]	5.1%
Schreuder	1	13	3	14	0.4	[0.0; 3.0]	2.6%
Random effects model	**99**	**827**	**349**	**1226**	**0.4**	**[0.3; 0.6]**	**100%**



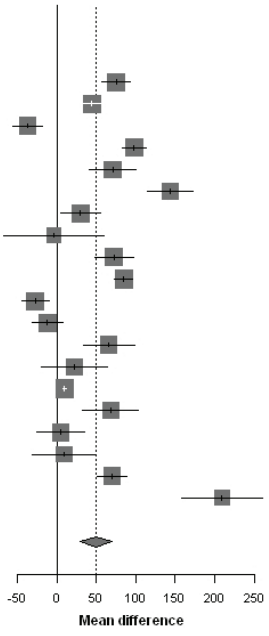
Operative time

Robot-assisted hysterectomy is associated with significantly longer average operating times (+49 minutes, 95% CI: 29 to 69) than open hysterectomy (Figure 3.29). This difference in time needs to be considered in the context of overall mean procedure times for robot-assisted and open hysterectomy (231 minutes and 181 minutes, respectively). A high degree of heterogeneity is observed in the results for this outcome (I^2 98.1%).

Subgroup analysis by type of hysterectomy was performed for radical and simple total hysterectomy with node staging. Results from 11 studies [68;72;76;80;81;91;93;94;96-98] indicate that mean operating times for robot-assisted radical hysterectomy are 35 minutes longer than for radical hysterectomy performed by open surgery (95% CI 1 – 68 mins, I^2 = 93.8%). Results from eight studies [71;75;77;82;87;88;90;92] comparing robot-assisted simple total hysterectomy with node staging to open simple total hysterectomy with node staging show an average increase in operating times of 66 minutes (95% CI 32 – 99 mins, I^2 = 98.5%) associated with robot-assisted surgery. Insufficient data was available to compare differences in operating time for any other types of hysterectomy.

Figure 3.29 Mean differences in operative time with robot-assisted versus open hysterectomy

Study	Robot-assisted Total	Mean	SD	Open Total	Mean	SD	MD	95%-CI	W(random)
Bell	40	184.00	41.30	40	108.60	41.40	75.4	[57.3; 93.5]	5.3%
Boggess	103	191.20	36.00	138	146.50	48.80	44.7	[34.0; 55.4]	5.5%
Boggess2	51	210.90	45.50	49	247.80	48.80	-36.9	[-55.4; -18.4]	5.3%
DeNardis	56	177.00	55.00	106	79.00	17.00	98.0	[83.2; 112.8]	5.4%
Ko	16	290.00	46.00	32	219.00	54.10	71.0	[41.7; 100.3]	5.0%
Veljovich	25	283.00	71.20	131	139.00	48.90	144.0	[114.9; 173.1]	5.0%
Estape	32	144.00	48.00	14	114.00	36.00	30.0	[4.9; 55.1]	5.1%
Lowe	7	260.00	59.90	7	264.00	60.80	-4.0	[-67.2; 59.2]	3.6%
Maggioni	40	272.27	42.30	40	199.60	65.60	72.7	[48.5; 96.9]	5.2%
Seamon2	92	228.00	43.00	162	143.00	47.00	85.0	[73.6; 96.4]	5.5%
Cantrell	63	213.00	51.40	64	240.00	46.30	-27.0	[-44.0; -10.0]	5.4%
Geisler	30	154.00	36.60	30	166.00	40.80	-12.0	[-31.6; 7.6]	5.3%
Göçmen	10	234.60	42.70	12	168.50	32.60	66.1	[33.8; 98.4]	4.9%
Göçmen2	8	233.00	33.30	7	210.80	47.70	22.2	[-20.0; 64.4]	4.5%
Goel	59	185.27	4.40	38	175.24	4.60	10.0	[8.2; 11.9]	5.6%
Halliday	16	351.00	51.00	24	283.00	63.00	68.0	[32.5; 103.5]	4.7%
Jung	28	193.18	60.42	56	187.85	76.55	5.3	[-24.7; 35.4]	5.0%
Nam	32	218.80	78.30	32	209.90	87.80	8.9	[-31.9; 49.7]	4.5%
Nevadunsky	66	204.00	57.00	43	134.00	43.70	70.0	[51.0; 89.0]	5.3%
Schreuder	13	434.00	86.70	14	225.00	39.60	209.0	[157.5; 260.5]	4.1%
Random effects model	**787**			**1039**			**49.1**	**[28.9; 69.3]**	**100%**



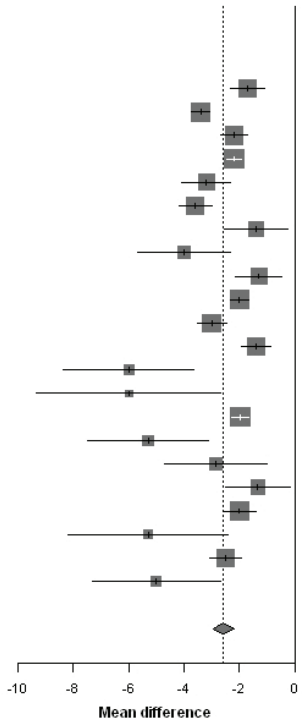
Length of hospital stay

Robot-assisted surgery is associated with an average decrease of 2.6 days in hospital stay per procedure (95% CI 2.2 to 2.9 days less) compared to open hysterectomy (Figure 3.30). This decrease in length of stay needs to be considered in the context of average hospital stays for robot-assisted and open hysterectomy of 1.9 and 4.4 days, respectively.
Sub-group analysis was carried out by separately limiting the included studies to non-US and European studies for duration of hospital stay. This was done to investigate the effect of different health systems on the reporting of this outcome following anecdotal evidence suggesting that, on average, patients undergoing surgical procedures in Europe and Australia tend to remain in hospital for longer than US patients. This analysis indicates that the average decrease in length of stay associated with the use of robot-assisted surgery in non-US studies is 4.3 days (95% CI 2.5 to 6.2) compared to the overall (US and non-US) average reduction of 2.6 days. When only European studies are included the mean reduction in length of stay between robot-assisted and open surgery is 4.6 days (95% CI: 2.1 – 7.0).

Further subgroup analysis by type of hysterectomy was performed for radical and simple total hysterectomy with node staging using data from all countries combined. Results from 11[68;71;72;76;80;81;91;93;94;96;98] indicate that average length of stay for robot-assisted radical hysterectomy is 2.9 days shorter than for radical hysterectomy performed by open surgery (95% CI -3.6 to -2.2 days, I^2 = 82.1%). Results from eight studies [71;75;77;82;86;88;90;92] indicate that average length of stay for robot-assisted simple total hysterectomy with node staging is 2.6 days shorter than for simple total hysterectomy with node staging performed by open surgery (95% CI -3.2 to -2.1 days, I^2 = 91.1%). Insufficient data was available to compare differences in length of stay for any other types of hysterectomy.

Figure 3.30 Mean differences in lengths of hospital stay with robot-assisted versus open hysterectomy

Study	Robot-assisted Total	Mean	SD	Open Total	Mean	SD	MD	95%-CI	W(random)
Bell	40	2.30	1.30	40	4.00	1.50	-1.7	[-2.3; -1.1]	5.8%
Boggess	103	1.00	0.20	138	4.40	2.00	-3.4	[-3.7; -3.1]	6.6%
Boggess2	51	1.00	0.65	49	3.20	1.61	-2.2	[-2.7; -1.7]	6.2%
DeNardis	56	1.00	0.50	106	3.20	1.20	-2.2	[-2.5; -1.9]	6.8%
Ko	16	1.70	0.82	32	4.90	2.30	-3.2	[-4.1; -2.3]	4.9%
Veljovich	25	1.70	0.85	131	5.30	2.87	-3.6	[-4.2; -3.0]	5.9%
Estape	32	2.60	2.10	14	4.00	1.70	-1.4	[-2.5; -0.3]	4.1%
Lowe	7	1.00	0.50	7	5.00	2.20	-4.0	[-5.7; -2.3]	2.8%
Maggioni	40	3.70	1.20	40	5.00	2.40	-1.3	[-2.1; -0.5]	5.1%
Seamon2	92	1.00	0.81	162	3.00	1.98	-2.0	[-2.3; -1.7]	6.6%
Cantrell	63	1.00	0.70	64	4.00	2.03	-3.0	[-3.5; -2.5]	6.1%
Geisler	30	1.40	0.80	30	2.80	1.20	-1.4	[-1.9; -0.9]	6.1%
Göçmen	10	2.80	1.28	12	8.80	3.94	-6.0	[-8.4; -3.6]	1.8%
Göçmen2	8	3.50	1.58	7	9.50	4.23	-6.0	[-9.3; -2.7]	1.0%
Goel	59	1.28	0.87	38	3.26	0.64	-2.0	[-2.3; -1.7]	6.7%
Halliday	16	1.90	0.90	24	7.20	5.30	-5.3	[-7.5; -3.1]	2.0%
Jung	28	7.92	3.61	56	10.78	4.99	-2.9	[-4.7; -1.0]	2.5%
Matthews(p1)	5	1.80	1.30	104	3.14	1.70	-1.3	[-2.5; -0.2]	4.0%
Matthews(p2)	65	1.50	0.70	113	3.50	3.20	-2.0	[-2.6; -1.4]	5.8%
Nam	32	11.60	4.20	32	16.90	7.20	-5.3	[-8.2; -2.4]	1.3%
Nevadunsky	66	1.30	0.84	43	3.80	1.85	-2.5	[-3.1; -1.9]	5.9%
Schreuder	13	4.00	1.82	14	9.00	4.03	-5.0	[-7.3; -2.7]	1.8%
Random effects model	**857**			**1256**			**-2.6**	**[-2.9; -2.2]**	**100%**



Sensitivity analysis

Sensitivity analysis performed by removal of outliers for estimated blood loss[72] reduced the decrease in average estimated blood loss associated with robot-assisted hysterectomy from 267ml to 247ml (95% CI: 197 to 297). Removal of outliers for operative time,[72] complication rate[96] and hospital stay[71] did not significantly affect the results of the meta-analysis for these outcomes. The asymmetry of funnel plots was tested using Egger's regression test and showed some evidence of publication bias associated with reported outcomes for blood loss (z=-6.7, p<0.0001) and hospital stay (z=-3.8, p=0.0001).

3.3.5 Robot-assisted hysterectomy compared to laparoscopic hysterectomy

Table 3.6 shows the overall results of a meta-analysis of pooled data from studies comparing robot-assisted and laparoscopic hysterectomy. Individual study results were combined for estimated blood loss, transfusion rate, complication rate, conversion rate, operative time and duration of hospital stay, as described in Chapter 2 and Appendix 3. Forest plots showing the spread of results for each outcome are also provided.

A summary of the main observations is provided below, followed by a description of the sensitivity and sub-groups analyses carried out and their impact on the estimate of the effect on relevant outcomes.

Estimated blood loss and transfusion

Robot-assisted hysterectomy was associated with a mean reduction in average estimated blood loss of 84ml compared to laparoscopic hysterectomy (95% CI: 52 to 117), (Figure 3.31). This was consistent with a finding in the pooled analysis of nine studies that the relative risk of transfusion is lower for robot-assisted compared to laparoscopic hysterectomy (RR 0.53; 95% CI: 0.28 to 0.99), (Figure 3.32).

Insufficient data was available to perform a subgroup analysis of estimated blood loss and risk of transfusion for different types of hysterectomy.

Figure 3.31 Mean differences in estimated blood loss (ml) with robot-assisted versus laparoscopic hysterectomy

Study	Robot-assisted Total	Mean	SD	Laparoscopic Total	Mean	SD	MD	95%-CI	W(random)
Sert	7	71.0	50.6	7	160.0	111.9	-89.0	[-180.0; 2.0]	4.9%
Bell	40	166.0	225.9	30	253.0	427.7	-87.0	[-255.3; 81.3]	2.5%
Boggess	103	74.5	101.2	81	145.8	105.6	-71.3	[-101.5; -41.1]	7.3%
Gehrig	49	50.0	28.1	32	150.0	91.5	-100.0	[-132.7; -67.3]	7.3%
Payne	100	61.0	60.9	100	113.0	85.9	-52.0	[-72.6; -31.4]	7.6%
Estape	32	130.0	119.4	17	209.4	169.9	-79.4	[-170.1; 11.3]	4.9%
Nezhat	26	250.0	127.2	50	300.0	136.2	-50.0	[-111.8; 11.8]	6.1%
Seamon	92	88.0	64.2	56	200.0	116.2	-112.0	[-145.1; -78.9]	7.2%
Shashoua	24	113.5	122.0	44	98.9	107.0	14.6	[-43.6; 72.8]	6.3%
Cardenas-Goicoechea	102	109.0	83.3	173	187.0	187.0	-78.0	[-110.2; -45.8]	7.3%
Giep	237	59.0	75.7	265	167.9	146.0	-108.9	[-128.9; -88.9]	7.6%
Holtz	13	84.6	32.0	20	150.0	111.0	-65.4	[-117.1; -13.7]	6.6%
Matthews(p1)	5	51.3	34.0	36	353.0	303.0	-301.7	[-405.1; -198.3]	4.4%
Matthews(p2)	65	82.3	106.0	21	260.0	208.0	-177.7	[-270.3; -85.1]	4.8%
Sarlos	40	81.0	42.3	40	50.0	44.4	31.0	[12.0; 50.0]	7.6%
Lim	122	81.1	45.9	122	207.4	109.4	-126.3	[-147.4; -105.2]	7.6%
Random effects model	**1057**			**1094**			**-84.4**	**[-117.1; -51.7]**	**100%**

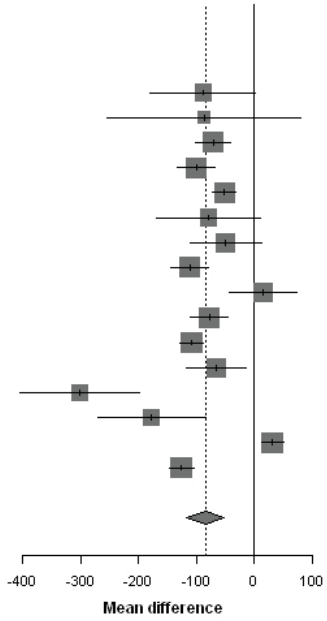
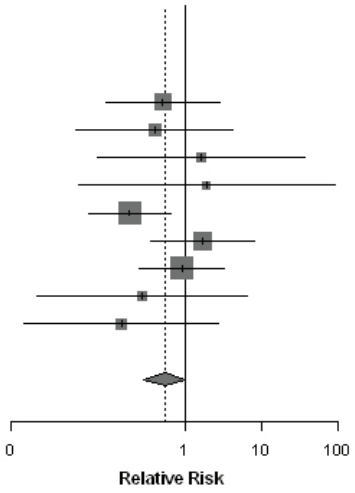


Figure 3.32 Relative risk of transfusion with robot-assisted versus laparoscopic hysterectomy

Study	Robot-assisted Events	Total	Laparoscopic Events	Total	RR	95%-CI	W(random)
Bell	2	40	3	30	0.5	[0.1; 2.8]	13.2%
Boggess	1	103	2	81	0.4	[0.0; 4.3]	6.9%
Estape	1	32	0	17	1.6	[0.1; 37.6]	4.0%
Nezhat	0	26	0	50	1.9	[0.0; 93.4]	2.6%
Seamon	3	92	10	56	0.2	[0.1; 0.6]	25.2%
Cardenas-Goicoechea	3	102	3	173	1.7	[0.3; 8.2]	15.7%
Jung	4	28	4	25	0.9	[0.2; 3.2]	24.1%
Matthews	0	70	1	57	0.3	[0.0; 6.5]	3.9%
Lim	0	122	3	122	0.1	[0.0; 2.7]	4.5%
Random effects model	**14**	**615**	**26**	**611**	**0.5**	**[0.3; 1.0]**	**100%**

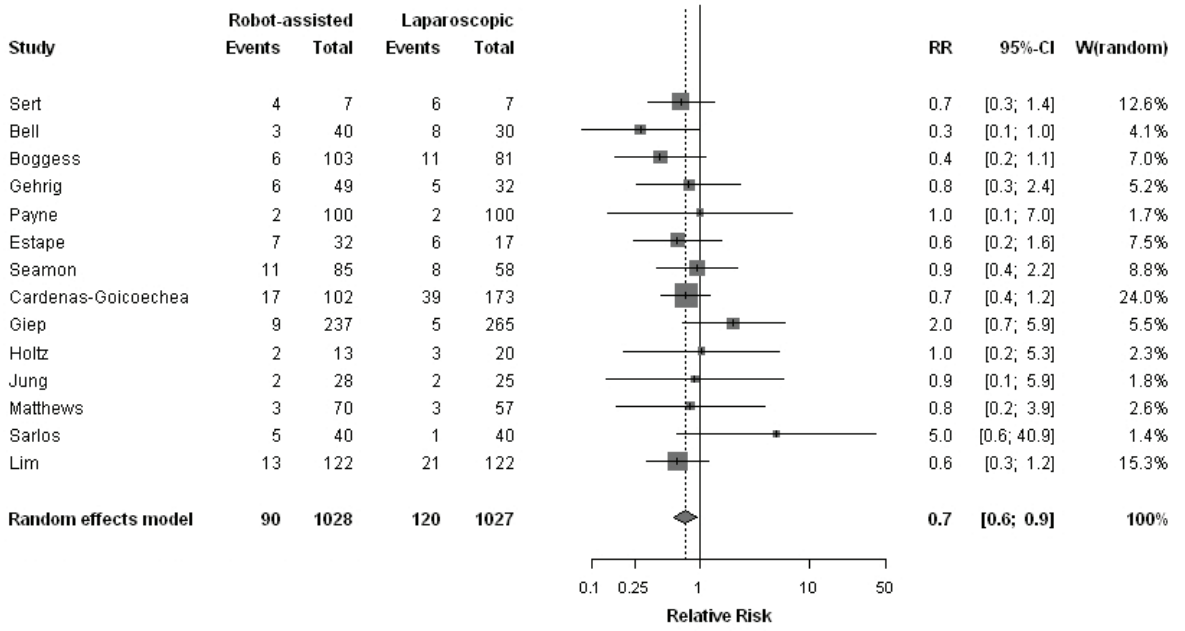


Complication rate

Relative risk of complications between the two groups was reported in 14 studies and show that there is a modest, but statistically significant difference in the rate of complications favouring robot-assisted surgery (RR 0.73; 95% CI: 0.57 to 0.94), (Figure 3.33). There was considerable variability in how this outcome was defined and recorded in the various studies.

Insufficient data was available to perform a subgroup analysis of complication rates for different types of hysterectomy.

Figure 3.33 Relative risk of complications with robot-assisted versus laparoscopic hysterectomy

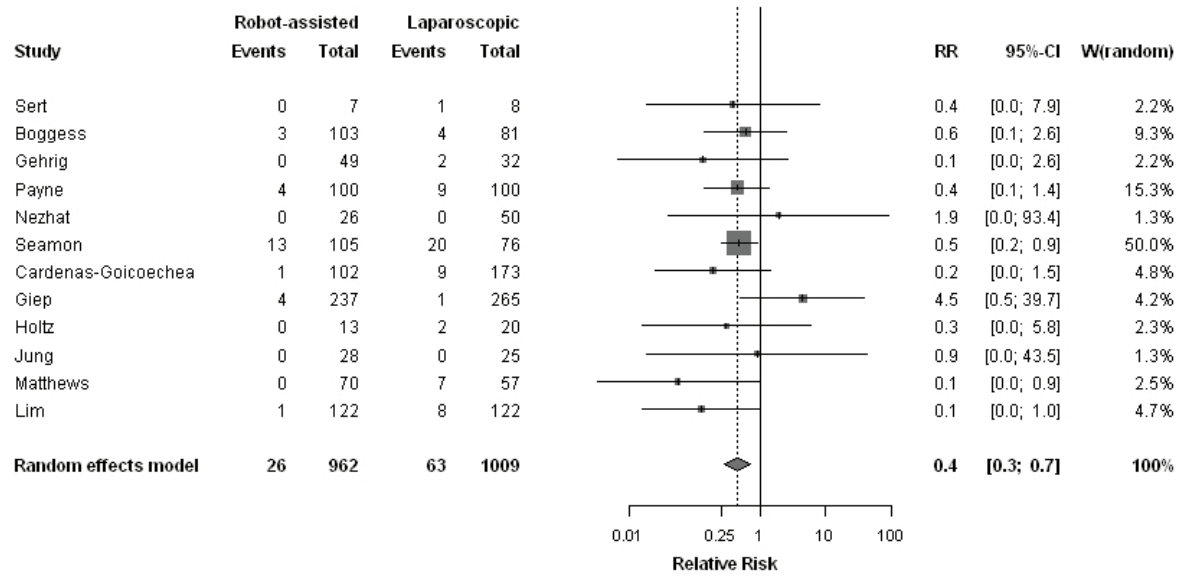


Rate of conversion to open surgery

Pooled data from 12 studies providing data on the rate of conversion to open surgery show that on average the risk of conversion is lower with robot-assisted hysterectomy (RR 0.44, 95% CI 0.28 to 0.69) compared to standard laparoscopic hysterectomy (Figure 3.34).

Insufficient data was available to perform a subgroup analysis of the rate of conversion to open surgery for different types of hysterectomy.

Figure 3.34 Relative risk of conversion to open surgery with robot-assisted versus laparoscopic hysterectomy



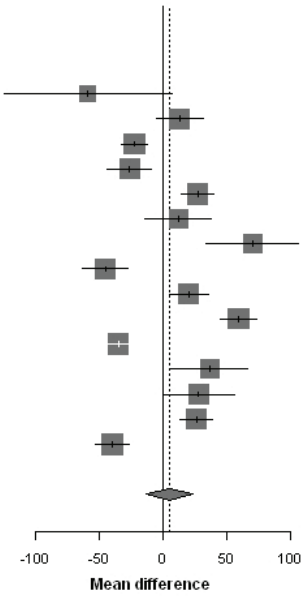
Operative time

Pooled analysis of 15 studies shows that a small increase in average operative time associated with robot-assisted surgery was not statistically significant (5 minutes longer; 95% CI: 14 minutes shorter to 24 minutes longer), (Figure 3.35). A high level of heterogeneity between the results of individual studies was observed (I^2 95.4%).

Insufficient data was available to perform a subgroup analysis of operative time for different types of hysterectomy.

Figure 3.35 Mean differences in average operative time with robot-assisted versus laparoscopic hysterectomy

	Robot-assisted			Laparoscopic					
Study	**Total**	**Mean**	**SD**	**Total**	**Mean**	**SD**	**MD**	**95%-CI**	**W(random)**
Sert	7	241.00	55.60	7	300.0	69.00	-59.0	[-124.6; 6.6]	3.9%
Bell	40	184.00	41.30	30	171.1	36.20	12.9	[-5.3; 31.1]	6.9%
Boggess	103	191.20	36.00	81	213.4	34.70	-22.2	[-32.5; -11.9]	7.3%
Gehrig	49	189.00	38.10	32	215.0	39.40	-26.0	[-43.3; -8.7]	7.0%
Payne	100	119.40	59.30	100	92.4	29.20	27.0	[14.0; 40.0]	7.2%
Estape	32	144.00	48.00	17	132.0	42.00	12.0	[-14.0; 38.0]	6.5%
Nezhat	26	276.00	79.20	50	206.0	70.50	70.0	[33.8; 106.2]	5.8%
Seamon	92	242.00	53.00	56	287.0	55.00	-45.0	[-63.0; -27.0]	7.0%
Shashoua	24	142.20	35.55	44	122.1	19.53	20.1	[4.8; 35.4]	7.1%
Cardenas-Goicoechea	102	237.00	57.00	173	178.0	58.90	59.0	[44.9; 73.1]	7.1%
Giep	237	89.90	37.50	265	124.8	48.70	-34.9	[-42.5; -27.3]	7.3%
Holtz	13	192.50	38.00	20	156.2	49.00	36.3	[6.5; 66.1]	6.2%
Jung	28	193.18	60.42	25	165.2	43.39	28.0	[-0.1; 56.1]	6.4%
Sarlos	40	108.90	36.10	40	82.9	21.20	26.0	[13.0; 39.0]	7.2%
Lim	122	147.20	48.20	122	186.8	59.80	-39.6	[-53.2; -26.0]	7.2%
Random effects model	**1015**			**1062**			**5.0**	**[-13.7; 23.6]**	**100%**



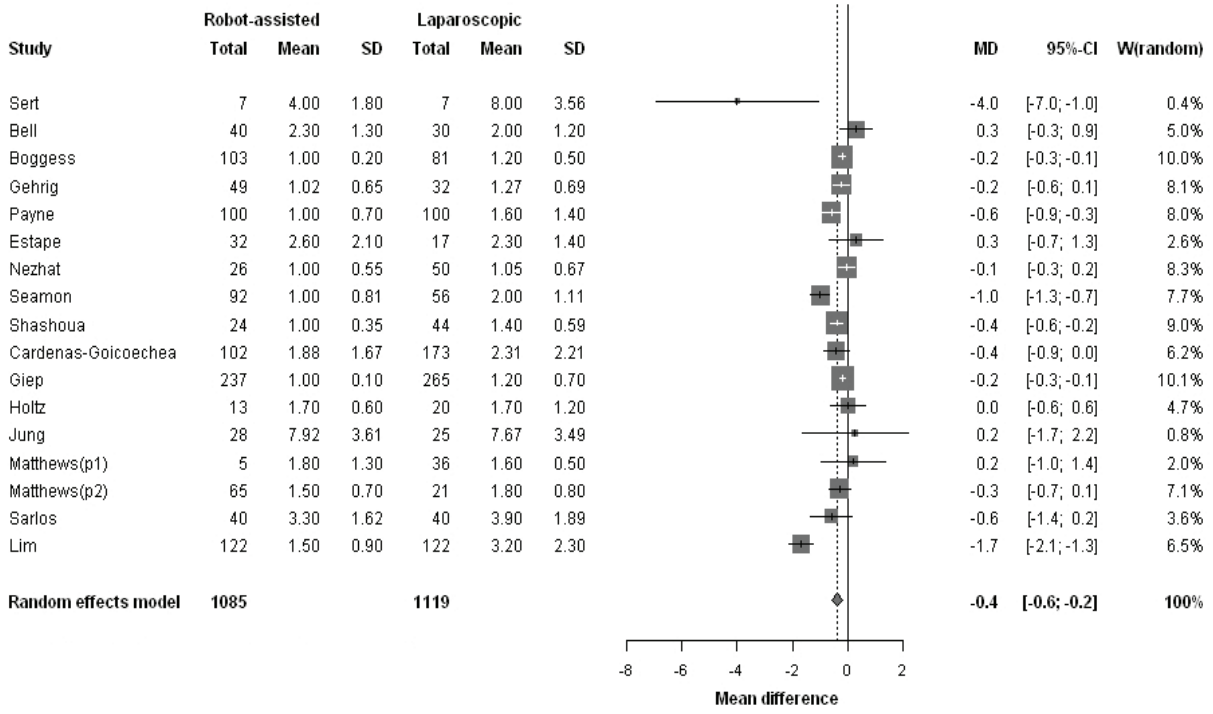
Length of hospital stay

Pooled results of 17 studies showed a small difference in the average length of hospital stay in favour of robot-assisted hysterectomy (0.4 days less; 95% CI: 0.6 to 0.2 days less) (Figure 3.36). A high level of heterogeneity between the results of individual studies was observed (I^2 90.9%).

A sub-group analysis was conducted that limited the pooled estimate of length of hospital stay to the three studies conducted outside the US. Results showed that the average length of stay in non-US studies was 4.9 days for robot-assisted hysterectomy and 6 days for laparoscopic hysterectomy. This resulted in a non-statistically significant reduction in length of stay of one day (95% CI: 2.8 days less to 0.7 days more) associated with robot-assisted hysterectomy. Similar analysis of two studies containing European-only length-of-stay data also failed to show a statistically significant difference (-2 days, 95% CI: -5.3 to +1.3 days).

Insufficient data was available to perform a subgroup analysis of length of stay for different types of hysterectomy.

Figure 3.36 Mean differences in average length of hospital stay with robot-assisted versus laparoscopic hysterectomy



Sensitivity analysis

Sensitivity analysis was carried out to investigate the change on the effect estimate of removing outliers for outcomes where these were identified. Removal of outliers for estimated blood loss,[83;89] hospital stay[70;79] and conversion rate[69] did not significantly alter the results of the meta-analysis for these outcomes. No evidence of publication bias was observed for any of the outcomes.

3.3.6 Summary

A meta-analysis was conducted comparing robot-assisted hysterectomy to both open hysterectomy and to standard laparoscopic hysterectomy. Study outcomes reported were limited to peri-operative complications and length of stay. The available data on specific clinical outcomes associated with hysterectomy were insufficient to perform meta-analysis of relevant outcomes in the treatment of individual conditions (e.g. uterine fibroids, etc.).

Robot-assisted hysterectomy is associated with a reduction in average estimated blood loss, a lower risk of transfusion or other peri-operative complications, shorter hospital stays and longer operating times than hysterectomy performed by open surgery. When compared to standard laparoscopic hysterectomy, the relative benefit for robot-assisted surgery is substantially reduced for each of these outcomes, while no significant difference in operating times was noted.

The results of this study are generally consistent with those from other recent HTA studies[8;18-20] and recently published reviews,[99;100] with robot-assisted surgery associated with decreases in estimated blood loss, length of stay and transfusion rates, but longer operating times compared to open hysterectomy. Three[8;19;20] out of four recent HTAs found a decrease in conversion rates associated with robotic surgery, while one reported no significant difference.[18] Overall, when compared to standard laparoscopic hysterectomy, results for the outcomes investigated are often either equivalent or tend to favour use of the robot-assisted approach.

These results need to be interpreted with caution due to the low quality of the evidence base at the time of this HTA, which is composed of prospective or retrospective observational studies with concurrent or historical controls, and the high level of heterogeneity observed for the outcomes that show the greatest difference between competing approaches (blood loss, operative time and hospital stay have I^2 values of between 90.9% and 98.8%).

3.4 Other urological indications

3.4.1 Nephrectomy

3.4.1.1 Description and epidemiology

Nephrectomy involves removal of a portion of the kidney containing a tumour or other anomaly (partial), removal of all of the kidney whilst sparing the adrenal gland (total) or removal of all of the kidney plus the adrenal gland (radical).[101] Partial and total nephrectomies are most commonly performed in patients diagnosed with clinically localised renal cancer, but are also performed in patients suffering from various benign conditions.[102] The role of robotic surgery in partial nephrectomy in particular has been highlighted as having the potential to overcome some of the technical challenges associated with laparoscopic partial nephrectomy[103] while preserving a minimally invasive approach.

Each year in Ireland, between 2005 and 2007, an average of 379 new cases of renal cancer were diagnosed.[104] In 2006, there were 193 deaths from renal cancer, accounting for 4.7% of all cancer related deaths.[104]

3.4.1.2 Summary of evidence

Seven identified studies concerning the clinical effectiveness of robot-assisted nephrectomy were identified. These include three recent HTAs [8;18;20] and four retrospective comparison studies that compared robot-assisted partial nephrectomy with laparoscopic partial nephrectomy.[102;105-107] A summary of the evidence from the studies is given below. Appendix 2 provides a more detailed comparison.

Data for a range of oncological and peri-operative outcomes as well as length of hospital stay were reported. Study details are provided in Appendix 2.

Operative time: Equivocal findings were obtained for studies that compared robot-assisted surgery to conventional laparoscopic or open surgery for either partial or radical nephrectomies; studies variably reporting shorter, longer or comparable operative times.

Length of hospital stay: For both partial and radical nephrectomies, length of hospital stay for robot-assisted surgery is comparable to, or shorter than that reported for laparoscopic or open surgery.

Estimated blood loss and transfusion rate: For both partial and radical nephrectomies, robot-assisted surgery is associated with comparable or reduced blood loss compared to laparoscopic or open surgery. Where reported, transfusion rates are comparable or lower for the robot-assisted approach.

Functional and oncological outcomes: Warm ischemic time

Robot-assisted partial nephrectomy is associated with comparable or reduced warm ischemic time to laparoscopic partial nephrectomy.

Complication rates: For both partial and radical nephrectomies, complication rates are comparable for robot-assisted surgery when compared to either laparoscopic or open surgery.

In summary, there is low quality evidence to support the use of robot-assisted nephrectomy, with evidence limited to non-randomised trials with concurrent or historical controls. Based on current evidence, it appears that both radical and partial nephrectomies may be safely performed with robot-assistance provided the surgeon has sufficient experience. While similar conclusions can be drawn for both procedures, the potential utility of using the device for partial nephrectomy may exceed that for radical nephrectomy, given the technical challenges and degree of precision involved. However, the available evidence at the time of this HTA did not confer any clear advantages compared to conventional laparoscopic or open surgical techniques for either procedure.

3.4.2 Radical cystectomy

3.4.2.1 Description and epidemiology

Cystectomy involves removal of all or part of the bladder in patients diagnosed with bladder cancer. Partial or segmental cystectomy removes part of the bladder; simple cystectomy removes the entire bladder; and radical cystectomy removes the bladder as well as other pelvic organs or structures.[108] Radical cystectomy remains the gold standard for treatment of patients with invasive bladder cancer;[109] bilateral pelvic lymphadenectomy is considered an integral part of this procedure.[110] The current standard approach to the removal of the bladder is via an open surgical procedure.[10] Laparoscopic cystectomy is a technically complex and demanding procedure[111] that is not currently being performed in Ireland, and is only offered in a limited number of centres in the US.[61]

Each year in Ireland between 2005 and 2007, an average 482 new cases of bladder cancer were diagnosed.[104] There were 188 deaths from bladder cancer in 2006, accounting for 4.6% of all cancer related deaths that year.[104]

3.4.2.2 Summary of evidence

Thirteen studies concerning the clinical effectiveness of robot-assisted radical cystectomy were identified. The studies included one RCT,[109] two HTAs,[8;20] four systematic reviews[110;112-114] and five individual studies.[115-119] A detailed summary of the studies retrieved is provided in Appendix 2.

Oncological outcomes and PSM rates: In the single RCT, no difference in lymph note yield was observed for robot-assisted compared to open radical cystectomy. No difference in PSM rates were observed for robot-assisted compared to laparoscopic and open radical cystectomy; there were difficulties in drawing conclusion due to differences in baseline population tumour grade between the study arms.

Operative time: Mean operative time for robot-assisted and open radical cystectomy varied considerably between studies. In the single RCT, a significant increase in operative time was observed for robot-assisted compared to open radical cystectomy. This was consistent with reports of increased operative time for robot-assisted compared to open radical cystectomy in the Grade III-2 and III-3 study reports. When compared to laparoscopic radical cystectomy, robot-assisted surgery was generally associated with shorter operative times.

Length of hospital stay: Mean duration of hospital stay varied considerably between studies for robot-assisted, laparoscopic and open radical cystectomy. Length of stay was generally shorter for robot-assisted versus open radical cystectomy, but was comparable to that of laparoscopic radical cystectomy.

Estimated blood loss and transfusion rate: Robot-assisted surgery is consistently associated with a significant reduction in mean estimated blood loss compared to open radical cystectomy or laparoscopic radical prostatectomy. This correlated with a reduction in observed transfusion rates for robot-assisted surgery compared to laparoscopic or open radical cystectomy.

Complication rates: No difference in complication rates was observed for robot-assisted surgery compared to open radical cystectomy.

In summary, there is limited evidence to support the use of robot-assistance for cystectomy procedures and the quality of this evidence is generally low. It appears that cystectomies may be safely performed with robot-assistance provided the surgeon has sufficient experience with the technique. However, robot-assisted surgery does not currently confer any clear advantages compared to conventional laparoscopic or open surgical techniques.

3.4.3 Pyeloplasty

3.4.3.1 Description and epidemiology

Pyeloplasty is the surgical reconstruction or revision of the renal pelvis to drain and decompress the kidney. Most commonly, the aim of pyeloplasty surgery is to relieve a uretero-pelvic junction obstruction(UPJO).[10] Open pyeloplasty remains the gold standard for management of UPJO.[120]

The number of kidney, ureter and major bladder procedures for non-neoplasm with or without catastrophic or severe complications in Ireland in 2009 was estimated as 1,017 (AR-DRG codes L04A to L04C).[121] This is an overestimate of the number of pyeloplasty procedures as it includes all kidney, ureter and major bladder procedures.

3.4.3.2 Summary of evidence

Three studies were selected for inclusion: two HTAs [8;20] and one systematic review.[120] Collectively, data from 15 different non-randomised trials with prospective or historical controls was included. A detailed summary of the studies retrieved is provided in Appendix 2.

Operative time: Equivocal findings were obtained for robot-assisted compared to conventional laparoscopic pyeloplasty; studies variably reporting shorter longer or comparable operative times.

Length of hospital stay: Limited data suggest that robot-assisted surgery is associated with comparable or reduced (WMD: -0.5 d; 95% CI: -0.6– -0.4; $p < 0.01$) hospital stay compared to conventional laparoscopic pyeloplasty.

Estimated blood loss: Limited data from two non-randomised trials suggest no difference in estimated blood loss between robot-assisted and conventional laparoscopic pyeloplasty.

Complication rates: Limited data suggest no difference in complication rates between robot-assisted and conventional laparoscopic pyeloplasty.

In summary, there is limited, low-quality evidence to suggest that comparable outcomes to open and laparoscopic pyeloplasty may be obtained with robot-assisted surgery.

3.4.4 Miscellaneous indications in urology surgery

3.4.4.1 Summary of evidence

Two studies relating to clinical effectiveness of robot-assisted surgery for miscellaneous indications in urology surgery were identified: one HTA [8] and a study comparing robot-assisted and conventional varicocelectomy.[122] The HTA listed two vasovaotomy, two inguinal herniorrhaphy, two adrenalectomy, four prolapse, one bladder diverticulectomy and one ureteral-re-implantation study. See Appendix 2 for more details.

There is limited, low-quality evidence indicating that robot-assisted surgery has been successfully used for a diverse range of miscellaneous urological indications. However, there is currently no evidence to suggest that it is superior to conventional surgical techniques.

3.5 Other gynaecological indications

3.5.1 Myomectomy

3.5.1.1 Description and epidemiology

Myomas are the most common tumour in women of reproductive age.[123] Myomectomy is the surgery to remove this tumour from the muscular wall of the uterus.

The number of endoscopic and laparoscopic procedures in Ireland for the female reproductive system in 2009 was estimated as 2,905 (AR-DRG code N08Z). There was an estimated additional 152 open procedures of the female reproductive system (AR-DRG N11Z) in that year. These numbers overestimate the number of myomectomy procedures as they include all procedures on the female reproductive system.[121]

3.5.1.2 Summary of evidence

Four studies were selected for inclusion: two HTAs [8;20] and two individual studies.[123;124] Collectively, data from 7 different non-randomised trials with prospective or historical controls was included. A detailed summary of the studies retrieved is provided in Appendix 2.

Operative time: Robot-assisted surgery is associated with longer operative time than for either conventional laparoscopic or open myomectomy procedures.

Length of hospital stay: Robot-assisted surgery is associated with a shorter length of stay than open myomectomy and with a comparable or shorter duration of stay than conventional laparoscopic surgery.

Estimated blood loss and transfusion rate:
Robot-assisted surgery is associated with a lower estimated blood loss compared to open myomectomy.

In summary, the evidence to support the use of robot-assistance for myomectomy procedures is limited and of low quality. Currently there is little evidence to support a claim that robot-assisted surgery for myomectomy is associated with superior clinical outcomes compared to conventional surgical techniques.

3.5.2 Tubal re-anastomosis

3.5.2.1 Description and epidemiology

Tubal re-anastomosis is a fertility restoring intervention. It is a procedure that involves microsurgical techniques to open and reconnect the fallopian tube segments that remain after a tubal ligation procedure. The laparoscopic approach has been hindered by the learning curve associated with precise intracorporeal suturing.[125]

As noted, there were 2,905 estimated endoscopic and laparoscopic procedures and 152 open procedures of the female reproductive system in Ireland in 2009. These numbers would include any tubal-anastomosis procedures that were performed.[121]

3.5.2.2 Summary of evidence

Three studies were selected for inclusion: two HTAs [8;20] and one individual study. [125] Collectively, the studies included data from six original non-randomised trials with prospective or historical controls. A summary of the studies is provided in Appendix 2.

Operative time: Robot-assisted surgery is associated with longer operative times compared to open tubal re-anastomosis.

Length of hospital stay: Robot-assisted surgery is associated with shorter hospital stays compared to open tubal re-anastomosis.[20;125]

Complication rates: Limited short-term post-operative follow-up indicate that robot-assisted surgery is associated with lower post-operative pregnancy rates and a higher rate of abnormal pregnancies.[125]

In summary, there is limited low quality evidence to support the use of robot-assisted tubal re-anastomosis compared to conventional surgical techniques. Robot-assisted surgery appears feasible with comparable, but not necessarily superior outcomes to conventional surgery.

3.5.3 Prolapse surgery (sacrocolpopexy)

3.5.3.1 Description and epidemiology

Vaginal vault prolapse occurs when the supporting structures for the vagina become weakened and it slips down from its normal position. Weakness of the supporting structures may be due to a hysterectomy, aging, changes in hormone levels and vaginal childbirth.[126] Surgical options include abdominal and vaginal sacrocolpopexy.[8]

In 2009 in Ireland, an estimated 1,410 prolapse repair procedures of the uterus, pelvic floor or enterocele (small bowel prolapse) were conducted (procedure block 1283); this overestimates the number of sacrocolpopexy procedures.[121]

3.5.3.2 Summary of evidence

Two HTAs [8;20] were selected for inclusion. A summary of the studies is provided in Appendix 2.

Operative time: The findings of a non-randomised cohort study[20] indicate that robot-assisted surgery is associated with a significant increase in operative time compared to open sacrocolpopexy.

Length of hospital stay: Based on a single non-randomised cohort study, robot-assisted surgery is associated with a shorter duration of hospital stay than open sacrocolpopexy.[20]

Estimated blood loss: Based on a single non-randomised cohort study, robot-assisted surgery is associated with a lower estimated blood loss than open sacrocolpopexy.[20]

Complication rates: There is no strong evidence regarding the difference in complication rates between robot-assisted and open sacrocolpopexy. In the one study identified, robot-assisted surgery appears to be associated with increased complications compared to open sacrocolpopexy, but the evidence for this is of poor quality and was not statistically analysed in the study.[20]

In summary, there is limited evidence to support the role of robot-assisted sacrocolpopexy compared to open sacrocolpopexy surgery. Early evidence suggests that the technique has comparable safety and efficacy and similar functional outcomes to conventional surgical techniques.

3.5.4 Miscellaneous indications in gynaecology surgery

3.5.4.1 Description and epidemiology

Uterine and adnexa procedures are commonly conducted in Ireland. In 2009, there was an estimated 4,514 (AR-DRG code N12A, N12B and N07Z) procedures. This overestimates numbers for adnexal mass as it also includes uterine procedures. Surgical procedures for endometriosis are included in data for endoscopic, laparoscopic and open procedures for the female reproductive system. In 2009, an estimated 2,905 (AR-DRG code N08Z) endoscopic and laparoscopic and 152 (AR-DRG N11Z) procedures were carried out. [121]

3.5.4.2 Summary of evidence

Three studies were identified describing surgery for locally advanced cervical cancer[127], endometriosis[128] and adnexal mass.[129] A detailed summary of the studies is provided in Appendix 2.

There is a limited and low quality evidence base for these various indications. Consistent with other indications, robot-assisted surgery may be associated with longer operative times, shorter hospital stay and comparable complication rates to conventional surgery. No firm conclusions can be drawn given the limited evidence and the variability in how outcomes are assessed and reported.

3.6 Cardiac Surgery

3.6.1 Description and epidemiology

Robot-assisted surgery has been assessed in the following cardiac interventions: mitral valve repair (MVR), coronary artery bypass grafting (CABG) and epicardial lead placement.

CABG surgery is a major surgical procedure that is commonly used to reduce the morbidity and mortality associated with coronary artery disease with bypasses for narrowed and blocked coronary arteries created during the procedure.[10;130] Robot-assisted minimally invasive CABG (mini-CABG) has been used as an alternative to conventional open CABG. In 2009, an estimated 2,018 CABG procedures (procedure block 0672-0679) were performed in Ireland.[121]

Cardiac surgery involving mitral valve replacement or repair is used in the management of mitral valve disease arising from stenosis or regurgitation of the mitral valve. Mitral valve repair is generally preferred to mitral valve replacement due to improved longevity and durability of repaired versus replaced valves and a simplified or reduced post-surgical pharmaceutical management. Mitral valve repairs are considered to be more technically challenging than mitral valve replacements, so they are only performed approximately 50% of the time.[10] In 2009, an estimated 477 cardiac valve procedures (AR-DRG codes F03A to F04B) were conducted in Ireland. This number likely overestimates mitral valve surgery as it includes all cardiac valve procedures.[121]

3.6.2 Summary of evidence

Seven study reports were selected for inclusion: three HTAs [8;18;20], one rapid response report,[131] and three individual studies.[132-134] Collectively, these include data from 23 different observational studies. A detailed summary of the studies retrieved is provided in Appendix 2.

Operative time: Robot-assisted CABG and mitral valve repairs are associated with longer operative times than their conventional open surgical equivalents.

Length of hospital stay: Robot-assisted minimally invasive CABG and mitral valve repairs are associated with shorter overall hospital stays compared to conventional open surgery. Data also suggest that robot-assisted CABG is associated with shorter intubation times and shorter intensive care unit (ICU) stays compared to conventional surgery. A similar reduction in the length of ICU stays is suggested for robot-assisted mitral valve repair compared to conventional surgery.[18;20;131-134]

Estimated blood loss and transfusion rate: Robot-assisted CABG is associated with lower transfusion requirements than conventional surgery.[131;133]

There is no difference in estimated blood loss or transfusion rates for robot-assisted versus conventional mitral valve repair.[20]

Complication rates: Rates of complications appear lower for robot-assisted CABG compared to conventional CABG.[131;133] The findings for robot-assisted mitral valve repair are indeterminate [20;132;134].

In summary, there is limited, low quality data to support a potential role of robot-assistance for a range of cardiac procedures. Interpretation of the available data is complicated by the considerable variability in study comparators and by the heterogeneity within study groups. Robot-assisted minimally invasive techniques may provide a promising alterative to current techniques for a range of surgical procedures. Outcomes are highly dependent on the specific technique and surgeon skill. Further research, including RCTs are required to inform the precise role and patient selection criteria for the various robot-assisted minimally invasive cardiac procedures.

3.7 Head and Neck Surgery

3.7.1 Description and epidemiology

Robot-assisted surgery has been assessed in the following head and neck disease interventions: thyroidectomy and oropharyngeal carcinoma procedures. Thyroidectomy is the surgical removal of part or all of the thyroid gland. Oropharyngeal carcinoma is the occurrence of malignant cells in the tissue of the oropharynx which may require surgery for its removal.

Between 2005 and 2007, the average annual number of head and neck cancers diagnosed in Ireland was 287.[104] There were an estimated 140 deaths from head and neck cancer in 2006, accounting for 3.3% of all cancer-related deaths.[104]

3.7.2 Summary of evidence

Three studies were selected for inclusion; two assessed robot-assisted thyroidectomy (RT) versus conventional thyroidectomy (CT)[135;136] and the third study assessed surgery for oropharyngeal carcinoma[137] (see Appendix 2).

Operative time (thyroidectomy only): Robot-assisted surgery is associated with longer operative time compared to conventional surgery.

Length of hospital stay (oropharyngeal carcinoma only): Robot-assisted endoscopic surgery is associated with shorter length of hospital stay for primary neoplasms compared to open surgery.

In summary, there is a very limited, low quality evidence base to support the use of robot-assisted surgery in preference to conventional surgical techniques for a number of diseases of the head and neck. Findings from these studies are consistent with general findings for robot-assisted surgery for a range of surgical procedures, that is, an increase in operative time and a reduction in the length of hospital stay. However, given the paucity of the data, no firm conclusions can be drawn.

3.8 Device-related issues

The safety profile of robot-assisted surgery for particular indications has been documented by analysis of the clinical outcomes associated with its use, including the rate and type of complications reported.[138;139] The results of a meta-analysis carried out for the two major indications of robot-assisted surgery (prostatectomy and hysterectomy) are described above (Sections 3.2 and 3.3 respectively) and form the basis of any assessment of the safety profile of robot-assisted surgery. In addition to this, a review of adverse events associated with the use of robot-assisted surgical systems is provided in order to highlight any risks specific to the device itself.

3.8.1 Surgeon ergonomics

Minimally invasive laparoscopic surgery was developed with the aim of reducing operative trauma to the patient in order to decrease pain and shorten post-operative recovery times compared to open surgery.[140] Traditional laparoscopy has, however, had certain limitations associated with its use that have prevented its widespread adoption. These included greater technical demands and a protracted learning curve for the surgeon. [63] Robot-assisted laparoscopic surgery attempts to overcome some of these limitations while retaining the benefits of a minimally invasive approach. Specific improvements associated with robot-assisted surgery include better visualisation through the use of three-dimensional magnification, availability of tools with seven degrees of freedom that mimic hand movements along with improved ergonomics and more intuitive hand-eye coordination when controlling surgical instruments.[5;63;141] However, this has been achieved at the cost of haptic and tactile feedback, as a result of the instruments being indirectly manipulated by the surgeon.[142]

Given the considerable differences that exist between conventional laparoscopic and robot-assisted surgery, it is pertinent to consider the implications that introduction of robot-assisted surgery has for surgeons using the device. Increases in fatigue, discomfort and morbidity associated with the use of traditional laparoscopic instruments are documented in published literature,[2-6] and include neck, shoulder and hand problems related to strain caused by long periods spent in an uncomfortable stance.

The ergonomics of laparoscopic instrument use result in difficult working angles for instruments and camera, requiring the surgeon to maintain a static head and neck position, along with shoulder strain, excessive wrist supination, and flexion and ulnar deviations that decrease transmission of force to the instrument handle.[3] Robot-assisted surgery differs from traditional laparoscopic surgery as the surgeon is in a seated position at the computer console and the movement of the instruments is coordinated using hand-operated controls with the elbows supported. A 2010 review[5] reported that improved ergonomics was the main advantage robot-assisted surgery had over traditional laparoscopic surgery and that this facilitated a shorter learning curve for surgeons. This is supported in an earlier consensus document[7] on robot-assisted surgery prepared by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the Minimally Invasive Robotic Association (MIRA), which states the following in regard to the ergonomics of the device:

> '*Both open and laparoscopic surgical procedures may be physically strenuous and have been associated with surgeon morbidity from repetitive use injury. Because the robotic surgeon sits comfortably in an ergonomically designed workstation, the performance of robotically controlled procedures generally is more ergonomic for the operating surgeon. However, this benefit may not apply to the patient-side assistant. Such ergonomic differences will be magnified for lengthier procedures.*'[7]

There is limited primary data available in regard to the effect of using the robotic device on surgeon morbidity and discomfort. A study[143] into the differences between musculoskeletal discomfort and ergonomic strain in laparoscopic versus robotic surgery for Roux-en-Y gastric bypass surgery found that robotic cases were associated with more discomfort in the neck, while laparoscopic cases were associated with greater discomfort in the upper back and in both shoulders. Analysis of ergonomic positioning during the procedures in the same study found that laparoscopic surgery was associated with poorer ergonomic positioning of the upper arm, lower arm, wrist and wrist twist, while robot-assisted surgery scored lower for trunk positioning. However, the ability to generalise based on studies in specific indications is limited, as the advantage of robotic-assisted surgery significantly depends on the type of the procedure.[5]

3.8.2 Device failure

Murphy et al.[139] summarises data on the incidence of device failure in prostatectomy, the highest volume indication for robot-assisted surgery at the time of this HTA.[144] Device failure rates reported in the literature range from 0.4% (34/8240) in a multi-institutional study[145] to 0.2-2.6% in some smaller studies.[146;147] This paper also identified two reports that reviewed data up to 2007 from the US FDA MAUDE database of reports of adverse events involving medical devices. One study estimated a device failure rate of 0.38% based on 168 malfunctions reported between 2000 and 2007.[148] Of the 38 system failures and 78 adverse events identified in a review of the data between May 2006 and April 2007,[149] most adverse events were related to broken instrument tips or failure of electrocautery elements of surgical instruments. Out of 38 unrecoverable system faults, 32 procedures were converted to open surgery. The authors of the review[139] make the point that this is a reflection on the general lack of experience in conventional laparoscopic radical prostatectomy in the US, and state that 'although device failure is rare, the increasing penetration of robot-assisted surgery into training programmes may lead to less availability of open radical prostatectomy (ORP) and LRP skills to deal with the consequences of such failure in the future'.

The reported rate of failure leading to conversion to open or laparoscopic surgery in papers published after the review by Murphy et al.[139] ranges from 0.6%[150] to 0.17%.[151] Nayyar et al.[150] reported 37 machine- or instrument-related errors during the course of 340 consecutive robot-assisted urological operations at one centre using one robotic machine (37/340; 10.9%). The overall conversions rate attributable to mechanical failures of the robot was 0.6% (2/340). The most frequent technical problems were related to robotic instruments (23/37). Kim et al.[151] reported 43 cases (2.4%) of mechanical failure with the device from a total of 1,797 robotic surgeries, including 24 (1.3%) cases of mechanical failure or malfunction and 19 cases (1.1%) of instrument malfunction. One open and two laparoscopic conversions (three cases; 0.17%) were performed.

A review of the MAUDE database for the period April 2007 to March 2011 was undertaken to estimate the number of device failures related to the da Vinci® surgical system. The search retrieved 25 reports between 1 April 2007 and 1 March 2011. Of the 25 malfunctions, most device failures were related to broken instrument tips, foot pedals not working, failure of electrocautery elements of surgical instruments (e.g. smoke emitting, working intermittently) and camera issues. As a consequence of the device failures, 4 of the 25 procedures were converted to open surgery.

In summary, reports of device failure rate relating to mechanical failures or instrument failure range from 0.17% to 10.9%. The majority of these events related to broken instrument tips or failure of electrocautery elements of surgical instruments. As a consequence, unrecoverable device failure can result in conversion to open surgery in a limited number of cases.

3.9 Conclusion

A review and comparison of robot-assisted laparoscopic surgery with conventional laparoscopic and open surgery was completed for a range of indications for surgery due to urological, gynaecological, cardiac diseases as well as diseases of the head and neck. Studies were identified by updating the searches completed in 2010 and 2008 as part of, respectively, the CADTH[18] and KCE[8] health technology assessments of robot-assisted surgery.

In summary, most studies conclude that robot-assisted surgery is feasible and technically safe with acceptable early operative outcomes that appear to be comparable to those achieved with open or laparoscopic surgery. The main clinical outcomes reported were operative time, length of hospital stay and estimated blood loss. Operative time can be affected by the surgeon experience (learning curve), the patient baseline characteristics and the type of surgery undertaken. However, in general, operation time was reported as longer for robot-assisted surgery compared to open and conventional laparoscopic surgery. Length of hospital stay can be influenced by a range of factors including surgeon preference, surgical complications, social circumstances and study location. Length of hospital stay for robot-assisted surgery was generally reported as being comparable to that of conventional laparoscopic surgery and shorter than for open surgery. Finally, estimated blood loss and transfusion rate were generally reported as being lower for robot-assisted surgery compared to open surgery. This appears due to the minimally invasive nature of robot-assisted surgery, but may also be impacted by the better 3D visualisation with the robot-assisted approach, which may facilitate better surgical precision.

Robot-assisted surgery is claimed in many studies to be less demanding for the surgeon, and in particular compared to conventional laparoscopic surgery. It is proposed as an option that will facilitate certain minimally invasive procedures that are otherwise difficult to perform. Clinical outcomes are, however, influenced by, and improve with increasing surgeon experience.[12]

It should be noted that study quality was generally poor with only two randomised controlled trials out of the more than 130 studies reviewed. The remaining studies were non-randomised cohort studies with prospective or retrospective controls. Patient study numbers in the robot-assisted arms tended to be small. Variable comparators were used within the studies; clinical outcomes were inconsistently defined and reported and there was evidence of intra- and inter-study heterogeneity in terms of patient characteristics. Long-term outcome data is generally lacking. These issues should be taken into account when considering the effectiveness and safety of robot-assisted procedures.

Key messages:

- The quality of the evidence to support the clinical effectiveness of robot-assisted surgery compared to either open or conventional laparoscopic surgery is poor, with a high level of heterogeneity between the results of different studies for some outcomes. These limitations must be considered when interpreting the results of the meta-analysis and the review of clinical evidence.
- Robot-assisted radical prostatectomy is associated with comparable (pT3) or better (pT2) oncological outcomes, superior functional and peri-operative outcomes, longer operative time and shorter hospital stays compared to open radical prostatectomy.
- Comparable results were observed for robot-assisted and conventional laparoscopic prostatectomy for most outcomes, with minor improvements in post-operative urinary continence and duration of hospital stay noted for the robot-assisted approach.
- Robot-assisted hysterectomy is associated with a reduction in estimated blood loss, lower risk of transfusion or complications, shorter hospital stays and longer operative times than hysterectomy performed by open surgery.
- Compared to conventional laparoscopic hysterectomy, the difference in the reported results for each of these outcomes is substantially reduced, with no significant difference in operating times.
- Unlike prostatectomy, there is an absence of data on functional or, where applicable, oncological outcomes for robot-assisted hysterectomy.
- Evidence to support the use of robot-assistance for a range of other urology, gynaecology, cardiac and head and neck procedures is limited in quantity and quality. It appears that robot-assisted surgery is safe and feasible for a range of such indications and may provide comparable, but not necessarily superior outcomes to conventional surgical techniques. Additional, higher quality research is required.
- There is general consensus that robot-assisted surgery is more ergonomic than laparoscopic surgery for the operating surgeon. However this benefit may not apply to the rest of the surgical team, including the assisting surgeon.
- Mechanical or instrument failure can arise during robot-assisted surgery, which if unrecoverable, can necessitate conversion of the procedure to open surgery in up to 0.6% of cases.

4. Economic evaluation

4.1 Introduction

As determined in the review of clinical effectiveness, robot-assisted prostatectomy and hysterectomy are associated with longer operative time, reduced blood transfusion and shorter hospital stays when compared to the open surgery equivalent. Robot-assisted radical prostatectomy is also associated with superior functional and comparable or better oncological outcomes. There is no evidence of improved functional outcomes for robot-assisted hysterectomy when compared to either open or conventional laparoscopic hysterectomy. Evidence to support the use of robot-assistance for a range of other urology, gynaecology, cardiac and head and neck procedures is limited in quantity and quality. Limiting the economic analysis to robot-assisted prostatectomy and hysterectomy is therefore justified on the grounds of the available evidence.

The purpose of this section is to:

- provide background on economic evaluation in HTA
- examine previously published economic analyses of robot-assisted surgeries for prostatectomy and hysterectomy
- develop an economic model for robot-assisted prostatectomy and hysterectomy in Ireland
- evaluate the budget impact of robot-assisted surgery in Ireland.

The layout of the remainder of this chapter is:

- Section 4.2 – background to economic evaluation
- Section 4.3 – review of economic analyses of robot-assisted prostatectomy and hysterectomy procedures
- Section 4.4 – description of the economic model
- Section 4.5 – definition of the model parameters
- Section 4.6 – results of the economic analyses
- Section 4.7 – limitations of the economic model
- Section 4.8 – summary of results.

4.2 Background – economic evaluation

Economic evaluation in HTA involves the comparative analysis of alternative courses of action. In this study the additional costs and, in the case of prostatectomy, health benefits associated with robot-assisted surgery in Ireland are being compared with the usual standard of care (that is a combination of conventional open and laparoscopic surgery). For prostatectomy the health benefits of robot-assisted surgery are defined as the impact of the technology on the quantity and quality of patient life, measured as the gain in quality-adjusted life years (QALYs).

When comparing two or more technologies, the question that arises is: what is the additional cost involved for the additional benefit achieved? To answer this question, the incremental cost-effectiveness of the technology compared to the alternative is calculated, with the results presented as an incremental cost-effectiveness ratio (ICER).[152] The ICER of A (robot-assisted surgery) compared to B (conventional surgical techniques) can be calculated as follows:

$$ICER = \frac{(Cost_A - Cost_B)}{(Effect_A - Effect_B)}$$

One of the implications of making comparisons between the cost-effectiveness of different technologies is that there is a threshold ratio above which a technology may not be considered cost-effective. If a technology has an ICER that is significantly higher than that of other healthcare technologies that are reimbursed, other factors such as the innovative nature of the technology or the wider costs and benefits to patients and society may be taken into consideration.[153] There is no specified ICER below which a health technology will be adopted. Economic evaluations of other interventions in an Irish setting which have been adopted following a determination that they were cost-effective include: population-based colorectal cancer screening (€1,696/QALY);[154] Human Papillomavirus vaccination programme at €17,383/life year gained (LYG);[155] universal infant pneumococcal conjugate vaccination at €5,997/LYG;[156] and of universal infant hepatitis B vaccination at €37,018/LYG.[157]

A separate form of economic analysis, a cost-minimisation analysis may be undertaken where alternative technologies are compared only in terms of their costs because their outcomes (effectiveness and safety) may be considered to be identical.

The types of evaluation used in this study are described in Section 4.4.4.

4.3 Review of published evaluations

A review of economic evaluation studies comparing robot-assisted surgery to either open or conventional laparoscopic surgery was undertaken. As only prostatectomy and hysterectomy are being considered for economic evaluation, the review was restricted to studies of these procedures.

A systematic review approach was taken to identify suitable studies as outlined in Chapter 2. The review used the data gathered in the HTA by the Canadian Agency for Drugs and Technologies in Health (CADTH)[18] and it updated the search to January 2011. Detailed descriptions of the literature search terms, inclusion and exclusion criteria, data extraction methods and study characteristics are provided in Appendix 4. A summary of the findings are presented in the following two sections while a full review is contained in Appendix 4.

4.3.1 Prostatectomy

A total of 12 economic evaluations were reviewed.[158-167] The studies were published between 2004 and 2011 with nine from the US[158-161;163;165-168] and one each from Australia,[164] Denmark[169] and the UK.[162] Of the 12 studies, two were cost-utility analyses[164;169], one a net-profit analysis[167] and the remainder were cost-minimisation analyses. One study compared only robot-assisted and laparoscopic surgery[167] with the remaining studies compared robot-assisted surgery to open surgery with four also including a comparison to standard laparoscopic surgery.[158;160-162] Three of the studies were published in abstract form only.[160;162;168] As abstracts typically have highly restricted word counts, they tend to evaluate as poor quality due to the limited information provided.

The evaluations were a mix of those conducted using costs derived from retrospective review of hospital records and those that applied a combination of costs derived from literature review and empirical data. A number of the studies either explicitly did not include the capital cost of the robot or else failed to specify if it was included, in which case it was assumed it was not.[159;160;162;163;165;168] Typically only direct costs were included although some studies also provided data on indirect costs relating to time to return to work.[164;169]

All but two of the evaluations concluded that robot-assisted surgery was more costly than open surgery. Of the two that found robot-assisted surgery to have a lower cost, neither included the cost of the robot and the incremental costs were found to be US$657 and US$1,740 lower, respectively.[163;165] In these two studies it is likely that the inclusion of the cost of the robot would have resulted in robot-assisted surgery being considered more costly than open surgery.

In studies reporting a higher incremental cost for robot-assisted surgery, the magnitude of the difference varied widely ranging from US$195(166) to US$7,797[159] per case. In the latter extreme, the large additional cost was due to open and robot-assisted cases having a comparable length of stay in the analysis.[159]

Of the two cost-utility analyses from Australia and Denmark, ICERs of AUS$24,457 per QALY[164] and the other €64,343 per QALY[169] were reported, respectively. The latter study calculated QALYs for patients who had successful treatment defined as urinary continence, erectile function and no residual cancer. This definition may be interpreted as overly restrictive and reducing the potential to observe differences between surgery types. Furthermore, the authors observed no difference in post-operative erectile function between their open and robot-assisted cohorts.

In summary there is broad agreement in the economic evaluations that, when the capital cost of the robot is taken into account, robot-assisted surgery is more costly per case than open surgery. However, the magnitude of the difference in costs is unclear.

4.3.2 Hysterectomy

Six studies were identified comparing the costs of robot-assisted and laparoscopic surgery.[73;75;83;170-172] The four US and two Swiss studies were published between 2008 and 2010. Two of the six studies were published as abstracts.[171;172]

All six studies were cost-minimisation analyses and contained a comparison of robot-assisted and standard laparoscopic surgery. Only three contained a comparison between robot-assisted and open surgery.[75;170;172] Two of the six studies explicitly included the cost of the robot in the analysis.[75;170]

All six studies found robot-assisted surgery to be more expensive than standard laparoscopic surgery. The additional cost per case for robot-assisted surgery compared to laparoscopic surgery ranges from US$438[75] to US$9,322.[172] In the comparison of robot-assisted to open surgery, two studies[170;172] reported a higher incremental cost and one study found robot-assisted surgery to be less expensive.[75] In that study, the lower cost of robot-assisted surgery relative to open surgery was explained by reductions in laboratory and hospital room and board costs. A higher daily room and board cost was applied to open surgery than to robot-assisted surgery which partly explains the lower cost for robot-assisted surgery.

In summary, there are a limited number of comparisons of robot-assisted and open surgery and the results are inconsistent. The comparison of robot-assisted and standard laparoscopic surgery is more common and shows the latter to be less expensive.

4.4 Description of the economic model

Economic modelling facilitates the combination of data on costs and benefits from different sources and allows these to be extrapolated into the future. The introduction of robot-assisted surgery into the publicly-funded system would incur ongoing running costs, while any benefits (e.g. QALYs) may extend over many years. Modelling allows the short-term nature of some costs to be offset against the long-term nature of any health benefits in the economic evaluation.

The budget impact analysis (BIA) provides a means to predict the potential financial impact of introducing a new technology into a healthcare system. Whereas an economic evaluation addresses the additional health benefit gained from investment in a technology, BIA addresses the affordability of the technology (e.g. the net annual financial cost of adopting the technology for a finite number of years).[173]

In this section, three economic models are presented based on the types of surgery for which the robot could be used:

- Model 1 – prostatectomy only.
- Model 2 – hysterectomy only.
- Model 3 – a combination of hysterectomy and prostatectomy.

4.4.1 Study question

Three questions are addressed in this study. Compared to the current mix of open and conventional laparoscopic surgery:

- What is the impact on costs and outcomes of introducing robot-assisted laparoscopic prostatectomy?
- What is the impact on costs of introducing robot-assisted laparoscopic hysterectomy?
- What is the impact on costs of introducing a combination of robot-assisted laparoscopic prostatectomy and hysterectomy?

4.4.2 Technology

The technology being assessed is robot-assisted laparoscopic surgery using the da Vinci S 4-arm System with HD Vision®. The economic models are based on the purchase of a single robot.

4.4.3 Comparators

Robot-assisted surgery is compared to routine care for prostatectomy and hysterectomy which comprises a mix of open and conventional laparoscopic surgery.

4.4.4 Type of evaluation

The preferred economic evaluation type for HTA in Ireland is a cost-utility analysis (CUA) with the outcomes expressed in terms of quality-adjusted life years (QALYs). A cost-minimisation analysis may be conducted where there is empirical evidence that there is no meaningful difference in terms of important patient outcomes between the technologies being compared.[153]

The systematic review of the clinical effectiveness of robot assisted prostatectomy (Chapter 3) showed that there were statistically significant differences in utility outcomes and positive surgical margins when compared to open surgery. For this reason a cost-utility analysis was applied for Model 1 in the evaluation of prostatectomy alone.

For hysterectomy, the systematic review indicated that the only differences were in operative parameters and that there was no demonstrable difference in patient outcomes. Thus, in Model 2 for hysterectomy when considered alone, a cost minimisation model was applied.

A cost minimisation model was also used for the combination of hysterectomy and prostatectomy. In the combined model (Model 3), the majority of operations will be hysterectomy, for which no difference in clinical effectiveness has been reported.

4.4.5 Study perspective

Costs are assessed from the perspective of the publicly-funded health and social care system in Ireland. Only direct medical costs (i.e. fixed and variable medical costs associated with the provision of a technology) are included. In the case of Model 1, all health benefits accruing to individuals are included in the assessment of outcomes. Indirect costs (such as decreased productivity due to disease or death) associated with robot-assisted laparoscopic surgery are excluded from the evaluation. Adoption of this perspective is consistent with national guidelines.[153]

4.4.6 Outline of the model structure

For all three models a patient cohort is modelled for each year of the robot lifespan. The cohort is characterised by the age and, in the case of prostatectomy, the pathological stage and life expectancy, of each patient. For both the current standard of care and for robot-assisted surgery, each patient is given operative characteristics (e.g., operative time, length of stay, number of units transfused). In Model 1 (cost-utility analysis of prostatectomy only) the outcomes for sexual function, urinary function and positive surgical margin are also simulated along with the implications for further treatment (i.e. continence pads, PDE5 inhibitors, adjuvant radiotherapy). The operative characteristics and outcomes are used to compute the total incremental cost of robot-assisted surgery for the cohort.

The process of modelling cohorts over the robot lifespan generates the data to compute the average incremental cost for a single simulation. The key model parameters are expressed as distributions rather than point estimates to account for the uncertainty around their values. The modelling process is repeated 10,000 times for each model to capture the effect of variation in the model parameters.

4.4.7 Sensitivity analysis

In an economic analysis, the use of a probabilistic sensitivity analysis is recommended to determine the impact of varying the values of key parameters within plausible ranges. As the structure of the economic models presented here is inherently stochastic, the outputs are equivalent to a multivariate probabilistic sensitivity analysis.

A univariate sensitivity analysis shows how influential each parameter is and how sensitive the results are to fluctuations in each parameter. Given the uncertainty around the parameters themselves, it is important to understand how this translates into uncertainty about the results. Each parameter in turn is fixed at its upper and lower bounds while all the other parameters are varied as per the fully probabilistic model. The variance in results due to each parameter can be displayed as a tornado plot. Univariate sensitivity analyses are included for incremental costs and five-year budget impact for all three models and for the ICER in Model 1.

There is no uncertainty about the discount rate in the fully probabilistic model, but uncertainty is incorporated as part of a univariate sensitivity analysis. The discount rate may vary between 0 and 6%. In line with the other parameters, the 95% confidence bounds are used for the upper and lower parameter values in the univariate sensitivity analysis. A beta distribution is used for discounting that results in lower and upper bounds of 1.7% and 5.7% respectively.

4.4.8 Budget impact analysis

The BIA is conducted from the perspective of the publicly-funded health and social care system and reports the costs for each year in which they occur,[173] in this case for a timeframe of five years. The data for the BIA are the same as those used in the economic analysis with the difference being that prices are inclusive of VAT, and no discounting is applied. The cost of all items of surgical equipment including the capital cost of the robot are subject to VAT at 21%. The cost of incineration and robot maintenance are subject to a reduced VAT rate of 13.5%. The results are reported as the annual and five-year incremental cost of a programme of robot-assisted surgery. As for the three economic models, the capital cost of the robot is annualised using straight-line depreciation over the time horizon.

4.5 Economic model parameters

The economic model requires a range of input parameters that describe the characteristics of the patients undergoing treatment, the operative characteristics, the clinical effectiveness and the costs associated with surgery. The following sections outline the key parameters and the values used in the models. The parameters are defined as distributions and presented as a median and 95% confidence interval.

4.5.1 Target population

Two target populations are relevant to this study: men requiring radical prostatectomy; and women requiring hysterectomy that cannot be completed vaginally. The age distribution of patients was obtained from the Hospital In-Patient Enquiry (HIPE) system (Table 4.1).[174]

Table 4.1. Age distribution of target population

Surgery	Sex	Age	
		Median	(95% CI)
Prostatectomy	Male	58	(47 – 71)
Hysterectomy	Female	49	(31 – 74)

For men undergoing radical prostatectomy, the probability of a positive surgical margin is dependent on the pathological status. Based on the analysis of clinical effectiveness studies approximately three quarters of patients are pT2 with the remainder being pT3 (see section 3.2.3).

Table 4.2. Pathological status in prostatectomy

Pathological status	Proportion of patients	
	Median	(95% CI)
pT2	0.75	(0.70 – 0.80)
pT3	0.25	(0.20 – 0.30)

The volume of patients that can be treated each year is constrained by logistical issues. The time taken to complete robot-assisted surgery is assumed to decrease with increasing surgeon and team experience. Based on the opinion of the Expert Advisory Group, it is assumed that this translates into increasing volumes until a steady state is reached within three to five years.

Table 4.3. Annual case volumes

Year	Annual volume of cases (median & 95% CI)		
	Model 1 Prostatectomy alone)	Model 2 (Hysterectomy alone)	Model 3 (Combined model)
1	99 (74 – 124)	99 (74 – 124)	99 (74 - 124)
2	164 (131 – 206)	158 (131 – 187)	158 (131 - 187)
3	196 (147 – 240)	216 (185 – 253)	215 (185 - 253)
4	199 (146 – 249)	269 (221 – 311)	268 (221 - 310)
5 onwards	198 (146 – 252)	297 (223 – 374)	297 (222 - 372)

It is presumed that steady state will typically be achieved in the third year for Model 1 and the fifth year in Models 2 and 3. As a linear increase is applied from starting volume to steady state volume, Model 1 has a higher volume on average in year 2 than Models 2 and 3.

4.5.2 Time horizon

The evaluation is restricted to operations taking place during the lifespan of the robot. Based on the opinion of the Expert Advisory Group and feedback from Intuitive Surgical Inc., the median robot lifespan is seven years with a range of 5 to 10 years. The potential range for robot lifespan is consistent with HSE accounting practice and with the recommendations in the national economic analysis guidelines.[153] The costs and benefits relating to outcomes are estimated to patient life-expectancy.

4.5.3 Efficacy and effectiveness

The data on the efficacy and effectiveness of robot-assisted prostatectomy and hysterectomy has been derived from a systematic review of the relevant studies (see Chapter 3). The parameters for hysterectomy have been derived using a weighted combination of the results for the three surgery types (i.e. radical, simple, and simple total with node staging). The weights were in proportion to the volume of each type of surgery carried out in Ireland.

Table 4.4. Operative parameters

Parameter	Median (95% CI)		
	Open	Laparoscopic	Robot-assisted
Prostatectomy			
Operative time (minutes)	190 (134 – 272)	203 (137 – 289)	227 (167 – 310)
Length of stay (days)	9 (4 – 16)	7 (2 – 15)	7 (2 – 14)
Transfusion (probability)	0.20 (0.13 – 0.29)	0.05 (0.03 – 0.08)	0.02 (0.01 – 0.04)
Hysterectomy			
Operative time (minutes)	108 (67 – 176)	160 (94 – 240)	172 (117 – 246)
Length of stay (days)	8	6	6
	(3 – 18)	(1 – 17)	(1 – 16)
Transfusion (probability)	0.09 (0.04 – 0.16)	0.03 (0.01 – 0.07)	0.01 (0.00 – 0.04)

4.5.4 Safety

There were insufficient data to determine if the differing rates of complications could be taken as evidence of difference in patient outcomes. Failure of the robot is typically associated with postponement of surgery or, if it occurs peri-operatively, conversion to open surgery. The rates of conversion from robot-assisted and conventional laparoscopic to open have been incorporated into the model. It is assumed that robot-assisted surgery converts to open rather than conventional laparoscopic. In the event of conversion to open prostatectomy, outcomes from open surgery are used.

Table 4.5. Probability of conversion

Parameter	Median (95% CI)	
	Laparoscopic	Robot-assisted
Prostatectomy	0.013	0.005
	(0.003 – 0.035)	(0.002 – 0.011)
Hysterectomy	0.052	0.022
	(0.010 – 0.146)	(0.007 – 0.050)

4.5.5 Resource use and costs

Only direct costs relevant to the publicly-funded health and social care system are included in the evaluation. Direct costs are estimated based on the difference in resource use between the three different procedures (i.e. open, laparoscopic and robot-assisted surgery) rather than the total costs for each. For all models this includes: robot capital and maintenance costs; theatre staff costs; theatre equipment costs; anaesthetic costs; blood transfusion costs; cost of cleaning and sterilising equipment; hospital stay costs; and incineration costs. The capital cost of the robot is annualised using straight-line depreciation over the time horizon. There is no maintenance cost in the first year after purchase of the robot. For Model 1 (prostatectomy alone) costs are also included for continence pads, PDE5 inhibitors and adjuvant radiotherapy. Prices are current with staff costs taken from the mid-point of published Department of Health 2010 pay scales,[175] adjusted for pay-related costs in accordance with national guidelines.[153] Location and theatre allowances are included. Transfer payments (VAT) are excluded. A detailed breakdown of costs is provided in Appendix 4.

4.5.6 Outcomes

For Model 1 (prostatectomy alone), the outcomes of positive surgical margin, sexual function and urinary continence are estimated. The presence of a positive surgical margin results in a probability of requiring adjuvant radiotherapy in preference to active surveillance. Differences in continence and sexual function are measured in quality-adjusted life years (QALYs).

Table 4.6. Outcome probabilities for prostatectomy

Parameter	Median (95% CI)		
	Open	Laparoscopic	Robot-assisted
Probability of positive surgical margin (pT2)	0.15 (0.11 – 0.19)	0.14 (0.10 – 0.18)	0.11 (0.09 – 0.13)
Probability of positive surgical margin (pT3)	0.42 (0.35 – 0.50)	0.32 (0.18 – 0.48)	0.43 (0.36 – 0.51)
Probability of sexual function at 12 months	0.40 (0.30 – 0.51)	0.37 (0.17 – 0.79)	0.62 (0.43 – 0.85)
Probability of urinary continence at 12 months	0.88 (0.83 – 0.92)	0.86 (0.78 – 0.93)	0.93 (0.87 – 0.99)

The probability of post-operative function is conditional on pre-operative function. For both sexual and urinary function, based on data available from the studies included in the meta-analysis it is assumed that on average 80% of patients (95% CI: 63% - 93%) are pre-operatively functional.

It is assumed that patients who lose urinary function following prostatectomy will require continence pads. The rate of pad use at 12 months is assumed to be one pad per day. On the basis of limited data available from the meta-analysis , it is assumed that 23% (95% CI: 4% - 58%) of patients who have sexual function following prostatectomy do so with the aid of phosphodiesterase type-5 (PDE5) inhibitors. Of patients requiring either continence pads or PDE5 inhibitors, it is assumed that 50% (95% CI: 21% - 79%) will be eligible for, and will avail of, those provided through the publicly-funded healthcare system.

The functional outcomes used in the analysis (urinary and sexual function) are expressed as utility values and used to compute QALYs. Utilities can range from zero (death) to one (perfect health). Based on a study with more than five years of follow-up data, it is assumed that the loss of quality of life associated with erectile dysfunction lasts on average four years (95% CI: 1–7).[176] It is acknowledged that there is a lack of longer term follow up data on urinary function post-prostatectomy. As such, the utility gain for urinary function is assumed to extend on average to a point halfway between four years post-operatively and life-expectancy. Where both urinary incontinence and erectile dysfunction are experienced, the combined loss of utility applies for on average four years (95% CI: 1–7) after which the loss of utility for urinary incontinence continues on average to a point halfway between four years and life expectancy. Utility values for urinary incontinence, erectile dysfunction and the combination of urinary incontinence and erectile dysfunction are derived from studies based on patients with diagnosed prostate cancer (see Table 4.8).[177;178]

Table 4.8 Utility values

Function	QALY	
	Median	(95% CI)
Urinary incontinence	0.90	(0.60 – 1.00)
Erectile dysfunction	0.93	(0.72 – 1.00)
Urinary incontinence and erectile dysfunction	0.87	(0.48 – 1.00)

It is assumed that only patients with a positive surgical margin will be considered for adjuvant radiotherapy. Estimates for the numbers of patients with positive surgical margin and the probability of adjuvant radiotherapy are based on a combination of data from clinical effectiveness studies and Irish data.[32] Guidelines suggest that best practice for adjuvant radiotherapy is to administer 1.8 Gry per session for a recommended total of 75 to 81 Gry.[179] However, shorter courses of 6.5 or 7 weeks at higher doses are also possible.[180] For the economic model it is presumed that courses of 33, 35 and 45 sessions are all equally probable.

Table 4.7 Adjuvant radiotherapy after finding a positive surgical margin

Pathological status	Probability of adjuvant radiotherapy in patients with a positive surgical margin	
	Median	(95% CI)
pT2	0.52	(0.42 – 0.62)
pT3	0.72	(0.63 – 0.80)

For Model 2 (hysterectomy alone), long-term clinical effectiveness is assumed to be equivalent for all surgical approaches and hence no outcomes are estimated. As Model 3 (combination of prostatectomy and hysterectomy) is also a cost-minimisation analysis, no long-term outcomes are included.

4.6 Results of the economic models

The three economic models provide estimates of the incremental cost of robot-assisted surgery for prostatectomy alone, hysterectomy alone and a combination of prostatectomy and hysterectomy, respectively. The results of the models are for a single robot. For Model 1 (prostatectomy alone) the steady state volume is the upper limit of the annual number of prostatectomy procedures carried out in the publicly-funded healthcare system in Ireland.

Model 1 uses a lower steady state volume of cases than the other two models. The typical life span of the robot is seven years during which time an estimated 1,290 prostatectomies will be carried out. The equivalent volumes for Model 2 (hysterectomy alone) and Model 3 (combined model) are 1,683 and 1,681 respectively.

Table 4.9 Total number of cases in each model per annum at steady state and over the robot life span

	Median	(95% CI)	Median	(95% CI)
Model 1 - Prostatectomy alone	198	(147 – 250)	1,290	(815 – 1,881)
Model 2 - Hysterectomy alone	297	(222 – 374)	1,683	(1,012 – 2,526)
Model 3 - Combined model	297	(221 – 373)	1,681	(1,006 – 2,537)
Of which prostatectomy	47	(14 – 104)	264	(74 – 637)
Of which hysterectomy	246	(171 – 326)	1,396	(813 – 2,191)

** Volume at steady state (i.e. year five onwards)*

Model 3 (combined model) is based on an annual steady state volume averaging at 47 prostatectomies and 246 hysterectomies respectively.

4.6.1 Incremental cost of surgery

The incremental cost represents the additional cost of using robot-assisted surgery compared to the current standard of care. The incremental cost is discounted and presented as the incremental cost per case (Table 4.10). For Model 1 (prostatectomy alone) the incremental cost per case is €2,487 (95% CI: €1,899 - €3,314). The incremental cost per case in Model 2 (hysterectomy alone) is higher at €3,019 (95% CI: €2,582 - €3,733). Model 3 (combined model) has an overall incremental cost of €2,864 (95% CI: €2,384 - €3,587) per case. The incremental cost of a hysterectomy case is comparable in Model 2 (hysterectomy alone) and Model 3 (combined model). However, the incremental cost of a prostatectomy case is lower in Model 3 as they benefit from larger overall volume of cases. A larger overall volume spreads the capital and maintenance cost of the robot over more cases, thereby reducing the incremental cost.

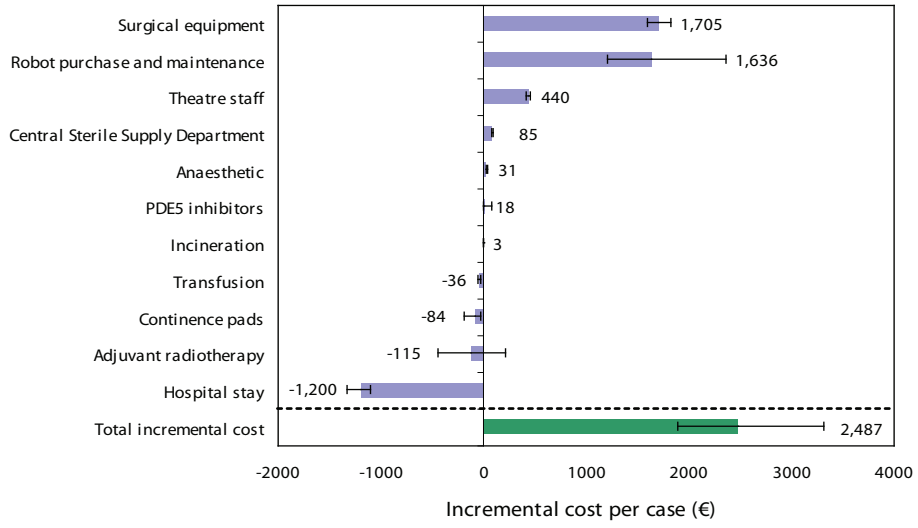
Table 4.10 Incremental cost per case in each model

Model	Per case (€)	
	Median	(95% CI)
Model 1 - Prostatectomy alone	2,487	(1,899 – 3,314)
Model 2 - Hysterectomy alone	3,019	(2,582 – 3,733)
Model 3 - Combined model	2,864	(2,384 – 3,587)
Of which prostatectomy	2,095	(1,408 – 3,072)
Of which hysterectomy	3,017	(2,575 – 3,743)

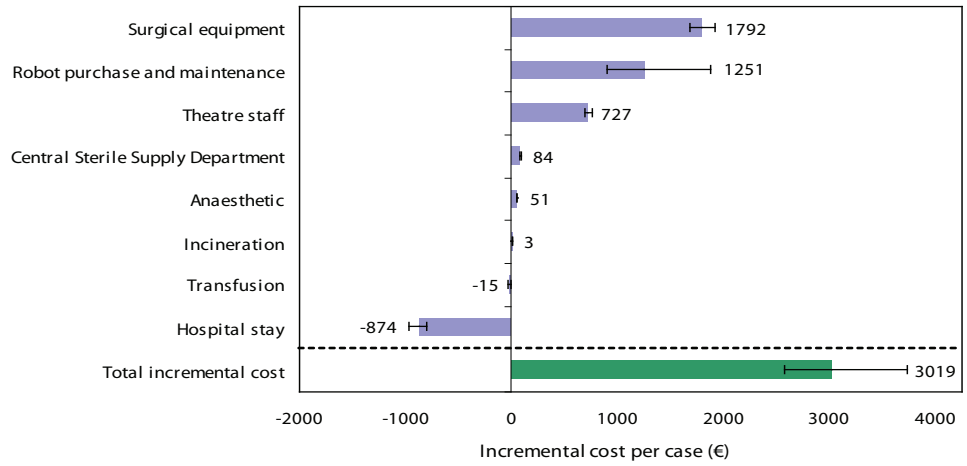
The main elements increasing the incremental cost per procedure are the increased cost of surgical equipment, the cost of robot purchase and maintenance, and the increase in theatre staff costs due to longer operative time. The main element reducing the incremental cost relative to the current standard of care is the reduction in length of hospital stay (Figure 4.1).

Figure 4.1 Contribution of different cost elements to the incremental cost of robot-assisted surgery

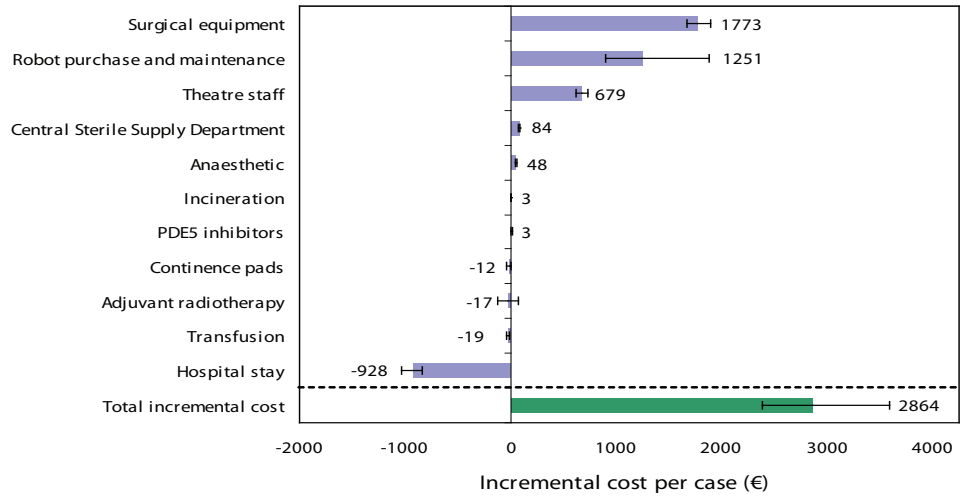
(a) Model 1 – Prostatectomy alone



(b) Model 2 – Hysterectomy alone



(c) Model 3 - Combined model



Note: error bars indicate 95% confidence bounds

Over the five-year time horizon, the use of robot assisted surgery reduced the bed days on average by 2,415 days for Model 1 (prostatectomy alone), 3,209 days for Model 2 (hysterectomy alone) and 3,191 days for Model 3 (combined prostatectomy and hysterectomy). The annual reduction in bed days at steady state is shown in Table 4.11.

Table 4.11 Annual reduction in bed days at steady state in each model

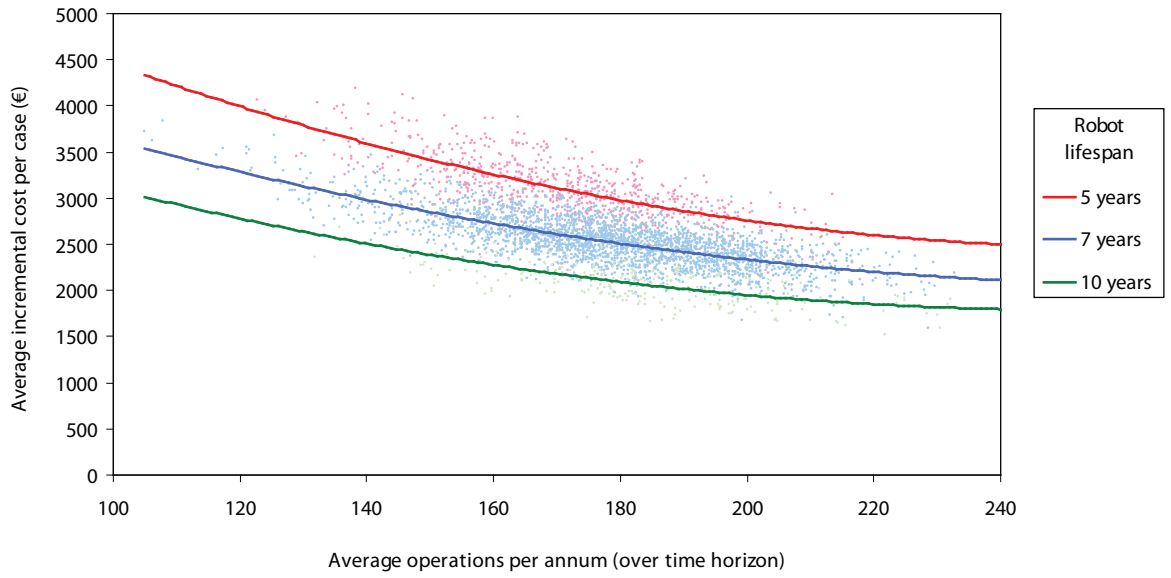
Model	Annual bed day reduction at steady state*	
	Median	(95% CI)
Model 1 - Prostatectomy alone	370	(273 – 472)
Model 2 - Hysterectomy alone	565	(422 – 721)
Model 3 – Combined model	558	(417 – 697)

** Steady state applies from year five onwards*

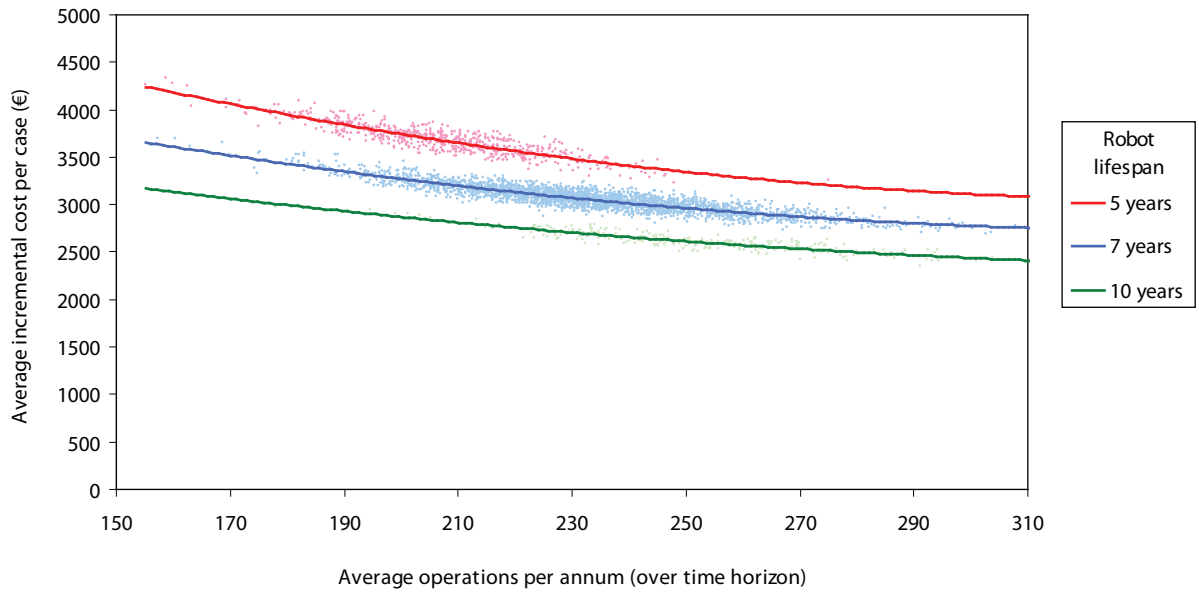
The purchase and maintenance costs of the robot add to each case. That additional cost is proportional to the volume of patients treated and the robot lifespan. The impact of different robot lifespans and annual case volumes on the incremental cost of robot-assisted surgery is shown in Figure 4.2. The benefit of increased volumes is most marked at lower volumes with the benefit of additional cases decreasing at higher volumes. At higher volumes the incremental cost of robot-assisted surgery is driven primarily by the increased cost of the surgical instruments and the theatre staff costs associated with the longer operative times.

Figure 4.2 Impact of robot lifespan and annual volume of operations on incremental cost

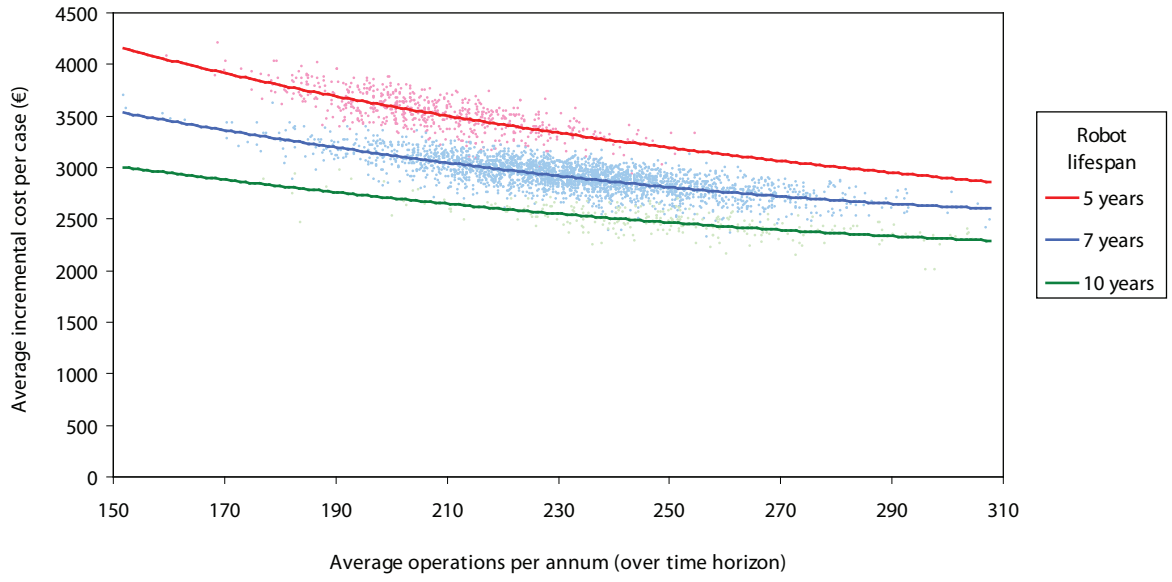
(a) Model 1 - Prostatectomy alone



(b) Model 2 - Hysterectomy alone



(c) Model 3 - Combined model



The trend lines in Figure 4.2 can be used to predict the incremental cost for a range of average annual caseloads and robot lifespans. For Model 1 (prostatectomy alone) the incremental cost can be reduced by 37% by doubling the caseload from 100 to 200 operations per annum (see Table 4.12).

Table 4.12 Predicted incremental cost of robot-assisted prostatectomy by average annual cases and robot lifespan

Average cases per annum	Robot lifespan		
	5 years	7 years	10 years
100	4,453	3,628	3,097
150	3,418	2,850	2,388
200	2,757	2,335	1,951
250	2,470	2,083	1,787

The incremental cost in Model 2 (hysterectomy alone) can be reduced by 25% by increasing the caseload from 150 to 300 operations per annum (Table 4.13).

Table 4.13 Predicted incremental cost of robot-assisted hysterectomy by average annual cases and robot lifespan

Average cases per annum	Robot lifespan		
	5 years	7 years	10 years
100	5,039	4,268	3,625
150	4,308	3,707	3,207
200	3,743	3,272	2,870
250	3,344	2,962	2,613
300	3,111	2,778	2,438
350	3,044	2,720	2,343

The incremental cost of Model 3 (combined prostatectomy and hysterectomy) can be reduced by 25% by increasing the caseload from 150 to 300 operations per annum (Table 4.14).

Table 4.14 Predicted incremental cost of robot-assisted procedure by average annual cases and robot lifespan

Average cases per annum	Robot lifespan		
	5 years	7 years	10 years
100	5,187	4,100	3,411
150	4,184	3,549	3,018
200	3,593	3,118	2,704
250	3,192	2,808	2,469
300	3,003	2,619	2,312
350	2,934	2,549	2,233

4.6.2 Budget impact analysis

The budget impact analysis results quantify the additional financial cost of robot-assisted surgery over the cost of the current standard of care. For Model 1 (prostatectomy alone), the budget impact ranges from €0.38 million in year one to €0.68 million per annum from year three onwards. The budget impact for Model 2 (hysterectomy alone) ranges from €0.49 million in year one to €1.15 million per annum in year five when steady state is reached. In Model 3 (the combined prostatectomy and hysterectomy model) the budget impact ranges from €0.48 million in year one to €1.11 million per annum in year five. The lower budget impact of Model 1 compared to Models 2 and 3 is due to the lower numbers of cases treated and the lower cost per case.

The lower cost in year one is due to a combination of the lack of maintenance fee in the first year and the lower volume of cases treated initially. The combined model has a smaller budget impact than the hysterectomy alone model due mainly to the reduced costs associated with operative time and length of stay in the prostatectomy subgroup.

Table 4.15 Estimated annual and total budget impact for each model (€ millions)

Year	Model 1 (Prostatectomy alone)		Model 2 (Hysterectomy alone)		Model 3 (Combined model)	
	Median	(95% CI)	Median	(95% CI)	Median	(95% CI)
1	0.38	(0.25 – 0.53)	0.49	(0.39 – 0.61)	0.48	(0.38 – 0.60)
2	0.64	(0.47 – 0.83)	0.81	(0.69 – 0.95)	0.78	(0.67 – 0.92)
3	0.68	(0.49 – 0.89)	0.95	(0.82 – 1.11)	0.92	(0.78 – 1.08)
4	0.69	(0.50 – 0.90)	1.08	(0.92 – 1.26)	1.04	(0.87 – 1.22)
5	0.68	(0.49 – 0.90)	1.15	(0.93 – 1.40)	1.11	(0.89 – 1.34)
Total	3.08	(2.50 – 3.76)	4.48	(3.95 – 5.14)	4.32	(3.77 – 4.99)

4.6.3 Model 1 - cost-utility analysis of prostatectomy alone

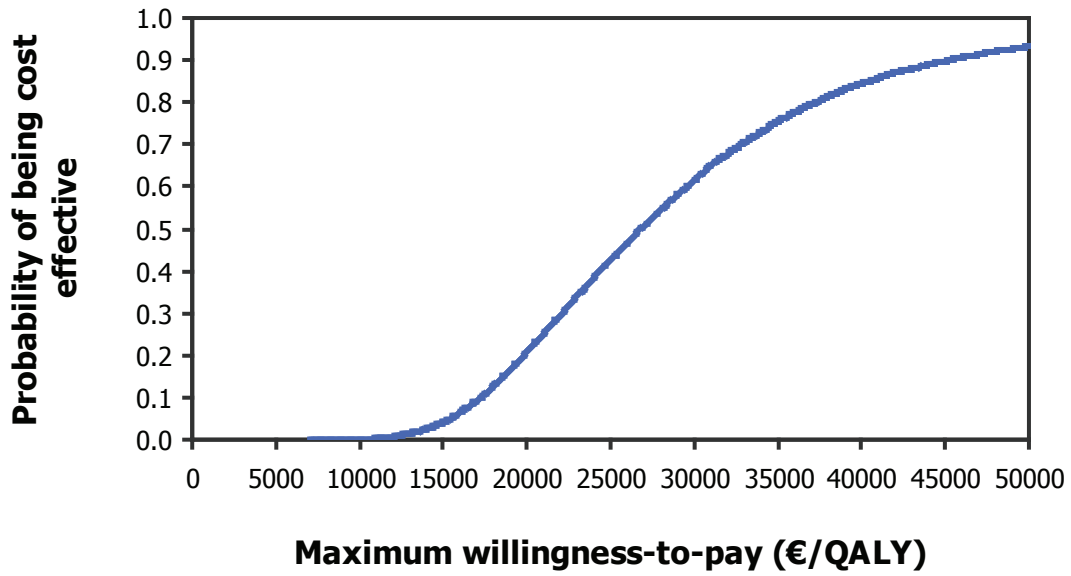
The assessment of clinical effectiveness in Chapter 3 showed that the use of robot-assisted surgery leads to, on average, improved positive surgical margin rates and improved outcomes for urinary continence and erectile dysfunction. The incremental cost-effectiveness ratio (ICER) is the ratio of incremental cost to incremental effectiveness, in this case QALYs. The median ICER is €26,647/QALY (95% CI: €14,241 - €61,220/QALY).

There is substantial uncertainty around the ICER which reflects the uncertainty around both the magnitude of the incremental effectiveness and also the duration over which the benefits persist post-operatively (Figure 4.3).

Figure 4.3 Incremental cost-effectiveness ratio for robot-assisted prostatectomy (Model 1)

The cost-effectiveness acceptability curve (CEAC) for robot-assisted prostatectomy is shown in Figure 4.4. The CEAC shows the probability that robot-assisted surgery is cost-effective over a range of willingness to pay thresholds. This allows the decision maker to set their own threshold ICER for how much they are willing to pay for an additional QALY and to see the probability that the technology would be cost-effective at this threshold. For robot-assisted prostatectomy, the probability of cost-effectiveness is zero below a willingness to pay threshold of €9,473 per QALY. Based on willingness to pay thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

Figure 4.4 Cost-effectiveness acceptability curve for robot-assisted prostatectomy (Model 1)



4.6.4 Univariate sensitivity analysis: incremental cost

In accordance with the national guidelines, univariate sensitivity analyses are presented to show how influential each parameter is and how sensitive the results are to fluctuations in each parameter.[153;173]

The three economic models contain many parameters, some of which are not influential. Although all the main parameters have been varied for the analysis, only those that result in a greater than 1% fluctuation from the median estimate are presented in the following tornado plots (Figure 4.5).

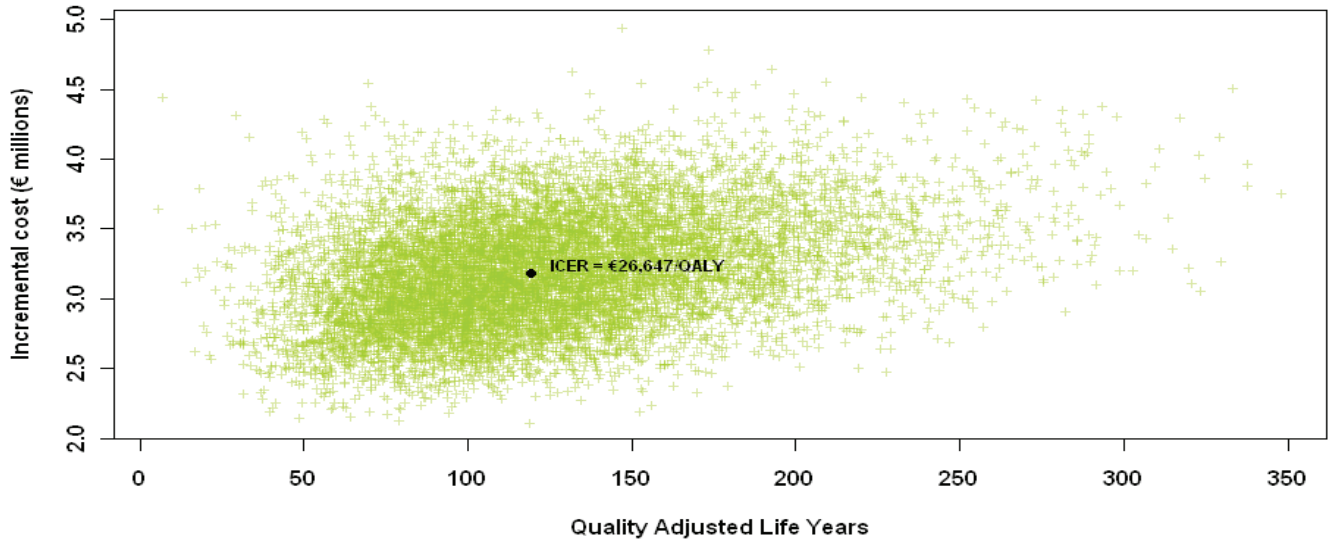
For Model 1 (prostatectomy alone) the length of stay is the most influential parameter followed by robot lifespan and volume of operations. The length of stay is the main parameter reducing the incremental cost of robot-assisted prostatectomy. The international data on length of stay vary. For the economic model only, data from European studies has been used on the grounds that they should be comparable to what might be observed in Ireland. It has already been shown that increasing the robot lifespan and volume of operations can significantly reduce the incremental costs. Another notable parameter is the positive surgical margin (PSM) rate for both robot-assisted and open surgery. Changes in the PSM rate impact on the numbers of patients likely to require adjuvant radiotherapy. The rates of PSM in patients who are tumour stage T2 are lower in robot-assisted surgery than in open surgery and consequently the numbers requiring adjuvant radiotherapy are lower. The model is clearly sensitive to changes in the PSM rate highlighting the importance of the clinical effectiveness data.

For Model 2 (hysterectomy alone) the robot lifespan is the most influential parameter affecting incremental cost followed by operative time. The length of stay is less important than in Model 1 (prostatectomy alone) and its influence is highly skewed due to the fact that the median difference between robot-assisted and open surgery is -2.1 days but the range is from -2.0 to -3.0.

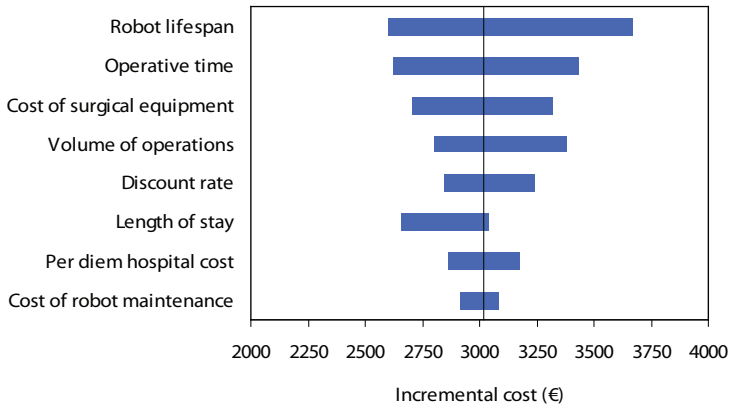
In Model 3 (combined model) the volume of operations and robot lifespan are the two most influential parameters. This feature highlights the importance of maximising the use of the robot to minimise incremental costs. The operative time, cost of surgical equipment and length of stay are also important. Length of stay is the key parameter reducing the incremental cost of robot-assisted surgery.

Figure 4.5 Univariate sensitivity analysis of incremental cost

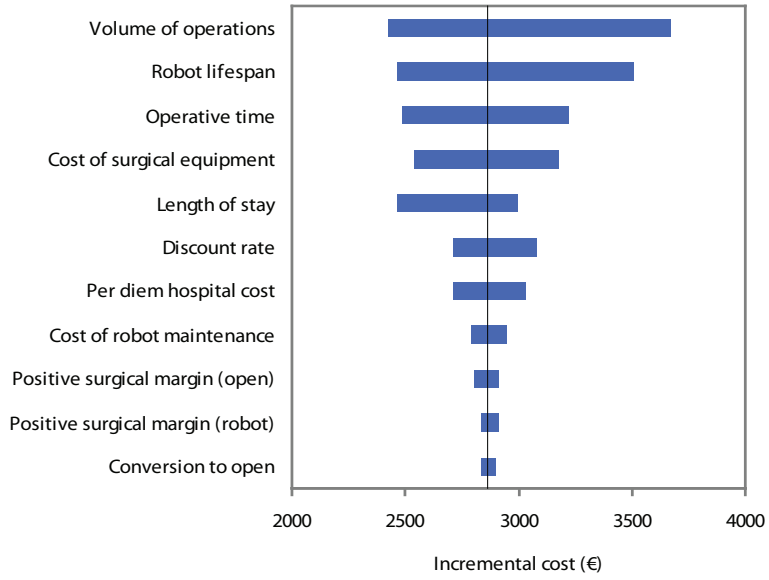
(a) Model 1 – Prostatectomy alone



(b) Model 2 – Hysterectomy alone



(c) Model 3 - Combined model



4.6.5 Univariate sensitivity analysis: five-year budget impact

For some parameters, most notably volume of operations, an increase in the number of procedures will reduce the incremental cost but increase the budget impact. Hence the univariate sensitivity analysis of five-year budget impact must be interpreted differently to that for incremental cost. As in the previous section all the main parameters have been varied for the analysis, but only those that result in a greater than 1% fluctuation from the median estimate are presented in the following tornado plots (Figure 4.6).

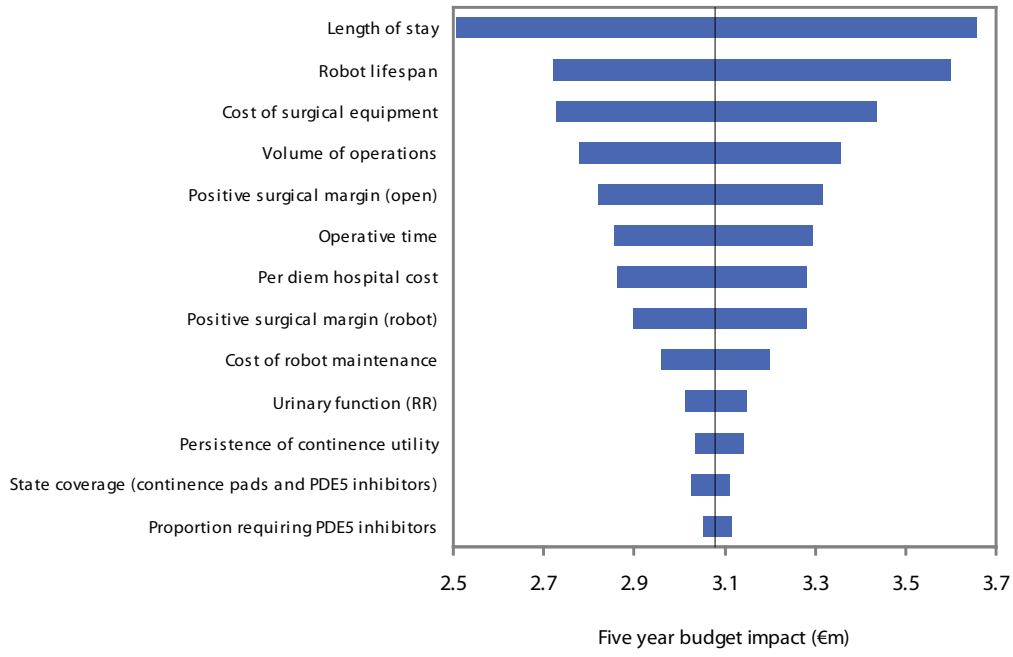
For Model 1 (prostatectomy alone), the ranking of important parameters is similar to the univariate sensitivity analysis for incremental costs. Length of stay is still the most influential parameter followed by robot lifespan. In terms of budget impact, a longer lifespan means that the cost of the robot is distributed over a longer period thereby reducing the annual cost.

In Model 2 (hysterectomy alone), the volume of operations is the most influential parameter affecting the five-year budget impact whereby a higher volume results in a higher budget impact. A higher volume reduces the incremental cost per procedure, but increases the budget impact. Variation in operative time, the cost of surgical equipment and the robot lifespan have comparable influence on budget impacts to volume of operations.

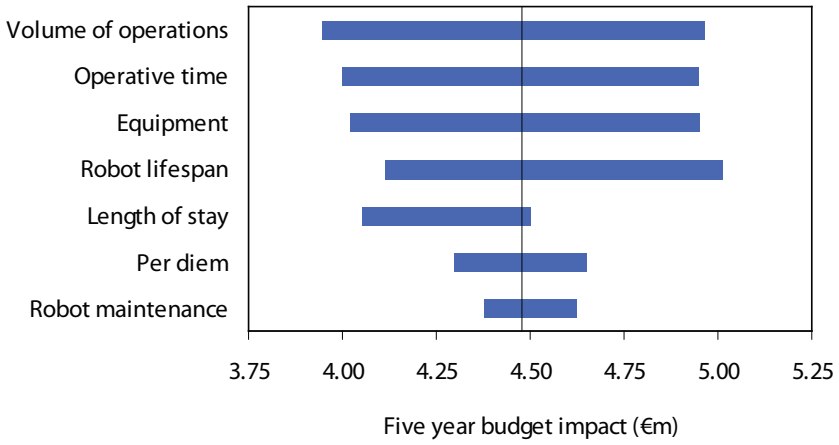
For Model 3 (combined model of prostatectomy and hysterectomy), the volume of operations is the single most influential parameter. The cost of surgical equipment, operative time and robot lifespan have equivalent influence to each other, but are less important than operation volume.

Figure 4.6 Univariate sensitivity analysis of five-year budget impact

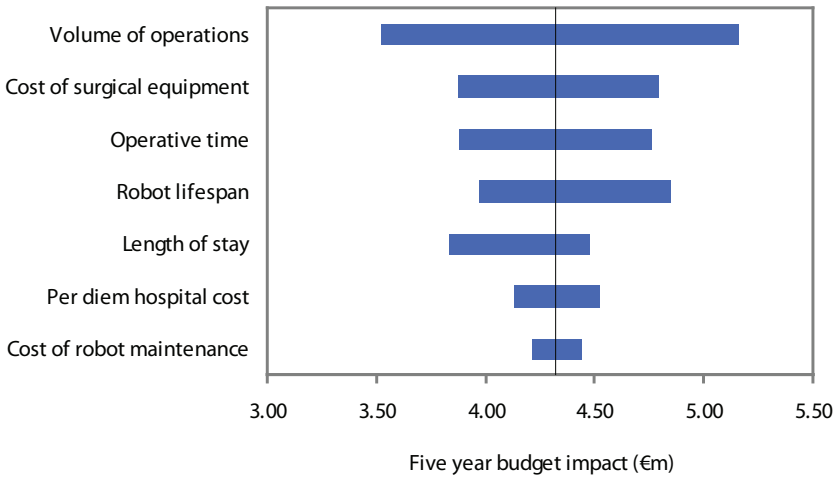
a) Model 1 – Prostatectomy alone



b) Model 2 – Hysterectomy alone



c) Model 3 - Combined model

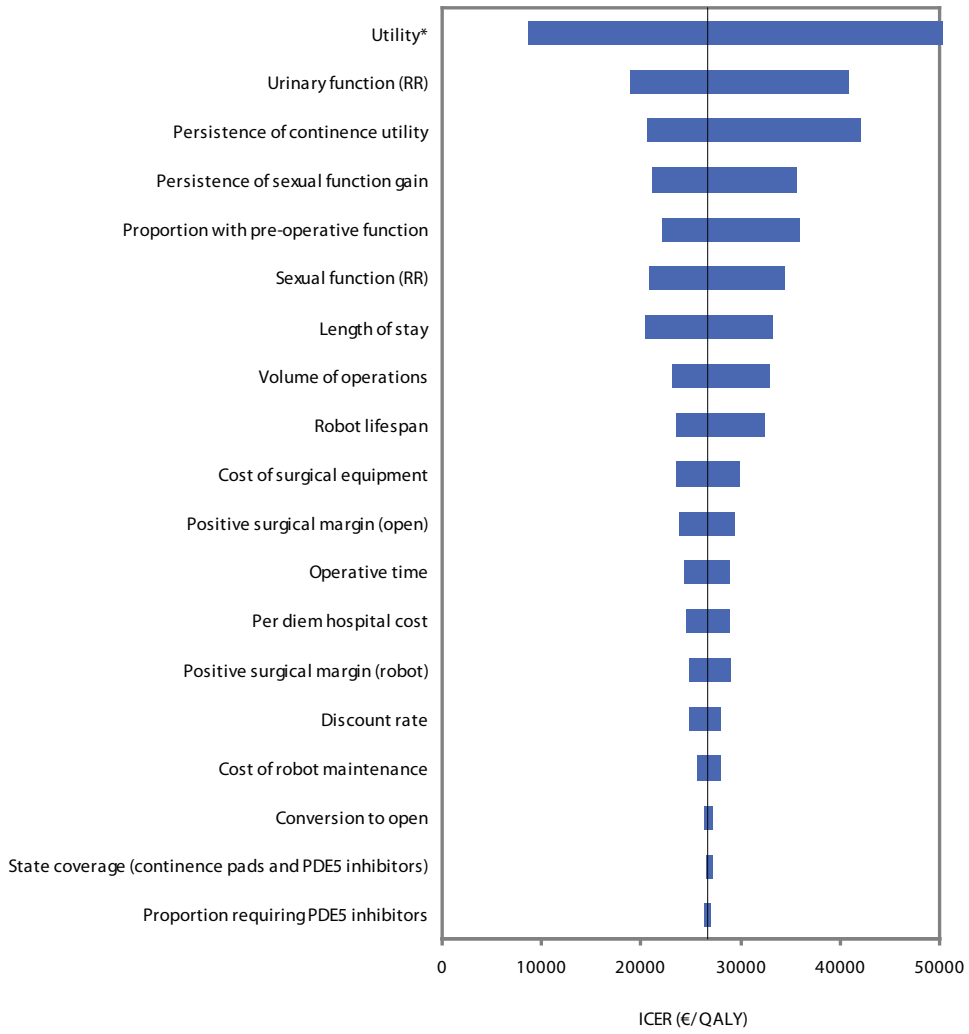


4.6.6 Univariate sensitivity analysis: incremental cost effectiveness for prostatectomy alone

Model 1 (prostatectomy alone) showed differences in functional outcomes that facilitated the estimation of an ICER for robot-assisted surgery. Where the incremental cost and budget impact are calculated based on costs, the utility gains are an important component of the ICER (Figure 4.7).

The single most influential parameter in estimating the ICER is the utility. For this analysis, all three utilities (urinary function, sexual function and combined urinary and sexual function) were simultaneously set to their upper and lower bounds, respectively. The upper bound for all three utility scores is 1, or perfect health. When all three utilities are set to 1 there is no utility gain and the ICER is estimated at infinity.

Figure 4.7 Univariate sensitivity analysis of incremental cost-effectiveness of robot-assisted prostatectomy (Model 1)



The top six most influential parameters all relate to utility gains, either directly or indirectly. These include: the relative risk of urinary function; the persistence of continence utility (i.e. the length of time over which the benefit of continence is experienced); the persistence of sexual function gain (that is the length of time over which the benefit of sexual function is experienced); proportion of patients who are pre-operatively functional; and the relative risk of sexual function. The main reason for these parameters being so influential is because of the uncertainty around their estimates.

The remaining influential parameters relate mostly to costs (length of stay, volume of operations, robot lifespan and cost of surgical equipment).

4.7 Limitations of the economic models

The three economic models presented are intended to accurately reflect the impact on costs and, in the case of prostatectomy, the outcomes of introducing robot-assisted surgery in Ireland. The extent to which the models achieve that goal is affected by a number of limitations.

4.7.1 Assumptions

Any economic model is necessarily a simplification of a real-world experience. Without access to detailed projections for future activity or patient profiles, assumptions have to be made in order to construct a workable model. For the current models the main assumptions fall into two categories: the applicability of international data to the Irish setting and the stability of model parameters over time.

International data are used to describe the difference between robot-assisted surgery and open and laparoscopic surgery for a number of operative characteristics and outcomes. It is assumed that relative differences in operative time, transfusion rates, urinary function and sexual function observed in the collected studies will apply in Ireland. The assessment of clinical effectiveness showed that for length of stay, US studies report much shorter durations due to a different definition of length of stay and discharge. Conversely, Asian studies were found to report unusually long lengths of stay, again due to the configuration of health services. Hence, the relative differences in length of stay between robot-assisted, open and laparoscopic surgery used in the economic models were based on European studies only. There is no clear reason to suspect that Ireland would be different from other countries. However, it is possible that the poor quality of available studies may mean that some of the reported series only include patients with the best outcomes. The results of those studies will not generalise well to a typical patient population.

A major assumption of the economic models is that some of the parameters will remain unchanged over the 10-year time horizon. The patient age profile and the relative differences in operative time, length of stay, transfusion rates, urinary function and sexual function are all assumed to remain stable over the study time horizon. The relative differences are obtained from international studies that include a mixture of experienced and inexperienced surgeons. Few of the studies include more than three to four years of robot-assisted surgical experience and hence it is possible that further reductions in operative time or length of stay might be observed with a longer study duration. However, it is suggested that the surgical learning curve reaches a plateau after which further improvements might be limited. As such it is assumed that the collected data are representative of what might be observed over the time horizon. It is also presumed that the current ratio of open to laparoscopic surgery will continue to apply.

Few studies assess functional outcomes and almost all of those that do are based in Europe. There are also limited data available on appropriate utility values for men undergoing radical prostatectomy. The utility values are the most important parameter affecting the ICER in Model 1. Two associated parameters are therefore also important: the proportion patients who are pre-operatively functional and the length of time over which the utility gain applies.

Few of the collected studies report clearly on the numbers of patients who were pre-operatively functional. The parameters on pre-operative function used in economic model are based on the limited data available extracted for the meta-analysis of clinical effectiveness. The length of time over which utility gains apply is difficult to determine due to the absence of long-term follow up after surgery. It is suggested that gains due regaining sexual function last no more than seven years post-operatively but for regaining continence they may extend to beyond seven years post-operatively.[176] It would be unreasonable to extrapolate that utility gains for regaining continence last to life expectancy, so the model allows them to extend to a random point after the utility gain for sexual function ceases. This approach used in the economic model reflects the uncertainty around utility data.

The analyses in this chapter are based on a single robot. The extent to which these results can be generalised to multiple robots depends on the indications being treated. For the model of prostatectomy alone the steady state volume is assumed to be 200 cases per annum. Given that there are fewer than 300 prostatectomies being carried out in the publicly-funded healthcare system in Ireland each year, it would not be possible to carry out 200 prostatectomies a year on each of two robots. However, the models for hysterectomy alone and the combination of prostatectomy and hysterectomy could potentially apply to multiple robots.

4.7.2 Quality of inputs

The quality of the outputs from the economic models is partly constrained by the quality of the inputs: accurate results cannot be obtained from inaccurate data. It has already been noted that most of the studies included in the meta-analyses of clinical effectiveness were of poor quality. The benefit of using meta-analysis to derive pooled values for the economic models is that representative-mean-effect estimates are used and that the associated confidence bounds reflect the heterogeneity of effect estimates across studies. The risk of poor quality studies is that they may introduce systematic bias to the meta-analyses and, consequently, to the economic models. An example of possible bias could be the inadequate attempts to follow up patients post-operatively resulting in over-estimates of functional outcomes. This could be a problem if follow up was different between the robot-assisted and open or laparoscopic arms of the included studies. It was assumed that where biases were present they applied in all study arms, thereby not biasing in favour of robot-assisted surgery. The use of relative differences for parameters (i.e. either weighted mean difference or relative risk) should further moderate the impact of such biases.

4.7.3 Plausibility of results

To test the method of computation, the economic models were also implemented as a deterministic model in Microsoft Excel. Equivalent results were obtained, although without any confidence bounds around the estimates. While this confirms that the model correctly combined the data, it does not evaluate the accuracy or plausibility of the results. By comparison to other studies, it is possible to determine whether the results are similar and hence plausible. For convenience, in the following comparisons the reported costs from the economic studies were transformed into equivalent 2010 Irish costs.The average incremental cost for robot-assisted prostatectomy compared to open surgery in economic analyses that included the cost of the robot is €2,520.

This is similar to the value of €2,487 estimated in the current study. The evidence around the incremental cost for hysterectomy is less clear as only two studies compared robot-assisted and open surgery including the cost of the robot. These studies, both from the US, calculated incremental costs of -€1,193 and €2,565, respectively.[75;170] The former found a cost saving in robot-assisted surgery although in that study a differential room and board cost was applied to the two types of surgery whereas other studies, including the present assessment, use an equivalent cost for each day. The latter reported cost is similar to, but lower than, the figure of €3,019 estimated in this study.

In terms of the ICER, only two other studies have estimated an ICER for robot-assisted prostatectomy. The reported ICERs from Australia and Denmark, €22,918 and €48,901 respectively, are both within the confidence bounds of the ICER estimated in this study.[164;169] It should be highlighted that the latter study used a retrospective cohort study which found no statistically significant difference in urinary and sexual function outcomes between robot-assisted and open surgery. This contrasts with the significant differences observed for both outcomes when data from multiple studies are combined.

The results reported in this study are broadly in line with published estimates for incremental cost and the ICER, supporting the view that the models in this study reflect the likely impact of introducing robot-surgery in Ireland.

4.7.4 Exclusion of indirect costs

The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. Some of the published economic evaluations for both robot-assisted prostatectomy and hysterectomy have incorporated indirect costs. Robot-assisted surgery is associated with a shorter length of stay but also a faster return to normal activity for patients which could translate into a large societal benefit. With regard to prostatectomy, one study reports that the return to work is two weeks' earlier after robot-assisted surgery compared to open surgery, equivalent to preventing €1,349 in lost earnings.[164] For a cost-utility analysis of robot-assisted prostatectomy, the ICER was reduced from €48,901/QALY to €10,271/QALY when absence of work was taken into account.[169] For hysterectomy, the average days to return to normal activity was 24.1 for robot-assisted surgery compared to 52.0 days for open surgery.[75] This reduction in days to normal activity was equivalent to €3,441 in lost wages and household productivity. If it is assumed that similar reductions in time to return to work could be achieved in Ireland then the societal benefits of robot-assisted surgery could be significant.

4.8 Summary

The incremental cost of robot-assisted surgery in prostatectomy has been evaluated in a number of studies with broad agreement that robot-assisted surgery is more costly than open surgery. Two cost-utility analyses have been published with inconsistent results.

In terms of robot-assisted hysterectomy, few economic analyses have been published and only three compared robot-assisted surgery to open surgery. While all the studies found robot-assisted surgery to be more costly than laparoscopic surgery, one of the comparisons to open surgery found robot-assisted surgery to be less costly. At the time of this HTA, there had been no cost-utility analyses of robot-assisted hysterectomy.

Economic models were developed for prostatectomy alone, hysterectomy alone and for a combination of prostatectomy and hysterectomy. Given the evidence around the difference in long-term clinical effectiveness of robot-assisted prostatectomy compared to conventional surgical techniques, the model for prostatectomy alone was a cost-utility analysis. In the absence of evidence of such a difference in clinical effectiveness for robot-assisted hysterectomy compared to conventional surgery, Model 2 (hysterectomy alone) was developed as cost-minimisation analysis. As the combined model contains predominantly hysterectomy procedures, this was also developed as a cost-minimisation analysis.

The models simulate the changes in costs (and outcomes for Model 1) for a cohort of patients who undergo robot-assisted surgery rather than the current standard of care. The models were developed using international clinical effectiveness data in combination with Irish data on patient characteristics, rates of adjuvant radiotherapy and costs. All of the key parameters were defined by distributions rather than point estimates and allowed to vary in a fully probabilistic model. Incremental cost, budget impact and, for the model of prostatectomy alone, the incremental cost effectiveness ratio were all presented as a median and associated confidence interval.

The median incremental cost for robot-assisted prostatectomy alone is €2,487 (95% CI: €1,899 – €3,314). For hysterectomy alone the median incremental cost is €3,019 (95% CI: €2,582 – €3,733) and for a combination of prostatectomy and hysterectomy the incremental cost is €2,864 (95% CI: €2,384 – €3,587). Within the combined model the incremental cost of robot-assisted hysterectomy is unchanged but the incremental cost of robot-assisted prostatectomy decreases to €2,095 (95% CI: €1,408 – €3,072) because of economies of scale. The main factors increasing the incremental cost are the surgical equipment, robot purchase and maintenance, and theatre staff costs. The main factor reducing the incremental cost relative to the current standard of care is the length of hospital stay.

The five-year budget impact per robot in the model for prostatectomy alone is estimated at €3.1 million, ranging from €0.4 million per annum in year-one to €0.7 million per annum from year-three onwards. For the hysterectomy alone model, the five-year budget impact per robot is estimated at €4.5 million, ranging from €0.5 million per annum in year-one to €1.2 million per annum in year-five. Finally, for the combined model the five-year budget impact per robot is estimated at €4.3 million, ranging from €0.5 million per annum in year one to €1.1 million per annum in year-five. The increasing budget impact is related to the increasing volume of operations being carried out.

Model 1, the cost-utility analysis for prostatectomy alone, estimated the median ICER to be €26,647/QALY (95% CI: €14,241 - €61,220/QALY). The cost-effectiveness is based on gains in urinary and sexual function and associated utilities in patients undergoing robot-assisted surgery. The wide confidence bounds reflect the uncertainty around many of the parameters related to the utilities in terms of both the number of patients who will experience gains and the magnitude of the benefit in those patients. Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

The economic models used in this study are restricted to the HSE perspective and exclude indirect costs. Robot-assisted surgery is associated with a shorter length of stay and a faster return to normal activity for patients. Inclusion of indirect cost savings associated with the faster return to work significantly reduce the ICER associated with robot-assisted surgery. If it is assumed that similar reductions in time to return to work could be achieved in Ireland then the societal benefits of robot-assisted surgery could be significant.

Key messages:

- Economic evaluation in HTA involves the comparative analysis of alternative courses of action. In this HTA, the additional costs (and in the case of prostatectomy, health benefits) associated with robot-assisted surgery are compared with the usual standard of care (that is open and standard laparoscopic surgery).
- Probabilistic models were used to carry out economic analyses of robot-assisted prostatectomy and hysterectomy in Ireland compared to the usual standard of care (i.e. open and laparoscopic surgery). Values for key parameters for the economic model were mainly informed through primary data collection and literature review and were endorsed by the Expert Advisory Group.
- The quality of the evidence supporting the key parameters for the model was poor leading to a higher likelihood of bias. It is not possible to predict how the results may have been affected by bias. This limitation must be considered when interpreting the economic findings.
- The incremental cost of robot-assisted surgery (over the robot lifespan) if a robot is used for prostatectomy alone is €2,487 (95% CI: €1,899 - €3,314), assuming a steady state volume of 200 cases per annum.
- The incremental cost of robot-assisted surgery (over the robot lifespan) if used for hysterectomy alone is €3,019 (95% CI: €2,582 - €3,733), assuming a steady state volume of 300 cases per annum.
- The incremental cost of robot-assisted surgery (over the robot lifespan) if a robot is used for a combination of prostatectomy and hysterectomy procedures is €2,864 (95% CI: €2,384 - €3,587), assuming a steady state volume of 300 cases per annum.
- The increased cost of robot-assisted surgery is primarily due to the additional costs associated with the specific surgical equipment used with the robot, the robot purchase and maintenance and the cost of theatre staff due to longer operative times. These costs are only partially offset by savings associated with shorter inpatient stays.
- Based on the steady state volumes used in the models, use of one robot to assist surgery compared to standard surgical techniques will reduce the annual number of bed days by 370 (95% CI: 273 – 472) if used for prostatectomy alone, 565 days (95% CI: 422 – 721) if used for hysterectomy alone and 558 days (95% CI: 417 – 697) if used for a combination of prostatectomy and hysterectomy.
- Increasing the annual volume of cases per robot reduces the incremental cost of robot-assisted surgery, as does extending the lifespan of the robot.
- The incremental budget impact of robot-assisted prostatectomy on a single robot is €0.4 million in the first year. Over five years, the incremental budget impact of robot-assisted prostatectomy is €3.1 million (95% CI: €2.5 million to €3.8 million).

- The incremental budget impact of robot-assisted hysterectomy on a single robot is €0.5 million in the first year. Over five years, the incremental budget impact of robot-assisted hysterectomy is €4.5 million (95% CI: €4.0 million to €5.1 million).
- The incremental budget impact of a combination of robot-assisted prostatectomy and hysterectomy on a single robot is €0.5 million in the first year. Over a five-year timeframe, the incremental budget impact of robot-assisted surgery is €4.3 million (95% CI: €3.8 million to €5.0 million).
- A cost-utility analysis for robot-assisted prostatectomy was also carried out. The estimated ICER is €26,647/QALY (95% CI: €14,241 - €61,220/QALY). The wide confidence bounds highlight the variability around the point estimate. That variability is primarily affected by the uncertainty around the utilities associated with urinary and sexual function. There is no specified threshold below which an ICER is deemed cost-effective. Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.
- The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days to return to normal activity appears substantially shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a significant societal benefit.

5. Organisation of health system and training requirements

5.1 Introduction

Assessment of the organisational aspects of delivering a new technology can help identify potential barriers and challenges to its implementation.[181] This chapter addresses those barriers and challenges specific to the introduction of a robot-assisted surgery programme.

Potential issues that may arise for an organisation were identified using the organisational domain of the EUnetHTA core model for HTA of medical and surgical interventions.[181] The key questions identified were:

- What are the implications for existing operative processes and specifically for training and credentialing of staff?
- What is the optimal profile for an organisation (e.g. caseload and existing theatre facilities) to allow the efficiency of such a programme to be maximised?
- What management issues would an organisation need to consider in the planning of a new programme?

5.2 Impact on existing processes

A new programme of robot-assisted surgery has the potential to impact on theatre processes and that of other auxiliary services. Robot-assisted surgery is additionally associated with a significant learning curve,[7;8;18;20;167;182] although it is generally felt that the use of robotics shortens the learning curve for laparoscopic surgery[8;183] and specifically for acquiring complex minimally surgical skills.[7] Internationally, it has been recommended that specific training and credentialing requirements are developed for those involved in delivering a programme of robot-assisted surgery so that patients receive safe care.[7;184-186] These issues are now explored in detail.

5.2.1 Processes

Patient admission and pre-theatre work-up

Hospital admission procedures are not expected to differ between robot-assisted and conventional surgical techniques.[187;188] As noted in Chapter 3, robot-assisted surgery may be associated with longer procedure times and therefore a longer duration of anaesthesia, particularly when surgeons are new to the technology. For the anaesthetist, this adds to other complexities common to robot-assisted surgery including extreme patient positioning, spatial restrictions and difficulty changing the patient's position when the robot is docked.[189;190] These must be considered by the anaesthetist in the pre-operative management of these patients.

Theatre time

A number of factors contribute to an increase in theatre time for robot-assisted surgery. These include: set up and docking of the robot and procedure-specific increases in operative time. Additionally, robot-assisted surgery is associated with a significant learning curve that impacts on each of these variables.

Additional theatre time is required at the beginning of each robot-assisted procedure to set up the robot and to dock the device to the patient. Data suggest that robot set-up time decreases from an additional 60 minutes initially to approximately 20 minutes per procedure with increasing staff experience.[191] Similarly, the time required to dock the machine to the patient (cart moved to patient side, robot arms clipped to patient ports, port depth checked and instruments inserted ready for use) reduces with increasing staff experience from an initial 20 minutes per procedure to approximately 5 minutes or less.[187;191]

As outlined in Chapter 3, mean operative time is significantly longer when using robot-assisted surgery for both radical prostatectomies and for hysterectomies compared to conventional open surgery. Increases in operative time were also noted for other robot-assisted gynaecological, cardiac and head and neck procedures.

Robot-assisted surgery is associated with a significant learning curve. [192-194] For robot-assisted prostatectomy, initial operative times of 8 to 9 hours are reported, with improvements of up to 10 minutes per case thereafter until cases are consistently performed within 3 to 4 hours. An average learning curve of 77 cases (range 13 to 200 cases) has been described.[167] Similar reductions in operative and theatre time have been documented for robot-assisted radical hysterectomy.[195]

Increases in overall theatre time become significant in an organisational context when additional personnel are required, overtime is paid, patients remain in theatre recovery overnight or fewer cases per shift can be accomplished.[7] Prolonged procedure and theatre time are improved by effective team training, attention to efficient procedures, surgeon and team experience and careful patient selection.[7] The costs associated with prolonged operative times while learning robot-assisted surgery may be minimised by limiting these programmes to high-volume centres that enable the learning curve to be rapidly traversed. Nonetheless these costs are substantial and an important consideration when deciding to introduce a programme at an individual institution.[167;183;196]

Surgeon-related factors

Compared to conventional surgical techniques, robot-assisted surgery is associated with reduced surgeon fatigue. This is due to the improved ergonomics provided by the robot set-up and positioning with the surgeon seated at an ergonomically designed workstation with arms resting during the procedure. This may reduce the risk of repetitive strain injuries that have been associated with both open and conventional surgical procedures.[7] These benefits may permit the experienced surgeon to complete more robot-assisted procedures per day than would be possible if using conventional surgical techniques with onward implications for theatre scheduling.[187;197]

Processes outside of theatre

Introduction of a robot-assisted surgery programme in an organisation has implications for other hospital services, particularly the central sterile supply department (CSSD). Cleaning of the robot equipment is time consuming and technically complex due to the size and complexity of the equipment involved and the requirement for manual cleaning of the EndoWrist® instruments.[198] Both steam and hydrogen peroxide sterilisation facilities are required. The latter may not be routinely available in all facilities and its introduction may involve additional capital expenditure costs.[199;200] While additional sets of the smaller limited-use instrumentation may routinely be held and is recommended,[18] the capital cost of carrying extra sets of items such as the camera is considerable. Close cooperation between theatre and CSSD is required to ensure rapid turnaround of equipment, particularly if more than one robot-assisted procedure is scheduled per day or if the CSSD is remotely located from the organisation.[199]

5.2.2 Training and credentialing

To deliver safe care, the introduction of any new technology, including robot-assisted surgery, necessitates the development of training and credentialing requirements.[12] This is necessary to ensure that surgical outcomes and patient safety are not compromised during the learning process,[185] that the best possible surgical outcome is obtained and best practice is adhered to by surgeons, their trainers and the responsible organisations.[12] There is currently no standardised training curriculum for independently performing robot-assisted surgery. Organisations will also need to develop standards and procedures enabling the authorisation of individual surgeons to have unrestricted privileges on the robot – it is recommended that these are developed on an inter-organisational or national basis with appropriate regulatory oversight.[12] In Ireland it is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of robotic surgery will fall to the various surgical training bodies, including, for example, the Royal College of Surgeons in Ireland (RCSI) or the Irish Society of Urology. Some information from other countries, most notably the United States, has been published specifically in relation to training in robotic surgery for surgeons and their organisations. Although this information is not specifically pertinent in Ireland, it is summarised in Appendix 5.

In addition to the significant training required for the lead surgeon, other members of the operating team require training in order to safely initiate and provide a robot-assisted surgical programme.[12] Some training courses are provided by the manufacturers.[202] It has been recommended that two to four teams of theatre personnel are trained, depending on the expected surgical volume.[196]

A number of the guidance documents that review best practices in robot-assisted and laparoscopic surgery training and credentialing referred to above also make specific recommendations for non-surgeon theatre staff.[7;184] The British Association of Urological Surgeons (BAUS) recommends that potential theatre teams visit a high-volume centre to learn all aspects of the surgery.[184] A consensus document on robotic surgery produced by the Society of American Gastrointestinal and Endoscopic Surgeons recommends that, at a minimum, theatre personnel should be trained according to the manufacturer's training

guidelines, and should have the opportunity to be partnered with an experienced nurse or theatre technician during their early experience.[7] It is also recommended that teams using such instruments (surgeons, technicians, nurses, manufacturing representative if possible) meet regularly to stay up to date with training and to learn of updates or changes to the hardware or software.[7]

Training for staff of the central sterile supply department (CSSD) should also be incorporated into the organisational training plan. This training is essential to ensure that it is appropriately cleaned and sterilised, to maximise the lifespan of the equipment and to minimise the turnaround time for equipment.[18;198;199]

5.3 Organisational profile

For an organisation to develop and implement a programme of robot-assisted surgery, there are two significant issues that should be considered:

- the overall surgical volume and casemix
- the capacity of the existing theatre infrastructure.

These are reviewed in detail in this section. Management issues that may arise during the introduction and initiation of a programme are discussed in section 5.4.

Organisational casemix

There are significant costs associated with the introduction of a robot-assisted surgery programme. These include the initial capital expenditure on the robot and an annual cost for its maintenance, service and repair, estimated at 10% of the capital acquisition cost. Organisations that can maximise their robot-assisted surgery caseload reduce the incremental cost per procedure and can therefore realise a greater return on their investment in robot-technology compared to those organisations with a lower surgical volume. Although robot-assisted surgery costs more per procedure than conventional open or laparoscopic surgery, the incremental costs may be partially offset by a reduced length of stay associated with the technology.

Health technology assessments published to date indicate that the principal indications for robot-assisted surgery are prostatectomy and hysterectomy, with increasing use of the technology in cardiac surgery.[8] There is growing use of the robot for the other indications for which it is approved although as noted in Chapter 3 the evidence to support these is more limited.

Data from HIPE report that 310 prostatectomies were performed in Ireland in 2009 in a total of 12 hospitals.[203] Procedure numbers ranged from a minimum of approximately five procedures‡ to a maximum of 76 procedures with a total of three hospitals carrying out greater than 45 procedures. During the same period, 1,922 hysterectomies (excluding vaginal procedures) were performed in a total of 28 hospitals.[203] Procedure numbers ranged from a minimum of 13 procedures to a maximum of 193 procedures with a total of 14 hospitals carrying out greater than 45 procedures. Surgical volume is critical to establishing a successful robot-assisted surgery programme.[196]

At the time of this HTA, a relatively small number of radical prostatectomy procedures were carried out in any single institution in Ireland. If planning a robot-assisted prostatectomy service, service managers should consider the need to direct more or all of these procedures to the centre, and/or ensure that the technology can be used for a range of other indications. These indications most likely include gynaecology with further potential indications developing over time. If planning a robotic surgery service for other primary indications (for example in gynaecology) consideration should be given to the potential annual caseload in order that the incremental cost per procedure is minimised.

Theatre size

To minimise the potential for damage to the robot, a dedicated operating theatre for the robot is recommended.[18;183;204;205] On an ongoing basis, sufficient physical space is required to accommodate the surgical console and cart, the robot itself, a stock of disposable and other instruments specific to the robot in case of malfunction, and a three-dimensional projection system. At the initiation of the programme during the early learning curve, multiple assistants in addition to the regular theatre staff as well as a second training console may also need to be accommodated. Recommended theatre sizes range from 37 to 65 square meters[18;183;204;205] with suggestions that 65 square meters be considered optimal. Three dedicated power outlets are recommended. This may mean make it difficult to accommodate the robot into existing theatre layouts.[18] If multi-specialty use of the robot is planned, then the additional theatre requirements associated with these disciplines must be considered. If including cardiac surgery as one of these multi-specialities, a hybrid of the robot-assisted surgery theatre requirements in addition to cardiac surgery imaging equipment requirements (angiography systems, mobile c-arms, ultrasound, endoscopy etc.) would need to be considered.[206]

5.4 Planning a new programme

5.4.1 Introduction

Planning a robot-assisted surgery programme in an organisation requires consideration of a number of leadership and management issues. These are outlined below.

Leadership

The importance of leadership in setting up a programme of robot-assisted surgery has been emphasised in the literature.[18;183;205] Effective leadership will motivate the organisation to embrace the technology, plan for the training programmes, articulate the commitments (short and long term) required, assess the suitability of the existing facilities for the service and continuously monitor and validate the outcomes from the programme as it develops.[18;196;205]

A lead surgeon, proficient in the use of the robot for the primary indication for which it is intended, is recommended.[183] To drive the successful implementation of a programme, the support of a multidisciplinary leadership team that comprises nursing, anaesthesia, technical support and administration is also needed to assess and plan the necessary operational, training and resource requirements.[205]

The merits of a partnering arrangement with an existing service location has been advocated as a valuable asset in terms of observing theatres, work flow, and learning from an experienced robot team and coordinator.(18)

Centralisation of services

Given national caseloads for certain procedures, such as radical prostatectomy, there may be merit in centralising access to robot-assisted surgery, with surgeons gaining admittance rights to operate on their patient at a designated centre. Such policy is consistent with policies of the HSE's National Cancer Control Programme to centralise care of prostate cancer in designated centres.[207] Appropriate governance would be required at an institutional level to ensure such a programme can be delivered to optimise the efficiency with which resources are used and to ensure safe and seamless care for the patient. Although potentially increasing the administrative burden, such an arrangement could ensure that a given robot is used at its maximal capacity reducing the incremental cost per case. Efficiencies may also be gained in the training of other theatre and auxiliary staff.

Capacity per robot

In planning a national access programme to robot-assisted surgery, consideration must be given to the capacity that can be achieved with a robot, both at programme initiation and at steady state when a fully trained and experience team are in place. Expert opinion agrees that the mean operation time for a robot-assisted prostatectomy would be approximately three hours with a turnaround time of one hour between surgeries. This would equate to two surgeries being planned per day with the possibility of a maximum of 10 per week when at a steady state. More realistically, it is considered that six cases per week are achievable and this is the typical caseload that has been modelled in Chapter 4. This would not be possible at the start of a robot-assisted programme, however, and typically it could take up to three years to get to a steady state. Expert opinion agrees that only one surgery should be planned in a day in the initial stages of a new programme.[208;209]

Monitoring outcomes

Measures to capture the efficiency and effectiveness of a new programme should be defined at the outset and audited at regular intervals to ensure the delivery of better, safer care. Such audit will be necessary in the planned National Competency Assurance Programmes for professional accreditation and is included as a key component of the National Standards for Safer Better Healthcare.[210] Effective audit measures both process and clinical outcomes, and includes a system to address shortcomings. Process measures include the caseload achieved and the resources consumed. Effectiveness measures include outcome measures specific to the procedure. For prostatectomy procedures, these include oncological outcomes, functional outcomes (continence, potency) and peri-operative outcomes (duration of procedure, transfusion rates, analgesic rates, complications, length of stay). A clear definition for each variable and the use of valid instruments that accurately capture patient reported outcomes will facilitate a robust, scientific audit.[18] The use of outcome registries for robot-assisted surgery indications has been recommended to enable the quality of outcomes to be documented and to allow for accurate comparison of robot-assisted surgery to traditional approaches.[7]

Patient selection

There will be limits to the number of patients that can access the technology in a single centre; this may cause difficulties in prioritising patients. Criteria for selecting patients for robot-assisted procedures should be defined at the outset. Ethical issues in relation to the selection of patients for robot-assisted procedures are discussed in Chapter 6. The selection of 'uncomplicated' patients for surgeons at the start of their learning curve helps facilitate successful outcomes in early procedures. The appropriate selection of patients is particularly relevant during the earlier learning curve, with recommendations to select patients for robot-assisted prostatectomy with a lower body mass index (BMI),[211] less extensive disease[212] and a prostate gland volume less than 60cm3.[213] Other relevant variables include complexity arising from co-morbidities or previous abdominal surgery and the ability to withstand a steep Trendelenburg position for a prolonged period.

5.4.2 Existing capacity in Irish healthcare system

At the time of this HTA, there were three surgical robots in use in hospitals in Ireland. Two of these were located in private facilities (the Mater Private Hospital in Dublin and the Galway Clinic) and one located in a public hospital (the Cork University Maternity Hospital). Before committing additional resources to the purchase, maintenance and development of new robot-assisted surgery programmes, decision makers should consider the potential of any of these facilities to meet the additional capacity required as part of a newly approved programme.

5.5 Key messages

- To successfully implement a safe and efficient programme of robot-assisted surgery careful planning is required that takes consideration of the optimal location for such a service, its potential impact on existing processes, appropriate selection of patients and the training requirements of surgeons and other staff.
- Robot-assisted surgery increases theatre time per procedure. In particular, operative time and associated costs are increased in the early stages of implementation when surgeons and auxiliary staff are new to robot-assisted surgery.
- A dedicated theatre is recommended for the robot – the dimensions, layout and facilities of which must be considered, particularly if multi-speciality use is planned.
- Appropriate governance arrangements must be considered when commencing a new robotic surgery programme. Additional arrangements may be required to facilitate access by different specialities and to enable surgeons from other institutions to access the technology.
- It is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of robotic surgery will fall to the various surgical training bodies.
- Training of other theatre staff and auxiliary staff is also required; the use of designated training programmes and a system of mentoring by experienced staff is recommended.

- The profile of a candidate organisation for a robot-assisted surgery programme needs careful consideration. Robot-assisted surgery has a significant capital and overhead cost. The incremental cost per case is reduced in organisations with a higher surgical caseload.
- Planning of a new programme of robot-assisted surgery should consider factors such as patient selection criteria, audit criteria and the appointment of a multidisciplinary leadership team.
- There is existing capacity in the Irish healthcare system for robot-assisted surgery. This capacity could be considered prior to any new investment in the technology in other facilities.

6. Ethical considerations

6.1 Introduction

The importance of incorporating a discussion of ethical issues in HTA is discussed in the first part of this chapter. This is followed with a discussion of the specific ethical issues of equity of access justice and autonomy, informed consent, and other potential ethical issues.

6.2 Importance of ethics in HTA

The rapid development of health technologies in recent years has been accompanied by escalating healthcare costs, and this rapid development has been a major contributor to the escalating costs.[214] HTA is considered to be a decision-support tool for healthcare policymakers. Traditionally it assesses, against existing standards of care, whether the technology works, for whom it works, and what the incremental costs and benefits are. There is widespread agreement, however, that it should also incorporate an ethical analysis, addressing the consequences of implementing a technology within the healthcare system.[215] The value of ethics in HTAs is said to be based on three observations:

- The implementation of certain technologies may have moral consequences, justifying the addition of an ethical analysis to customary deliberation on cost and effectiveness.
- Technology may challenge prevailing moral principles or societal rules.
- The entire HTA 'enterprise' is value laden.[216]

Further, the fundamental issues in HTA – such as safety, efficacy, effectiveness and efficiency – raise ethical questions. These include how society defines safety, how efficacy is measured, and what criteria should be applied when assessing effectiveness and efficiency?

The development of a health technology is a process that is intended to promote a moral good, for instance, the alleviation of pain or improving health status and, therefore, places ethics within the realm of HTA.[217] Another reason for integrating ethics into HTA is because new health technologies can be morally challenging. Past experience has demonstrated that technology can confront fundamental moral principles (autonomy, integrity, dignity, beneficence, and justice) and ethical perceptions, such as the moral status of embryos. Indeed, in recent years, controversial technologies have necessitated in-depth ethical analysis, such as genetic testing, pre-implantation genetic diagnosis (PGD) and in vitro fertilisation (IVF).

Decisions to implement new technologies could imply devaluing or discarding other technologies or may result in the reallocation of resources within the healthcare system. In addition, policymakers are required to balance individual and wider societal interests and are expected to operate in a transparent, honest and equitable fashion. Ethical analysis within HTAs can provide insight into these issues as well as highlight patient perspectives and community views and assist policymakers in interpreting information in a relevant way.

6.3 Equity of access and justice

Ethical issues within the context of equity of access and justice arise in the context of any decision not to invest in robot-assisted surgery, as well as in the context of a decision to invest. These are discussed below.

Failure to invest in robot-assisted surgery

The fair distribution of healthcare resources requires limiting expenditure to interventions with proven safety and efficacy. If a decision is taken not to invest in robot-assisted surgery, ethical questions may arise regarding the equity of access to healthcare, autonomy and justice. However, it is important to note that this would only be the case were the technology shown to be superior to the existing laparoscopic or open surgery techniques. Failure to provide the technology, in that situation, would result in a system of inequity between public and private healthcare patients because the service would not be available for patients who do not have private health insurance or an independent means to pay for the surgery. Undoubtedly, limiting availability of a superior surgical intervention to private patients would be ethically problematic.

The principles of solidarity, equity and justice prescribe that, as far as possible, patients should have equal access to medical treatments and that all sections of society should get a 'fair share' of those resources.[218] It has long been accepted that the provision of healthcare services should be decided on the basis of medical need rather than on non-medical criteria, such as the ability to pay. Equity imposes an obligation to provide the best possible service in as fair a manner as possible so that no member of society who otherwise could have a claim on those services is excluded or disadvantaged.

Restricting the choice of public patients in relation to the type of surgical procedure they may wish to avail of could also be considered an infringement on the right to personal autonomy (entitlement to make decisions or take actions based on personal convictions and free from external influences). However, it should be noted that the right to personal autonomy, particularly in the healthcare setting, is not absolute. Healthcare budgets are finite and an individual's right to choose certain treatments/services may conflict with other values or priorities, such as equity or the need to benefit the wider community. There is also a belief that while a patient's right to autonomy should be valued as an ideal, in reality the options of both patients and doctors are often restricted. Many decisions are made without a patient's input or indeed in the absence of the patient, which in effect means, that many aspects of 'choice' are beyond his/her reach.[219] This is true of both public and private patients.

Investment in robot-assisted surgery

When new technologies are implemented, resources may need to be diverted from other effective treatments for the same conditions or from the overall healthcare fund. Innovative surgical interventions are almost inevitably more expensive than other forms of treatment, as is the case with robot-assisted surgery. Its introduction therefore has a significant opportunity cost (i.e. the cost of an alternative that must be forgone in order to pursue a certain action), particularly where this would divert resources from cheaper options. If an investment were to be made in robot-assisted surgery, questions of equity and justice would persist, but for other reasons.

In the economic climate at the time of this HTA, an investment in a robotic surgery programme would almost certainly necessitate the diversion of resources from existing services. Where resources are limited and it is impossible to provide universal services, any decisions to reallocate resources within the public health system or to allocate services to one patient group instead of another is a decision that must be open to strict inspection. The difficulty lies in trying to ensure fairness and justice in the rationing process and policymakers must attempt to balance competing concerns.

The principle of justice requires that any action taken would be on the basis of fair decision making between competing claims. Concepts of justice vary widely and there is little agreement on which theory should take precedence. In his 'Theory of Justice' John Rawls states that resources should be allocated to ensure that those in poorest health, or greatest need, should be as well off, in health terms, as they can be. Whatever theory of justice is applied, the challenge will be to strike a balance between different patient expectations and to distribute resources fairly in order to ensure the best medical outcomes for the most people. In line with the findings of the current report, in the case of robot-assisted surgery, this may involve assessing the feasibility of exploiting existing capacity in the Irish healthcare system.

A more just distribution of healthcare resources can be secured when empirical evidence, as set out in the current HTA report is available on which to base funding decisions. This can aid in determining where best to invest precious resources. Legitimacy requires that patients see any resource allocation system as just and accept allocation decisions as fair. It is therefore important that any policy decision relating to the whether or not robot-assisted surgery should be implemented is made in a transparent and equitable manner.

Limited investment in robot-assisted surgery

Surgical volume is critical in establishing a successful robot-assisted surgery programme, as outlined in Chapter 5. The consequence of this is that an investment in the smaller number of centres could raise issues of equity and justice if only a restricted number of patients benefitted as a result of the location of the service. This would be particularly important if robot-assisted surgery was considered to be superior to conventional surgical approaches, and could give rise to inequities in access. The issue of geographical access is, however, complex. The quality of care provided in centralised services may be higher than if they were more evenly dispersed. Thus, improving access to central services may be more appropriate than providing localised services in some contexts. This has to be balanced against the risk, however, that some patients may be offered an alternative procedure as a result of their location. In that context, it is worth noting that most surgeries performed using robot-assisted surgery would in fact be elective procedures, meaning patients would have the time to decide if they wished to access a centre offering robot-assisted surgery.

6.4 Informed consent

In the event of introducing a new robotic surgery programme, the question arises of what information needs to be shared with patients during the informed consent process. The primary ethical principle underlying informed consent requirements is respect for patient autonomy. Therefore, one goal of the informed consent process is to enable patients to make medical care decisions that reflect their values and desires. The informed consent process has come to be accepted as an appropriate and necessary expression of respect for autonomy that provides overall benefit to patients.

In the contemporary environment of shared decision making, it is currently common practice for a surgeon to discuss with a patient the nature of the surgery, its risks and benefits, potential alternatives and the expected post-operative course. When a surgeon is obtaining consent for innovative procedures, such as robot-assisted surgery, the short- and long-term risks and benefits of the procedure may not be fully known. The surgeon would therefore have less information to share with their patient than they would for more conventional open or laparoscopic methods. This lack of information can make the informed consent process challenging for both surgeons and patients.

To further complicate matters, there is an overwhelming assumption by the public that 'new is better', leading to additional difficulties in the way patients objectively consider the risks of innovative procedures. The allure of new surgical technological developments affects not only patients but also surgeons. The desire to do 'cutting-edge' procedures is strong for many surgeons, a fact that makes the objective assessment of the value of innovative surgical techniques difficult for both surgeons and patients.[220] As outlined in Chapter 5, there is an associated learning curve for the surgeon when commencing robot-assisted surgery, as is the case for most surgical procedures. This raises the issue of how best to ensure that patient's safety is maintained while the surgeon gains the necessary skills and experience in the new procedure. In order to support the decision making by the patient, as part of any informed consent process involving robot-assisted surgery, the surgeon should fully disclose to the patient the degree of experience he or she has with the procedure. In the case of robot-assisted surgery being adopted, the patient should be advised that the technique is new and the potential risks of the procedure (including any areas of uncertainty) should be outlined to patients as accurately as possible. Information should be provided about alternative interventions and patients should have access to information about how many of these procedures have been performed at the hospital and by the surgeon who will perform the procedure. The potential advantages of such disclosure are enhanced patient autonomy, better patient decision-making, and the promotion of a culture of openness and accountability, thereby supporting physician-patient trust.

The introduction of a system of monitoring patient outcomes with robust data collection systems, that should accompany the introduction of a new programme, would provide surgeons with information in relation to currently unknown long-term risks and benefits of robot-assisted surgery in various surgical applications. This would prove helpful in securing genuine consent from patients.

6.5 Other ethical issues

Surgeon autonomy

The autonomy of the patient has been discussed in some detail. However, it is also important to acknowledge the autonomy of the surgeon delivering care. A surgeon's perception of a technology is the most important factor in its voluntary use. There are surgeons who will choose not to incorporate robotic-assisted surgery into their routine practice for a range of reasons, including a belief that traditional practices are sufficient to treat their patients.[221] Section 9.1 of the 2009 Guide to Professional Conduct and Ethics for Registered Medical Practitioners allows doctors to refuse specific treatments in cases where they consider the treatment would not work or that it could cause more harm than good. This is within their rights to do so, but their duty of care to a patient who wishes to access this service is that they should refer them on to another surgeon who can provide the service.

Monopoly issues

The da Vinci robot is manufactured by Intuitive© Surgical, Inc which sells the robot, the instruments for the robot and its service contract. At the time of this HTA, the da Vinci was the only actively marketed surgical system to have received approval from the US Food and Drug Administration, and the only system to have received approval for cutting and suturing. This effectively means that pricing and production decisions can be made independent of competitive forces. Such a monopoly may hinder clinical use and thwart advances in the field, as a monopolist has no incentive to develop new techniques to secure its survival and/or development. In the 2009 health technology assessment on robot-assisted surgery, completed by the Belgian Healthcare Knowledge Centre,[8] the issue of whether it was ethically acceptable to use public funds to pay a manufacturer in a monopoly position was raised. The report concluded that while this was not the ideal situation, for the reasons outlined above, comparable situations arose in relation to pharmaceuticals and these products were reimbursed using public funds. Nonetheless, the monopoly situation which exists in relation to robot-assisted surgery should be an issue of consideration for policymakers in deciding whether or not to invest in such technology. It is imperative that value for money be achieved and that limited public funds are spent in improving outcomes for surgical patients at an affordable cost for the entire community.

6.6 Key messages

- Policymakers are required to balance individual and wider societal interests and are expected to operate in a transparent, honest and equitable fashion. Ethical analysis within HTAs can provide insight into these issues as well as highlight patient perspectives and community views and assist policymakers in interpreting information in a relevant way.
- Ethical issues of equity, justice or autonomy could arise in the context of any decision not to invest in robot-assisted surgery. Such issues, however, also arise in the context of a decision to invest in the technology – although for different reasons. These issues are significant if the technology is considered to be superior to existing surgical approaches.

- Non-provision of the technology to those without private health insurance or the ability to pay could lead to issues of equity for some patients, and could affect their personal autonomy.
- Provision of this more expensive technology implies that the opportunity of providing other healthcare services may be lost, and policymakers must balance competing demands for healthcare resources within the context of equity and justice for all patients.
- In keeping with the principles of fairness and justice, the challenge for policy makers will be to strike a balance between different patient expectations and to distribute resources fairly in order to ensure the best medical outcomes for most people. In line with the findings of this report, in the case of robot-assisted surgery, this may involve assessing the feasibility of exploiting existing capacity in the Irish healthcare system.
- When considering a robot-assisted procedure, the surgeon must fully disclose to the patient the degree of experience he/she has with the technique.

7. Summary and conclusions

7.1 Introduction

Health technology assessment supports evidence-based decision making in regard to the optimum use of resources in healthcare services. Measured investment and disinvestment decisions are essential to ensure that overall population health gain is maximised particularly with finite healthcare budgets and increasing demands for services provided.

This HTA assesses the following questions to aid the decision maker when considering an investment in robot-assisted surgery in the publically funded healthcare system in Ireland. These assessments are summarised in the sections that follow:

- What is the evidence for the effectiveness and safety of robot-assisted surgery compared to traditional surgical approaches?
- Is it cost-effective to introduce robot-assisted surgery?
- What would be the overall cost of introducing robot-assisted surgery?
- What organisational issues (including training and credentialing) should be considered so that robot-assisted surgery is introduced as safely and effectively, efficiently and cost-effectively as possible?
- What overall ethical issues should be considered in relation to a decision to invest, or not to invest?

In accordance with the Terms of Reference, procedures in urology, gynaecology, cardiology and diseases of the head and neck were assessed in this HTA. Of these, prostatectomy and hysterectomy are the two procedures for which the most evidence existed at the time of this HTA in relation to the clinical effectiveness of robot-assisted surgery. Therefore, this HTA has generated the data to inform a decision whether or not to expand access to the technology for these indications in Ireland. Information on the use of the robot in other indications continues to emerge.

7.2 Evidence of effectiveness and safety of robot-assisted surgery

A systematic review of the literature indicated that the overall quality of the evidence regarding the clinical effectiveness of robot-assisted surgery in prostatectomy and hysterectomy was poor. There was a high level of heterogeneity between the results of different studies for some of the outcomes under consideration. These limitations must be considered when interpreting the results of the meta-analysis and the review of clinical evidence.

The available evidence at the time of this HTA indicated that robot-assisted prostatectomy procedures were superior to open procedures across a range of outcomes evaluated.

There is a decreased risk of positive surgical margins for pathological stage pT2 tumours, superior functional outcomes (urinary continence and sexual function) and a reduction in peri-operative transfusion requirements. Duration of hospital stay is reduced. The robot-assisted procedure is, however, associated with a longer operating time.

The evidence available at the time of this HTA indicated that the benefits of robot-assisted prostatectomy over a laparoscopic approach were minor. There are comparable oncologic outcomes, marginal improvements in urinary continence and equivocal data on sexual function. Reductions in length of stay are obtained, although these are less pronounced than the reductions obtained by comparison with open surgery. No significant differences were observed for transfusion, operative time or in the rate of conversion to open surgery.

Robot-assisted hysterectomy when compared with open surgery is associated with a reduction in estimated blood loss, lower risk of transfusion or complications and shorter hospital stays. Operating times are, however, longer. Compared to conventional laparoscopic hysterectomy, the difference in the reported results for each of these outcomes is substantially reduced, with no significant difference in operating times. Unlike prostatectomy, however, there is an absence of data in relation to differences in functional and oncological outcomes (where applicable) for robot-assisted hysterectomy compared to alternative approaches.

Evidence to support the use of robot-assistance for a range of other urology, gynaecology, cardiac and head and neck procedures was limited in quantity and quality. Based on the review it is predicted that robot-assisted surgery is safe and feasible for a range of such indications and may provide comparable but not necessarily superior outcomes to conventional surgical techniques. Additional, higher quality research is required for these indications.

Robot-assisted surgery is more ergonomic than laparoscopic surgery for the operating surgeon. However this ergonomic benefit does not apply to the rest of the surgical team, including the assisting surgeon. Mechanical or instrument failure can arise during robot-assisted surgery, which if unrecoverable, can necessitate conversion of the procedure to open surgery in up to 0.6% of cases.

7.3 Cost-effectiveness and budget impact

Economic evaluation in HTA involves the comparative analysis of alternative courses of action. In this case, the additional costs and additional health benefits associated with robot-assisted procedures were compared with the usual standard of care (i.e. open and laparoscopic approaches).

Three different scenarios were modelled in this HTA. The first, a prostatectomy-only model, was based on a steady state caseload of approximately 200 cases per annum. As there are superior outcomes associated with this procedure, a cost-utility analysis was undertaken. The second, a hysterectomy-only model, was based on a steady state caseload of approximately 300 cases per annum. As there are no demonstrable improved clinical outcomes for this procedure, a cost-minimisation analysis was undertaken.

The third scenario, a combined prostatectomy/hysterectomy model, was based on a caseload of approximately 300 cases per annum. In this model, the number of hysterectomy procedures was significantly in excess of the prostatectomy procedures, so a cost-minimisation analysis was carried out.

The perspective of the evaluation is the publicly funded healthcare system in Ireland. Values for key model parameters were informed primarily through primary data collection and literature review, and were endorsed by the Expert Advisory Group. National guidelines for the economic evaluation of health technologies in Ireland, as published by the Authority, were applied. A seven-year timeframe (lifespan of the robot) was applied with a discount rate of 4% for costs and benefits.

The results of these economic evaluations are shown in Table 7.1

Table 7.1 – Summary of economic evaluation

Result	Model 1 (Prostatectomy alone)		Model 2 (Hysterectomy alone)		Model 3 (Combined model)	
	Median	(95% CI)	Median	(95% CI)	Median	(95% CI)
Annual caseload (at steady state)	198	(147 – 250)	297	(222 – 374)	297	(221 – 373)
Incremental cost						
(€ per case)	2,487	(1,899 – 3,314)	3,019	(2,582 – 3,733)	2,864	(2,384 – 3,587)
5 year budget impact						
(€ millions)	3.08	(2.50 – 3.76)	4.48	(3.95 – 5.14)	4.32	(3.77 – 4.99)
Annual reduction in bed days	360	(273 – 472)	565	(422 – 721)	558	(417 – 697)
ICER (€/QALY)	26,647	(14,241 - 61,220)				

The incremental costs associated with robot-assisted procedures in each of the models are indicated above. These are primarily due to the costs associated with surgical equipment, robot purchase and maintenance and the additional cost of theatre staff due to longer operative times. Based on the steady state volumes used in the models, however, the use of robot-assisted surgery will reduce the annual number of bed days. Increasing the annual volume of cases would reduce the incremental cost of robot-assisted surgery, as would extending the lifespan of the robot.

The incremental budget impact of robot-assisted procedures on a single robot in the first year is predicted as €0.4 million (prostatectomy only), €0.5 million (hysterectomy only) and €0.5 million (combination of both). Over five years, the estimated incremental budget impact of robot-assisted procedures is predicted as €3.1 million, €4.5 million and €4.3 million respectively.

The cost-utility analysis in the prostatectomy-only model, based on an annual steady state caseload of 200 procedures, predicted an incremental cost effectiveness ratio (ICER) of €26,647/QALY (95% CI: €14,241 - €61,220/QALY). There is no specified threshold in Ireland below which an ICER is deemed cost-effective.

To facilitate comparison however, economic evaluations of other interventions in an Irish setting which have been adopted include: population-based colorectal cancer screening (€1,696/QALY);[154] human papillomavirus vaccination programme at €17,383/life year gained (LYG);[155] universal infant pneumococcal conjugate vaccination at €5,997/LYG;[156] and of universal infant hepatitis B vaccination at €37,018/LYG.(157) Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days to return to normal activity is significantly shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a societal cost benefit which has not been factored into these models.

7.4 Organisation and training requirements

The introduction of a new robot-assisted surgery programme in an organisation will introduce new processes and change existing ones. For example, robot-assisted surgery increases theatre time and associated costs per procedure. This is increased further in the early stages of implementation when staff are new to the technology. Arrangements for leadership, identification of multidisciplinary robot-assisted surgery teams, coordination of access to the programme for a range of specialities, identification of the optimal theatre space, careful patient selection and a commitment to monitor and report clinical outcomes of the surgeries performed are all issues that should be assessed carefully. Additional arrangements may be required to facilitate access by surgeons from other institutions to the existing robotic-surgery resource.

There will be significant training requirements for individual surgeons in an organisation if they have not previously been fellowship trained in the technique in another institution. It is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of robotic surgery will fall to the various surgical training bodies. Ongoing training to ensure currency of skills and training of other theatre staff and auxiliary staff is required. The use of designated training programmes and a system of mentoring by experienced staff is recommended.

Robot-assisted surgery has a significant capital and overhead cost. The incremental cost per case is, however, reduced in organisations with a high surgical caseload. A high surgical caseload can be achieved by using the device across a range of specialities, or within organisations with an ability to undertake the volumes of prostatectomy and hysterectomy cases that have been modelled in the economic analysis. Further, there is existing capacity in the Irish healthcare system in the area of robot-assisted surgery and this capacity could be considered prior to any new investment in the technology in other facilities.

7.5 Ethical issues

Potential ethical issues arising from a decision to adopt, not to adopt, or to adopt in a limited manner, robot-assisted surgery are considered as part of this HTA.

A decision not to invest may result in ethical issues regarding the equity of access to healthcare, autonomy and justice. However, healthcare budgets are finite and an individual's right to choose certain treatments or services may conflict with other values or priorities of decision making, such as the need to benefit the wider community.

A decision to invest in robot-assisted surgery may have implications for the resource allocation of existing technologies and services for a given finite healthcare budget. Decisions to allocate resources within the public health system, or to allocate services to one group rather than another, should be open and transparent. Policy makers should strike a balance between patient expectations and the fair distribution of resources in order to ensure the best medical outcomes for the most people. In the case of robot-assisted surgery, an assessment of the existing capacity in the Irish healthcare system should be explored by the HSE prior to any new investment decision.

Limited adoption of robot-assisted surgery would raise further issues of equity and justice if a restricted number of patients benefitted from the location of that service. Improving access to centralised services may be an important consideration.

Informed patient consent is a key ethical principle in the context of robot-assisted surgery. Patients should be advised that the technique is new, the potential risks, alternative interventions and the number of such procedures that have been undertaken by the surgeon. This should help enhance patient autonomy, patient decision-making, and the promotion of a culture of openness and accountability and ultimately supporting physician-patient trust. It is within a surgeon's rights not to adopt a new technology, but their duty of care is to refer patients to another surgeon if the alternative service is requested.

7.6 Conclusions

Prostatectomy and hysterectomy are the two procedures for which the most evidence existed at the time of this HTA in relation to robot-assisted surgery, and represent the only procedures for which firm conclusions can be made. However, the quality of the evidence to support clinical-effectiveness was poor. This should be taken into account when interpreting the findings of this HTA.

Evidence available at the time of this HTA indicated that robot-assisted prostatectomy procedures were superior to open prostatectomy procedures across a range of outcomes evaluated. There is a decreased risk of positive surgical margins for pathological stage pT2 tumours, superior functional outcomes (urinary continence and sexual function) and a reduction in peri-operative transfusion requirements. Overall duration of stay is reduced. The procedure is, however, associated with a longer operating time.

The available evidence indicates that the benefits of robot-assisted prostatectomy over laparoscopic approaches are minor. There are comparable oncologic outcomes, marginal improvements in urinary continence and equivocal data on sexual function. Reductions in length of stay are obtained, although these are less pronounced than those reductions obtained by comparison with open surgery. No significant differences were observed for transfusion, operative time or in the rate of conversion to open surgery.

Robot-assisted hysterectomy when compared with open surgery is associated with a reduction in estimated blood loss, lower risk of transfusion or complications and shorter hospital stays. Operating times are, however, longer. Compared to conventional laparoscopic hysterectomy, the difference in the reported results for each of these outcomes is substantially reduced, with no significant difference in operating times. Unlike prostatectomy, there is an absence of data on functional or oncological outcomes (where applicable) for robot-assisted hysterectomy. Evidence to support the use of robot-assisted surgery for a range of other urology, gynaecology, cardiac and head and neck procedures was limited in quantity and quality. Based on the review it is concluded that robot-assisted surgery is safe and feasible for a range of such indications and may provide comparable, but not necessarily superior, outcomes to conventional surgical techniques. Additional, higher quality research is required for these indications.

Robot-assisted surgery is more ergonomic than laparoscopic surgery for the operating surgeon. However this ergonomic benefit does not apply to the rest of the surgical team, including the assisting surgeon. Mechanical or instrument failure can arise during robot-assisted surgery, which if unrecoverable, can necessitate conversion of the procedure to open surgery in up to 0.6% of cases.

A cost-utility analysis of robot-assisted prostatectomy was carried out as there is data available to demonstrate improved clinical outcomes for patients. This predicted an incremental cost effectiveness ratio (ICER) of €26,647/QALY (95% CI: €14,241 – €61,220/QALY). There is no specified threshold in Ireland below which an ICER is deemed cost-effective. To facilitate comparison, however, economic evaluations of other interventions in an Irish setting which have been adopted include:

- population-based colorectal cancer screening (€1,696/QALY);[154]
- human papillomavirus vaccination programme at €17,383/life year gained (LYG);[155]
- universal infant pneumococcal conjugate vaccination at €5,997/LYG;[156]
- universal infant hepatitis B vaccination at €37,018/LYG.[157]

Based on 'willingness to pay' thresholds, the probability of robot-assisted surgery being cost-effective is 0.20 at a threshold of €20,000 per QALY, 0.63 at €30,000 per QALY and 0.85 at €40,000 per QALY.

The economic models used in this study are restricted to the HSE perspective and only incorporate direct costs. The number of days for patients to return to normal activity is significantly shorter after robot-assisted surgery compared to open surgery. As such, robot-assisted surgery may offer a societal cost benefit which has not been factored into these models.

A robot-assisted surgical procedure has an incremental cost over conventional open or laparoscopic approaches. The increased costs associated with the technology (equipment purchase, maintenance, consumables, personnel and theatre time) are partly offset by the reduction in length of stay in hospital. In developed economic models in this HTA, these incremental procedure costs ranged from €2,487 to €3,019 for prostatectomy and hysterectomy respectively at the steady state caseloads indicated. The incremental budget impact for the publicly funded system for introducing a single robot ranged from €3.1 million to €4.5 million, for prostatectomy and hysterectomy procedures respectively, over a five-year period. There is a projected reduction in bed days of 360 and 565 annually for the prostatectomy and hysterectomy models respectively.

Robot-assisted surgery has a significant capital and overhead cost. The incremental cost per case is, however, reduced in organisations with a high surgical caseload. A high surgical caseload can be achieved by using the device across a range of specialities, or within organisations with an ability to undertake the volumes of prostatectomy and hysterectomy cases that have been modelled in the economic analysis. Further, there is existing capacity in the Irish healthcare system in the area of robot-assisted surgery and this capacity could be considered prior to any new investment in the technology in other facilities.

There are significant issues to be considered by an organisation prior to the introduction of a new robotic surgery programme. Arrangements for training, leadership, identification of multidisciplinary robot-assisted surgery teams, coordination of access to the programme for a range of specialities, identification of the optimal theatre space, careful patient selection and a commitment to monitor and report clinical outcomes of the surgeries performed are all issues that should be assessed carefully. Additional arrangements may be required to facilitate access to the robot device by surgeons from other institutions.

Finally, any decision in relation to the provision of robot-assisted surgery may give rise to ethical issues regarding the equity of access to healthcare, autonomy and justice. However, healthcare budgets are finite and the allocation of resources to this technology may conflict with other values or priorities of decision making, such as the need to benefit the wider community.

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9. Glossary of terms

Absolute risk reduction	A measure of treatment effect that compares the probability (or mean) of a type of outcome in the control group with that of a treatment group.
Adenocarcinoma	A malignant tumour formed from glandular structures in epithelial tissue.
Adnexa	Conjoined, subordinate, or associated anatomic parts e.g., the uterine adnexa include the ovaries and fallopian tubes.
Adnexectomy	Excision of the uterine tube and ovary.
Adrenalectomy	Surgical removal of one or both adrenal glands.
Adjuvant radiotherapy	Radiotherapy given to a patient in addition to surgical treatment (e.g. prostatectomy) when it is considered that the patient may be at elevated risk of relapse.
Adverse event	Any noxious, pathological or unintended change in anatomical, physical or metabolic functions as indicated by physical signs, symptoms and/or laboratory changes occurring in any phase of a clinical study whether or not considered treatment related. It includes exacerbation of pre-existing conditions or events, intercurrent illnesses, accidents, drug interaction or the significant worsening of disease.
Analgesia	Relief from pain.
Anastomosis	The joining together two hollow tubes usually to restore continuity after resection.
Asymptomatic	Without symptoms. For example, an asymptomatic infection is an infection with no symptoms.
Autonomy	The patient's right of self-determination concerning medical care. It may be used in various senses including freedom of action, effective deliberation and authenticity. It supports such moral and legal principles as respect for persons and informed consent. Making decisions for oneself, in light of a personal system of values and beliefs.
Bayesian analysis	A statistical approach that can be used in single studies or meta-analysis which explicitly incorporates a prior probability distribution based on subjective opinion and objective evidence, such as the results of previous research.

Bias	In general, any factor that distorts the true nature of an event or observation. In clinical investigations, a bias is any systematic factor other than the intervention of interest that affects the magnitude of (i.e. tends to increase or decrease) an observed difference in the outcomes of a treatment group and a control group.
Bilateral pelvic lymphadenectomy	Surgical removal of lymph nodes from both sides of pelvis.
Bladder Diverticulectomy	The repair of diverticulum, which is an abnormal sac or pouch causing incomplete voiding of the urinary bladder.
Blinding (masking)	Also known as 'masking', the knowledge of patients and/or investigators about whether individual patients are receiving the investigational intervention(s) or the control (or standard) intervention(s) in a clinical trial.
BMI	Body Mass Index.
Brachytherapy	A form of radiotherapy where a radiation source is placed inside or next to the area requiring treatment.
Budget impact analysis	The financial impact of the introduction of a technology or service on the capital and operating budgets of a government or agency.
Capital costs	The non-recurring cost of investment in items that remains useful beyond the period when costs are incurred.
Cardiopulmonary bypass	A type of heart surgery where the blood is taken from the body via a device and diverted through a heart-lung machine which oxygenates the blood prior to returning it to the systemic circulation under pressure. This allows the surgeon adequate time to perform primary heart surgery.
Cardiothoracic	Of or pertaining to both the heart and the chest.
Case series	An uncontrolled study (prospective or retrospective) of a series (succession) of consecutive patients who receive a particular intervention and are followed to observe their outcomes.
Case-control study	A retrospective observational study designed to determine the relationship between a particular outcome of interest (e.g. disease or condition) and a potential cause (e.g. an intervention, risk factor, or exposure).

Case-mix	Features of a study population that may influence the outcome or the choice of treatment (e.g. severity of disease, coexisting conditions); such features must be taken into account when assessing treatment outcomes.
Cervix	The narrow lower or outer end of the uterus.
Clinical outcome	An outcome of major clinical importance that is defined on the basis of the disease being studied (e.g. fracture in osteoporosis, peptic ulcer healing and relapse rates).
Clinical significance	A conclusion that an intervention has an effect that is of practical meaning to patients and healthcare providers.
Clinical trial	A carefully controlled and monitored research study on human subjects or patients evaluating one or more health interventions (including diagnostic methods and prophylactic interventions). Each trial is designed to answer specific scientific questions.
Cohort study	An observational study in which outcomes in a group of patients that received an intervention are compared with outcomes in a similar group i.e. the cohort, either contemporary or historical, of patients that did not receive the intervention.
Comparator	The technology to which an intervention is compared.
Complication	A secondary disease or condition that develops in the course of a primary disease or condition and arises either as a result of it or from independent causes.
Concealment of allocation	The process used to assign patients to alternative groups in an RCT in a manner that prevents foreknowledge (by the person managing the allocation as well as the patients) of this assignment.
Concurrent control	A control group that is observed by investigators at the same time as the treatment group, but that was not established using random assignment of patients to control and treatment groups.
Confidence interval (CI)	Depicts the range of uncertainty about an estimate of a treatment effect.
Confounding factor	A factor that is causally linked to the treatment (exposure) and the outcome under study.
Congenital	Present from or before birth.

Console time	The time taken to remove the organ using the console.
Contamination	In clinical trials, the inadvertent application of the intervention being evaluated to people in the control group or inadvertent failure to apply the intervention to people assigned to the intervention group.
Continence	The ability to retain a bodily discharge voluntarily.
Contraindication	A clinical symptom or circumstance indicating that the use of an otherwise advisable intervention would be inappropriate.
Control group	A group of patients that serves as the basis of comparison when assessing the effects of the intervention of interest that is given to the patients in the treatment group.
Controlled clinical trial (CCT)	A prospective experiment in which investigators compare outcomes of a group of patients receiving an intervention to a group of similar patients not receiving the intervention. Not all clinical trials are randomised controlled trials (RCTs), though all RCTs are clinical trials. See Randomised Controlled Trial.
Conversion	Changing from one type of surgery to another.
Coronary artery bypass grafting	A piece of a vein from another place in the body, such as a leg, is attached to the coronary artery above and below a narrowed area or blockage. This allows blood to bypass the blockage and proceed onto the cardiac muscle.
Cost per QALY	A measure used in cost utility analysis (CUA) to assist in comparisons among programmes; expressed as monetary cost per unit of outcome.
Cost-benefit analysis	A comparison of alternative interventions in which costs and outcomes are quantified in common monetary units.
Cost-effectiveness analysis (CEA)	A comparison of alternative interventions in which costs are measured in monetary units and outcomes are measured in non-monetary units, e.g. reduced mortality or morbidity. (See also Cost per QALY).
Cost-minimisation analysis (CMA)	A determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes.

Cost-utility analysis (CUA)	A form of cost-effectiveness analysis of alternative interventions in which costs are measured in monetary units and outcomes are measured in terms of their utility, usually to the patient, e.g. using QALYs.
Credentialing	The systematic approach to the collection, review, and verification of a practitioner's professional qualification.
Cystectomy	The removal of all or a portion of the urinary bladder.
Didactic	Intended to instruct.
Discount rate	The interest rate used to discount or calculate future costs and benefits so as to arrive at their present values, e.g. 3% or 5%. This is also known as the opportunity cost of capital investment.
Discounting	The process used in cost analyses to reduce mathematically future costs and/or benefits/outcomes to their present value.
Docking time	The time taken to position the robot alongside the patient at the optimal height and distance from the patient.
DRG	The diagnosis related group (DRG) is a code that classifies a hospital episode according to three components: the major diagnosis category; surgical, medical or 'other' episode type; and severity of episode. DRGs are used as the basis for costing hospital episodes. In Ireland the Australian refined (AR) version of DRGs are used.
Economic evaluation	The comparative analysis of alternative courses of action, in terms of their costs and consequences.
Economic model	In healthcare, a mathematical model of the patient pathway that describes the essential choices and consequences for the interventions under study and can be used to extrapolate from intermediate outcomes to long-term outcomes of importance to patients.
Effect size	A generic term for the estimate of effect determined in a study.
Effectiveness	The benefit (e.g. to health outcomes) of using a technology for a particular problem under general or routine conditions.
Efficacy	The benefit of using a technology for a particular problem under ideal conditions, for example, in a laboratory setting or within the protocol of a carefully managed randomized controlled trial.

Efficiency	The extent to which the maximum possible benefit is achieved out of available resources.
Electrocautery	To burn, sear or destroy tissue using an electric current.
Endometriosis	The presence and growth of functioning endometrial tissue in places other than the uterus that often results in severe pain and infertility.
Epidemiology	The study of the distribution and determinants of health-related states or events in specified populations.
Equipoise	A state of uncertainty regarding whether alternative health care interventions will confer more favorable outcomes, including balance of benefits and harms.
Equity	Fairness in the allocation of resources or treatments among different individuals or groups.
Erectile dysfunction	Chronic inability to achieve or maintain an erection satisfactory for sexual intercourse.
Ergonomics	An applied science concerned with the characteristics of people that need to be considered in designing things that they use in order that people and things will interact most effectively and safely.
Ethics	A general term for what is often described as the science of morality. In philosophy, ethical behaviour is that which is good. The goal of a theory of ethics is to determine what is good, both for the individual and for society as a whole.
Evidence-based medicine	The use of current best evidence from scientific and medical research to make decisions about the care of individual patients. It involves formulating questions relevant to the care of particular patients, systematically searching the scientific and medical literature, identifying and critically appraising relevant research results, and applying the findings to patients.
External validity	The extent to which the findings obtained from an investigation conducted under particular circumstances can be generalized to other circumstances.
Fibroids	Resembling, forming, or consisting of fibrous tissue.
Forest plot	A plot showing a series of lines and symbols which represent the results of a meta-analysis.

Funnel plot	A graphical display of sample size plotted against effect size that can be used to investigate publication bias.
Gastrointestinal	Of or relating to the stomach and the intestines.
Gleason Score	A system of grading prostate cancer. The Gleason grading system assigns a grade to each of the two largest areas of cancer in the tissue samples. Grades range from 1 to 5, with 1 being the least aggressive and 5 the most aggressive. The Gleason Score is the sum of the Gleason grades of the two largest areas of cancer in the tissue samples.
Gold standard	The method, procedure or measurement that is widely accepted as being the best available against which new interventions should be compared.
Gry	The gray (Gy) is the SI unit of absorbed radiation dose of ionizing radiation.
Haptic	Relating to or based on the sense of touch.
Health economics	The application of the principles and rules of economics in the area of health and healthcare, including the evaluation of health policy and the health system from an economic perspective; health system planning; the demand for and supply of healthcare; economic evaluation of medical technologies and procedures; the determinants of health and its valuation, and analysis of the performance of healthcare systems in terms of equity and allocative efficiency.
Health outcomes	The results or impact on health of any type of intervention (or lack of) (e.g. a clinical procedure, health policy or programme, etc.).
Health-related quality of life	A multi-dimensional measure comprising the physical and mental health perceptions of a patient in terms of health status, health risks, functional status, social support, and socioeconomic status.
Health technology	Any intervention that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. This includes the pharmaceuticals, devices, procedures and organisational systems used in healthcare.

Health technology assessment (HTA)	Health technology assessment (HTA): the systematic evaluation of properties, effects, and/or impacts of health care technology. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in healthcare. HTA is conducted by interdisciplinary groups using explicit analytical frameworks drawing from a variety of methods.
Herniorrhaphy	A surgical procedure for correcting hernia.
Heterogeneity	In meta-analysis heterogeneity refers to variability or differences in the estimates of effects among studies. Statistical tests of heterogeneity are used to assess whether the observed variability in study results (effect sizes) is greater than that expected to occur by chance.
Hierarchy of evidence	Studies are often grouped into a hierarchy according to their validity or the degree to which they are not susceptible to bias. The hierarchy indicates which studies should be given most weight in an evaluation.
Historical control	A control group that is chosen from a group of patients who were observed at some previous time.
HTA	Health technology assessment.
Hysterectomy	Surgical removal of the uterus.
IIEF-5	International Index of Erectile Dysfunction. A diagnostic tool for erectile dysfunction in men.
Incidence	The rate of occurrence of new cases of a disease or condition in a population at risk during a given period of time, usually one year.
Incontinence	Inability of the body to control the evacuative functions.
Incontinence pads	A pad worn in underwear to absorb urine/faeces.
Incremental cost	The additional costs that one intervention imposes over another.
Incremental cost effectiveness ratio (ICER)	The additional cost of the more expensive intervention as compared with the less expensive intervention divided by the difference in effect or patient outcome between the interventions, e.g. additional cost per QALY.

Indication	A clinical symptom, risk factor, or circumstance for which the use of a particular intervention would be appropriate as determined or specified.
Informed consent	The legal and ethical requirement that no significant medical procedure can be performed until the competent patient has been informed of the nature of the procedure, risks and alternatives, as well as the prognosis if the procedure is not done. The patient must freely and voluntarily agree to have the procedure done.
Inguinal herniorrhaphy	An operation for hernia in the groin area that involves opening the hernial sac, returning the contents to their normal place, obliterating the hernial sac, and closing the opening with strong sutures.
International Network of Agencies for Health Technology Assessment (INAHTA)	An international association of non-profit, health technology assessment agencies (www.inahta.org).
Intracorporeal	Situated or occurring within the body.
Intraoperative	Occurring, carried out, or encountered in the course of surgery.
Intuitive Surgical Inc.	The name of the American company who designed and sells the Da Vinci Surgical System.
Investigational Device Exemption (IDE)	A regulatory category and process in which the US Food and Drug Administration (FDA) allows specified use of an unapproved health device in controlled settings for purposes of collecting data on safety and efficacy/effectiveness; this information may be used subsequently in a pre-marketing approval application.
Justice	The principle that states that fairness requires equals to be treated equally.
Laparoscope	A usually rigid endoscope that is inserted through an incision in the abdominal wall and is used to examine visually the interior of the peritoneal cavity.
Laparoscopy	Visual examination of the inside of the abdomen by means of a laparoscope.
Laparotomy	A surgical incision into the abdominal cavity, for diagnosis or in preparation for major surgery.

Learning curve	Progress in learning measured against time to achieve mastery in the task i.e. the time taken to learn how to become very good at performing robotic surgery.
Licensing	A marketing authorisation for medicines which meet standards of safety, quality and efficacy.
Literature review	A summary and interpretation of research findings reported in the literature. May include unstructured qualitative reviews by single authors as well as various systematic and quantitative procedures such as meta-analysis. (Also known as overview.)
Localised	Confined or restricted to a particular location.
LRP	Laparoscopic radical prostatectomy.
Lymphadenectomy	The surgical removal of one or more groups of lymph nodes.
Malignant	Tending to invade normal tissue or to recur after removal; cancerous.
MAUDE	Manufacturer and User Facility Device Experience. MAUDE data represents report of adverse events involving medical devices. The data are collected by the FDA.
Mean (arithmetic mean)	The average value, calculated by summing all the observations and dividing by the number of observations.
Median	The middle value in a ranked group of observations. This can be a better estimate of the average value if there are extreme outlying values that may skew the arithmetic mean.
MEDLINE	An electronic database produced by the United States National Library of Medicine.
Melanoma	A tumour of melanin-forming cells, typically a malignant tumour associated with skin cancer.
Meta-analysis	Systematic methods that use statistical techniques for combining results from different studies to obtain a quantitative estimate of the overall effect of a particular intervention or variable on a defined outcome.

Metastasis	The development of secondary malignant growths at a distance from the primary site.
Methodological quality	The extent to which the design and conduct of a study are likely to have prevented systematic errors (bias).
Minimally invasive surgery	Surgery done with only a small incision or no incision at all, such as through a cannula with a laparoscope or endoscope.
Mitral valve repair	Surgical repair of the valve in the heart that guards the opening between the left atrium and the left ventricle.
Myomectomy	Surgical excision of a myoma or fibroid.
Narrative review	An overview of primary studies which have not been identified or analysed in a systematic (standardised and objective) way.
Natural history	The course of a disease from onset (inception) to resolution. Many diseases have well-defined stages such as pathological onset, pre-symptomatic and clinically manifest disease.
Neoplasm	A new and abnormal growth of tissue in some part of the body, especially as a characteristic of cancer.
Nephrectomy	Surgical removal of a kidney.
Null hypothesis	In hypothesis testing, the hypothesis that an intervention has no effect, i.e. that there is no true difference in outcomes between a treatment group and a control group.
Observational study	A study in which the investigators do not manipulate the use of, or deliver, an intervention (e.g. do not assign patients to treatment and control groups), but only observe patients who are (and sometimes patients who are not as a basis of comparison) exposed to the intervention, and interpret the outcomes.
Obstetrics	The branch of medicine and surgery concerned with childbirth and the care of women giving birth.
Odds ratio (OR)	A measure of treatment effect that compares the probability of a type of outcome in the treatment group with the outcome of a control group.
Oesophagectomy	The surgical removal of all or part of the oesophagus.
Oncology	The study of tumours.
Opportunity cost	The amount that could be spent on alternative healthcare strategies if the health technology in question was not used.

Oropharyngeal carcinoma	A malignant tumour of epithelial origin in the area of the oropharynex.
Oropharynx	The part of the pharynx between the soft palate and the epiglottis.
ORP	Open radical prostatectomy.
Outcomes	Components of patients' clinical and functional status after an intervention has been applied.
Outlier	An observation differing so widely from the rest of the data as to lead one to suspect that a gross error may have been committed.
Ovaries	One of the typically paired essential female reproductive organs that produce eggs and in vertebrates, female sex hormones, that occur in the adult human as oval flattened bodies.
p value	In hypothesis testing, the probability that an observed difference between the intervention and control groups is due to chance alone if the null hypothesis is true.
Parametrium	The connective tissue and fat adjacent to the uterus.
Pathology	The anatomic and physiological deviations from the normal that constitute disease or characterize a particular disease.
Patient selection bias	A bias that occurs when patients assigned to the treatment group differ from patients assigned to the control group in ways that can affect outcomes, e.g. age or disease severity.
Peer review	The process by which manuscripts submitted to health, biomedical, and other scientifically oriented journals and other publications are evaluated by experts in appropriate fields (usually anonymous to the authors) to determine if the manuscripts are of adequate quality for publication.
Performance bias	Systematic differences in care provided apart from the intervention being evaluated. For example, if patients know they are in the control group they may be more likely to use other forms of care, patients who know they are in the experimental (intervention) group may experience placebo effects, and care providers may treat patients differently according to what group they are in.
Perineal	Relating to the area of tissue that marks externally the approximate boundary of the pelvic outlet and gives passage to the urogenital ducts and rectum; also the area between the anus and the posterior part of the external genitalia especially in the female.

Perioperative	Relating to, occurring in, or being the period around the time of a surgical operation.
Peritoneum	The membrane lining the cavity of the abdomen and covering the abdominal organs.
Phosphodiesterase Type-5 Inhibitors	A group of drugs used to treat erectile dysfunction in men. They work by suppressing a phosphodiesterase enzyme thereby suppressing the enzyme's inhibitory effect on the hormone cyclic GMP, and that enables the cyclic GMP produced during sexual arousal to initiate the muscular and vascular changes which produce an erection.
Placebo	An inactive substance or treatment given to satisfy a patient's expectation for treatment. In some controlled trials (particularly investigations of drug treatments) placebos that are made to be indistinguishable by patients (and providers when possible) from the true intervention are given to the control group to be used as a comparative basis for determining the effect of the investigational treatment.
Placebo effect	The effect on patient outcomes (improved or worsened) that may occur due to the expectation by a patient (or provider) that a particular intervention will have an effect. The placebo effect (also known as the Hawthorne effect) is independent of the true effect (pharmacological, surgical, etc.) of a particular intervention.
Positive surgical margin	The border of tissue between the outer edge of the tissue surrounding the tumour and the tumour is called the surgical margin. Positive margin occurs when cancer cells or tumour extends into the tissue outside of the tumour.
Postoperative	Relating to, occurring in, or being the period following a surgical operation.
Preceptor	A teacher or instructor.

Precision	1. The degree to which a measurement (e.g. the mean estimate of a treatment effect) is derived from a set of observations having small variation (i.e. close in magnitude to each other). A narrow confidence interval indicates a more precise estimate of effect than a wide confidence interval. A precise estimate is not necessarily an accurate one. 2. A measure of the likelihood of random errors in the results of a study, meta-analysis or measurement. Confidence intervals around the estimate of effect from each study are a measure of precision, and the weight given to the results of each study in a meta-analysis (typically the inverse of the variance of the estimate of effect) is a measure of precision (i.e. the degree to which a study influences the overall estimate of effect in a meta-analysis is determined by the precision of its estimate of effect).
Preference	Preference is a generic term and a concept that refers to the desirability of a health outcome. Both utility and value are special cases of the general term/concept of preference.
Prevalence	The number of people in a population with a specific disease or condition at a given time, usually expressed as a proportion of the number of affected people to the total population.
Primary (research) study	'Original research' in which data are first collected. The term primary research is sometimes used to distinguish it from 'secondary research' (re-analysis of previously collected data), meta-analysis, and other ways of combining studies (such as economic analysis and decision analysis).
Procedure block	Every surgical procedure has an associated procedure code. A procedure block is a 4-digit code used to group related surgical procedure codes together.
Proctor	Someone who supervises a student during an examination or other activity.
Prolapse	The falling down or slipping of a body part from its usual position or relations.
Prospective study	A study in which the investigators plan and manage the intervention of interest in selected groups of patients. As such, investigators do not know what the outcomes will be when they undertake the study.

Prostate	A firm partly muscular partly glandular body that is situated about the base of the mammalian male urethra and secretes an alkaline viscid fluid which is a major constituent of the ejaculatory fluid. Also called the prostate gland.
Prostate Specific Antigen	A protein produced by the cells of the prostate gland. Used as a marker for prostate cancer.
Prostatectomy	Surgical removal or resection of the prostate gland.
PSA	Prostate Specific Antigen.
PSM	Positive Surgical Margin.
pT2	Prostate cancer cells are confined to the prostate gland organ.
pT3	Prostate cancer cells have extended beyond the prostate gland.
Publication bias	Unrepresentative publication of research reports that is not due to the scientific quality of the research but to other characteristics, e.g. tendencies of investigators to submit, and publishers to accept, positive research reports (i.e. ones with results showing a beneficial treatment effect of a new intervention).
PubMed	A service of the National Library of Medicine that includes over 14 million citations for biomedical articles back to the 1950s.
Pyeloplasty	Plastic surgery of the renal pelvis of a kidney.
Quality of evidence	Degree to which bias has been prevented through the design and conduct of research from which evidence is derived.
Quality of life (QOL)	See Health-related quality of life.
Quality score	A value assigned to represent the validity of a study either for a specific criterion, such as allocation concealment, or overall.
Quality-adjusted life year (QALY)	A unit of healthcare outcomes that adjusts gains (or losses) in years of life subsequent to a healthcare intervention by the quality of life during those years.

RAH	Robot-assisted hysterectomy.
RALP	Robot-assisted laparoscopic prostatectomy.
Random effects model	A statistical model sometimes used in meta-analysis in which both within-study sampling error (variance) and between-studies variation are included in the assessment of the uncertainty (confidence interval) of the results of a meta-analysis.
Randomised controlled trial (RCT)	An experiment of two or more interventions in which eligible people are allocated to an intervention by randomisation. The use of randomisation then permits the valid use of a variety of statistical methods to compare outcomes of the interventions.
RARP	Robot-assisted radical prostatectomy.
RCT	see Randomised Controlled Trial.
Relative risk (RR) (risk ratio)	The ratio of (statistical) risk in the intervention group to the risk in the control group. A relative risk of one indicates no difference between comparison groups. For undesirable outcomes an RR that is less than one indicates that the intervention was effective in reducing the risk of that outcome.
Reliability	The extent to which an observation that is repeated in the same, stable population yields the same result (i.e. test-retest reliability).
Resection	Surgical removal of part of an organ or structure.
Retroperitoneal	Anatomical space in the abdominal cavity behind the peritoneum.
Retropubic	Behind the pubic bone.
Retrospective study	A study in which investigators select groups of patients that have already been treated and analyse data from the events experienced by these patients.
Review	1. A systematic review. 2. A review article in the medical literature which summarises a number of different studies and may draw conclusions about a particular intervention. Review articles are often not systematic. Review articles are also sometimes called overviews.

Risk assessment	The qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards or from the absence of beneficial influences.
Risk difference	See Absolute risk reduction.
Risk factor	An aspect of a person's condition, lifestyle or environment that increases the probability of occurrence of a disease. For example, cigarette smoking is a risk factor for lung cancer.
Risk ratio	See Relative risk.
Roux-en-y Bypass	A surgical procedure in the treatment of severe obesity that involves partitioning off part of the upper stomach to form a small pouch.
RR	See Relative risk.
Sacrocolpopexy	An operation that aims to provide support for the pelvic organs in their natural position. This is achieved by attaching a piece of material (mesh), usually from the top and back of the vagina, to a ligament of the lower back bone.
Sample size	Sample size: the number of patients studied in a trial, including the treatment and control groups, where applicable.
SD	Standard deviation.
Secondary research	Research that does not generate primary data but that involves the qualitative or quantitative synthesis of information from multiple primary studies. Examples are literature reviews, meta-analyses, decision analyses and consensus statements.
Selection bias	Error due to systematic differences in characteristics between those who are selected for study and those who are not.
Sensitivity analysis	A means to determine the robustness of a mathematical model or analysis (such as a cost-effectiveness analysis or decision analysis) that tests a plausible range of estimates of key independent variables (e.g. costs, outcomes, probabilities of events) to determine if such variations make meaningful changes the results of the analysis.
SHIM	Sexual Health Inventory for Men. A five-question diagnostic tool for erectile dysfunction in men.
Single-arm studies	Usually refers to an analysis or evaluation where groups receiving the new technology and the standard (control) are taken from different studies for comparison.

Skin-to-skin time	Used with reference to operating times. Usually the time from the first incision to skin closure.
Staging	The classification of the severity of a disease in distinct stages on the basis of established signs and symptomatic criteria.
Standard deviation (SD)	A measure of the dispersion of a set of data from its mean.
Standardised mean difference (SMD)	The difference between two means divided by an estimate of the within-group standard deviation. When an outcome (such as pain) is measured in a variety of ways across studies (using different scales) it may not be possible directly to compare or combine study results in a systematic review. By expressing the effects as a standardised value the results can be combined since they have no units.
Statistical significance	Statistical significance: a conclusion that an intervention has a true effect, based upon observed differences in outcomes between the treatment and control groups that are sufficiently large so that these differences are unlikely to have occurred due to chance, as determined by a statistical test.
Sternotomy	An incision into or through the sternum.
Study validity	The degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).
Subgroup analysis	The process of analysing data from subpopulations of patients. Sub-group analyses should be planned at the outset of the study and even then their results should only be considered as exploratory.
Surrogate	Something that serves as a substitute.
Systematic review (systematic overview)	A form of structure literature review that addresses a question that is formulated to be answered by analysis of evidence, and involves objective means of searching the literature, applying predetermined inclusion and exclusion criteria to this literature, critically appraising the relevant literature, and extraction and synthesis of data from the evidence base to formulate findings.

Tactile	Relating to, mediated by, or affecting the sense of touch.
Technological imperative	The inclination to use a technology that has potential for some benefit, however marginal or unsubstantiated, based on an abiding fascination with technology, the expectation that new is better, and financial and other professional incentives.
Technology assessment	See Health technology assessment.
Thoracotomy	A surgical opening into the thoracic cavity.
Thymextomy	Surgical removal of the thymus gland.
Thyroidectomy	Surgical excision of thyroid gland tissue.
Tracheotomy	An incision in the windpipe made to relieve an obstruction to breathing.
Treatment effect	The effect of a treatment (intervention) on outcomes, i.e. attributable only to the effect of the intervention. Investigators seek to estimate the true treatment effect using the difference between the observed outcomes of a treatment group and a control group.
Tubal ligation	Binding of the fallopian tubes thereby preventing passage of ova from the ovaries to the uterus serves as a method of female sterilization.
Tubal re-anastomosis	The reuniting (as by surgery or healing) of a divided vessel e.g. tubes.
Ureteral re-implantation	Treatment in ureteral reflux to stop urine moving upwards back into kidneys. The ureter is disconnected from the bladder and re-implanted in a new and longer submucosal tunnel from the luminal side of the bladder.
Urological	Relating to the urinary system or urogenital organs.
Uterine fibroid	A benign tumour of the uterine wall that consists of fibrous and muscular tissue.
Uterus	A muscular, hollow organ of the female reproductive tract. The uterus contains and nourishes the embryo and fetus from the time the fertilized egg is implanted until birth.

Utility	In economic and decision analysis, the desirability of a specific level of health status or health outcome, usually expressed as being between zero and one (e.g. death typically has a utility value of zero and a full healthy life has a value of one).
Validity	The degree to which a result (of a measurement or study) is likely to be true and free of bias (systematic errors). Also, the degree to which a measure or parameter accurately reflects or assesses a concept of interest.
Value	A cardinal measure of the preference for, or desirability of, a specific level of health status or a specific health outcome, measured under certainty.
Variable	Any quantity that varies. A factor that can have different values.
Variance	A measure of the variation shown by a set of observations, defined by the sum of the squares of deviations from the mean, divided by the number of degrees of freedom in the set of observations.
Varicocele	Varicose enlargement of the veins of the spermatic cord producing a soft compressible tumour mass in the scrotum.
Varicocelectomy	Surgical treatment of varicocele by excision of the affected veins often with removal of part of the scrotum.
Vasovaotomy	A surgical procedure that attempts to restore the function of the vas deferens after a vasectomy.
Warm ischemic time	In surgery, the time a tissue/organ remains at body temperature after its blood supply has been reduced or cut off but before it is cooled or reconnected to a blood supply.
Weighted mean difference (WMD)	A method of meta-analysis used to combine measures on continuous scales (such as weight), where the mean, standard deviation and sample size in each group are known.
Willingness to pay (WTP)	The maximum amount that a person is willing to pay: (i) to achieve a particular good health state or outcome, or to increase its probability of occurrence; or (ii) to avoid particular bad health state or outcome, or to decrease its probability.

Appendix 1.

Literature search strategies

1.1 Search strategy for data on effectiveness and safety of robot-assisted surgery for prostatectomy and hysterectomy

The search strategy adopted for the identification of relevant studies comparing robot-assisted surgery to open and laparoscopic surgery for prostatectomy and hysterectomy was modelled on the search documented in the HTA on robot-assisted surgery carried out by the Canadian HTA agency, CADTH[18]. This search strategy was chosen following a review of the evidence base identified by four recent HTAs[8;18-20] and analysis of the search methodology employed by each. The updated search results were individually screened by two independent reviewers according to predefined inclusion criteria, with any disagreements being resolved through discussion. Data extraction tables were prepared and data extraction was performed by two reviewers independently. Any disagreements were again resolved following discussion between the two reviewers. A summary of the search is provided in Table App 1, with a flowchart showing the results provided in Figure App 1 below. The detailed search strategy, including search strings and limits used is also provided.

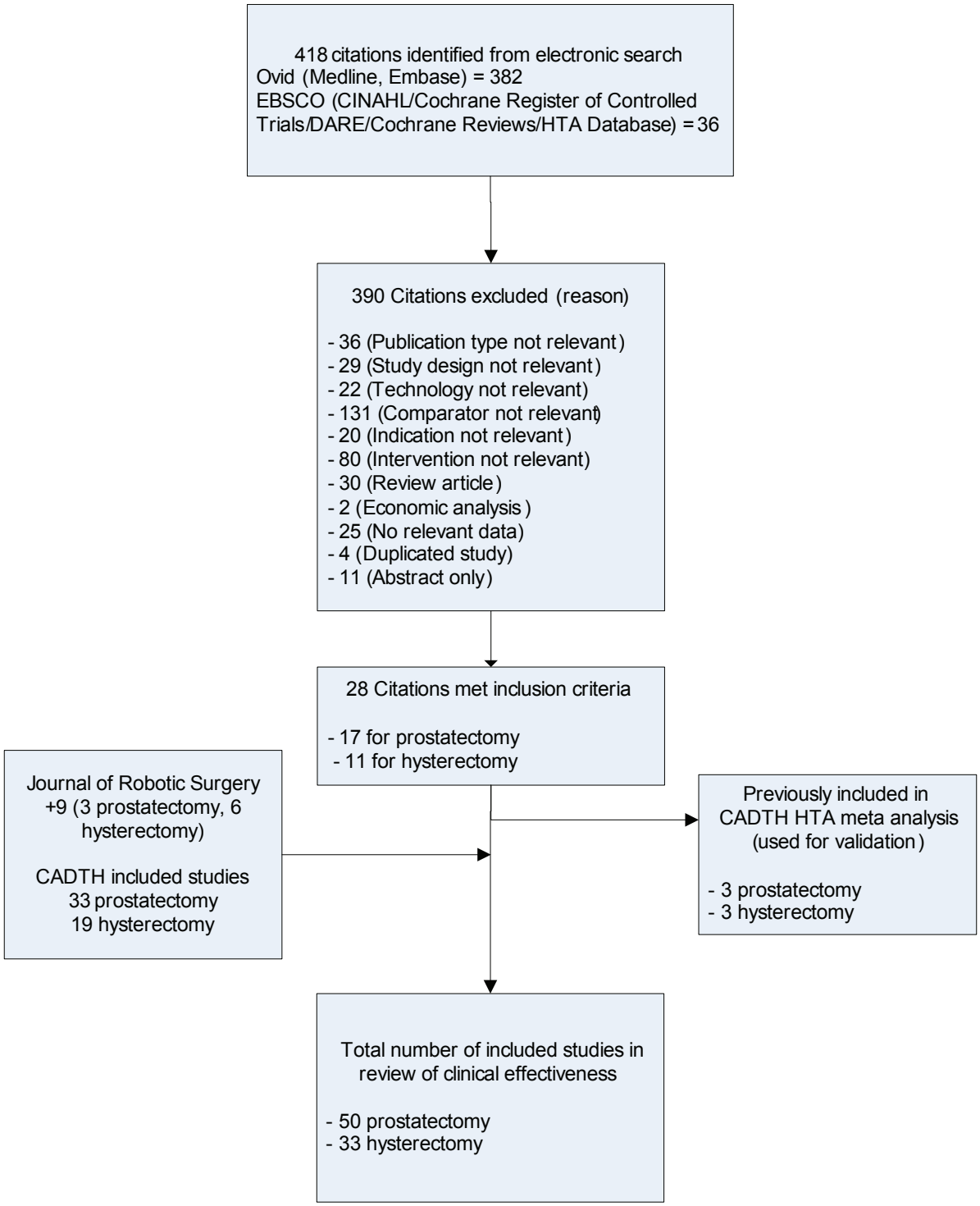
Study quality was assessed using an appraisal form that took into account both study design and study performance, modified from Hailey et al.[21], which was used in the CADTH HTA(18) on robot-assisted surgery. The assessment rates studies on a scale of A to E, where A (overall score 11.5 to 15.0) indicates a high quality with high degree of confidence in study findings; B (overall score 9.5 to 11.0) indicates good quality with some uncertainty regarding the study findings; C (overall score 7.5 to 9.0) indicates fair to good quality with some limitations that should be considered in any implementation of the study findings; D (overall score 5.5 to 7.0) indicates poor to fair quality with substantial limitations in the study findings and should be used cautiously; and E (overall score 1 to 5.0) indicates poor quality with unacceptable uncertainty for study findings.

Further details of the search that was performed, including full search strings, is available on request.

Table App 1 Search summary (prostatectomy and hysterectomy)

Interface	Ovid	EBSCO	Other
Databases	MEDLINE	CINAHL	Journal of Robotic Surgery
	EMBASE	Cochrane Library	
		DARE	
		Cochrane Register of Controlled Trials	
		HTA Database	
Date	25/03/2011		
Study Types	Systematic reviews; meta-analyses; technology assessments; randomized controlled trials; controlled clinical trials; observational studies, clinical practice guidelines		
Limits	English or French language; Year 2010 - 2011		

Figure App 1 Search results for review of clinical effectiveness of robot-assisted surgery versus open and laparoscopic surgery in prostatectomy and hysterectomy



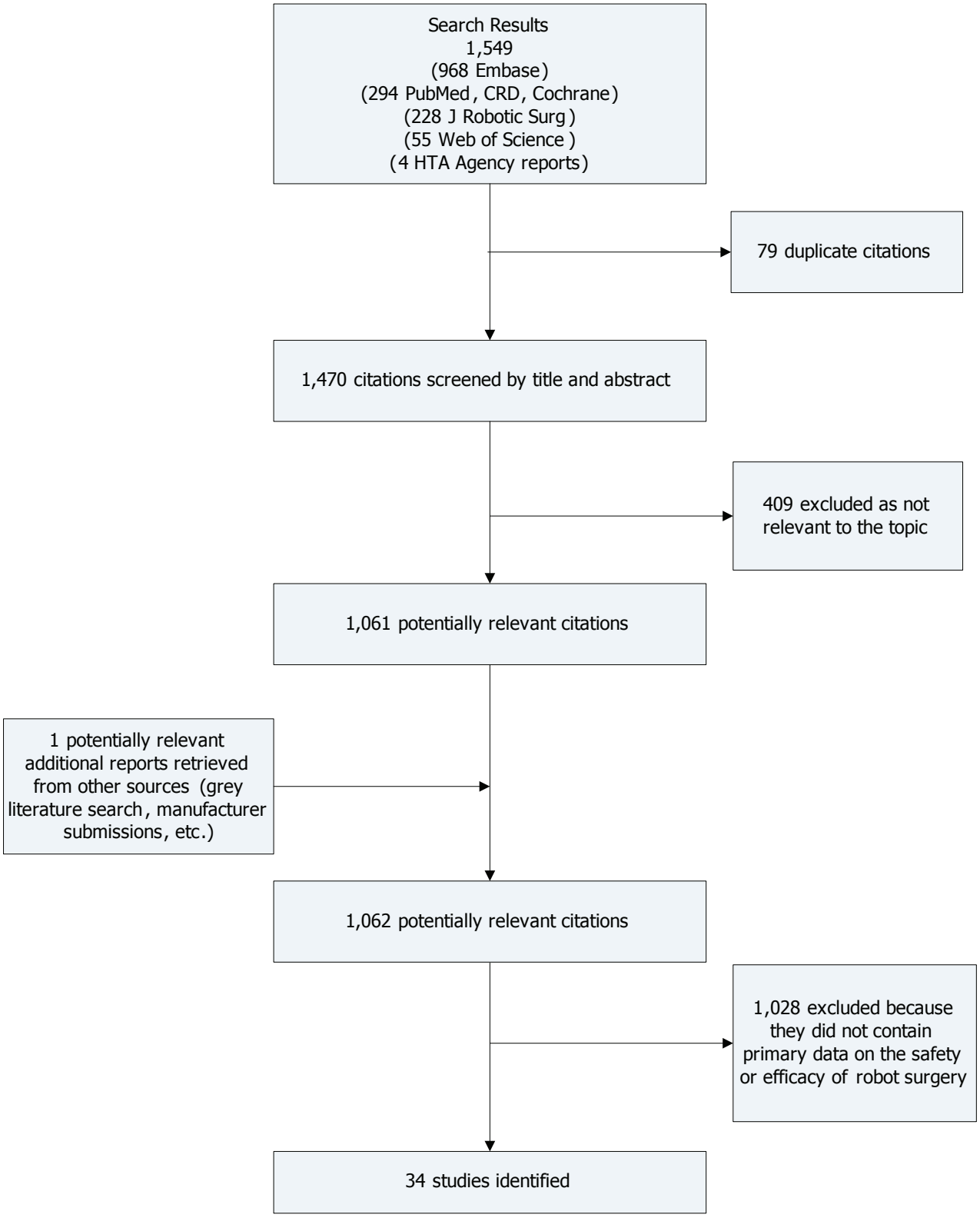
1.2 Search strategy for data on effectiveness and safety of robot-assisted surgery for indications other than prostatectomy and hysterectomy

The search strategy was based on the search strategy used in a HTA conducted by the Belgian agency KCE in 2008.[8] The purpose of this current literature search was to update the KCE search by identifying relevant studies published from October 2008 to January 2011; the included studies are summarised in Chapter 3. The published literature was identified by searching the following sources:

- Pubmed (Medline)
- Centre for Reviews and Dissemination (CRD) database
- Cochrane Library
- Embase
- Journal of Robotic Surgery
- Web of Science
- HTA websites (INAHTA members).

As in the KCE HTA, a search was conducted for systematic reviews, clinical trials, prospective studies, multi-centre trials and HTAs using the MeSH terms 'Robotics' and 'Surgery, computer assisted' and additionally the keywords (surgery) and [(da vinci) or (davinci)]. Full details of the search performed, including complete search strings, are available on request.

Figure App 1.2 Flow chart of included studies (effectiveness and safety of da Vinci® surgical system for indications other than prostatectomy and hysterectomy)



Appendix 2.

Summary of included studies

Table App 2.1 – Prostatectomy (urology): studies retrieved

First Author / year	Study type	Comparator	Country where study was carried out	# Patients in Robot Arm	# Patients in comparator Arm(s)	Total # Patients in Study	# Robotic Surgeons involved in study	Mean age (Robot arm)	Mean age (Comparator arm)	Mean BMI (Robot arm)	Mean BMI (Comparator arm)	Mean PSA level (Robot arm)	Mean PSA level (Comparator arm)	Quality*
Ahlering 2004[56]	Retrospective	Open	US	60	60	120	1	62.9	62.7	26.3	26.5	8.1	8.4	Fair to good
Ball 2006[222]	Prospective	Both	US	82	259	341	2	60	60	N/A	N/A	6	7.51	High
Barocas 2010[39]	Prospective	Open	US	1413	491	1904	4	61	62	N/A	N/A	N/A	N/A	Good
Burgess 2006[159]	Retrospective	Open	US	78	32	110	1	N/A	N/A	N/A	N/A	N/A	N/A	Fair to good
Chino 2009[223]	Retrospective	Open	US	368	536	904	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Good
D'Alonzo 2009[45]	Retrospective	Open	US	256	280	536	7	59	60	N/A	N/A	6	7.3	Fair to good
Drouin 2009[224]	Retrospective	Both	France	71	168	239	3	60.4	61.2	22.6	23.2	7.8	9.05	Good
Durand 2008[225]	Retrospective	Both	France	34	52	86	2	62.2	63.3	N/A	N/A	6.97	8.14	Fair to good
Farnham 2006[226]	Prospective	Open	US	176	103	279	1	59	60	N/A	N/A	6.5	8.3	Fair to good
Ficarra 2006[57]	Prospective	Open	Italy	103	105	208	2	N/A	N/A	N/A	N/A	N/A	N/A	High
Fracalanza 2008[140]	Prospective	Open	Italy	35	26	61	1	N/A	N/A	25.5	26.4	N/A	N/A	Fair to good
Hakimi 2009[40]	Retrospective	Laparoscopic	US	75	75	150	1	59.8	59.6	N/A	N/A	8.4	7.5	Good
Hohwu 2009[227]	Retrospective	Open	Sweden	127	147	274	N/A	57.9	58	25.9	26.9	7.7	11.7	Fair to good
Hu 2006[41]	Retrospective	Laparoscopic	US	322	358	680	3	62.1	63.7	27.5	27.4	N/A	N/A	Fair to good
Joseph 2005[52]	Retrospective	Laparoscopic	US	50	50	100	N/A	59.6	61.8	N/A	N/A	7.3	6	Fair to good
Krambeck 2009[42]	Retrospective	Open	US	294	588	882	3	61	61	N/A	N/A	4.9	5	Good
Laurila 2009[228]	Retrospective	Open	US	94	98	192	1	59.8	58.8	N/A	N/A	6.7	5.9	Fair to good

* Study quality was assessed using an appraisal form modified from Hailey et al.,[21] taken from the CADTH HTA[18] on robot-assisted surgery.

First Author / year	Study type	Comparator	Country where study was carried out	# Patients in Robot Arm	# Patients in comparator Arm(s)	Total # Patients in Study	# Robotic Surgeons involved in study	Mean age (Robot arm)	Mean age (Comparator arm)	Mean BMI (Robot arm)	Mean BMI (Comparator arm)	Mean PSA level (Robot arm)	Mean PSA level (Comparator arm)	Quality*
Lo 2010[38]	Retrospective	Open	Hong Kong	20	20	40	N/A	64	66	N/A	N/A	14.2	14.5	Poor to fair
Menon 2002[48]	Prospective	Laparoscopic	US	40	40	80	2	60.7	62.8	27.7	27.7	5.7	6.9	Good
Miller 2007[229]	Prospective	Open	US	42	120	162	N/A	61.1	60.6	N/A	N/A	N/A	N/A	Fair to good
Nelson 2007[230]	Prospective	Open	US	629	374	1003	N/A	59.3	59.9	N/A	N/A	6.7	8.4	Fair to good
Ou 2009[43]	Retrospective	Open	Taiwan	30	30	60	1	67.3	70	24.2	24.1	6.13	6.22	Fair to good
Ploussard 2009[53]	Prospective	Laparoscopic	France	83	205	288	1	62.8	62.9	26.6	26.3	9.2	8.2	Fair to good
Rocco 2009[49]	Retrospective	Open	Italy	120	240	360	3	N/A	N/A	N/A	N/A	N/A	N/A	Poor to fair
Rozet 2007[54]	Retrospective	Laparoscopic	France	133	133	266	4	62	62.5	24.8	25.3	7.6	7.8	Fair to good
Schroeck 2008[231]	Retrospective	Open	US	362	435	797	4	N/A	N/A	N/A	N/A	N/A	N/A	Fair to good
Smith 2007[232]	Retrospective	Open	US	200	200	400	2	60.3	61.1	28.5	27.8	6.4	8.3	Fair to good
Tewari 2003[50]	Prospective	Open	US	200	100	300	1	59.9	63.1	27.7	27.6	6.4	7.3	Good
Trabulsi 2010[51]	Retrospective	Laparoscopic	US	205	45	250	1	59.9	58.1	N/A	N/A	6.4	6.2	Fair to good
Trabulsi 2008[44]	Retrospective	Laparoscopic	US	50	190	240	N/A	57.7	58.6	28.4	26.8	5.5	6.5	Fair to good
Webster 2005[233]	Prospective	Open	US	159	154	313	N/A	59.4	60.1	N/A	N/A	6.31	8.62	Fair to good
White 2009[46]	Retrospective	Open	US	50	50	100	1	62	64.7	N/A	N/A	4.63	5.04	Fair to good
Wood 2007[234]	Prospective	Open	US	165	152	317	N/A	60.2	59.2	N/A	N/A	6.5	6.5	Good
Asimakopoulos 2011[37]	RCT	Laparoscopic	Italy	52	60	112	1	59.6	61.1	25.8	26.3	8.9	7.37	High
Bolenz 2010[158]	Retrospective	Both	US	262	381	643	2	N/A	N/A	N/A	N/A	N/A	N/A	Poor to fair

* Study quality was assessed using an appraisal form modified from Hailey et al.,[21] taken from the CADTH HTA[18] on robot-assisted surgery.

First Author / year	Study type	Comparator	Country where study was carried out	# Patients in Robot Arm	# Patients in comparator Arm(s)	Total # Patients in Study	# Robotic Surgeons involved in study	Mean age (Robot arm)	Mean age (Comparator arm)	Mean BMI (Robot arm)	Mean BMI (Comparator arm)	Mean PSA level (Robot arm)	Mean PSA level (Comparator arm)	Quality*
Breyer 2010[235]	Prospective	Open	US	283	695	978	N/A	59.7	59.2	N/A	N/A	7.1	7.6	Poor to fair
Carlsson 2010[236]	Prospective	Open	Sweden	1253	485	1738	6	N/A	N/A	N/A	N/A	N/A	N/A	Fair to good
Coronato 2009[237]	Retrospective	Open	US	98	57	155	2	59.8	59.4	N/A	N/A	6.5	8.4	Poor to fair
Di Pierro 2011[55]	Prospective	Open	Switzerland	75	75	150	1	N/A	N/A	N/A	N/A	N/A	N/A	Good
Doumerc 2010[238]	Prospective	Open	Australia	212	502	714	1	59.8	60.1	N/A	N/A	7.1	8.3	Good
Ham 2008[59]	Prospective	Open	South Korea	223	199	422	1	59.8	66.1	24.6	23.7	20.3	40.7	Good
Hong 2010[239]	Prospective	Open	South Korea	26	25	51	1	59.8	68.6	N/A	N/A	N/A	N/A	Fair to good
Kordan 2010[240]	Prospective	Open	US	830	414	1244	2	59.8	61.5	28.2	28	N/A	N/A	Fair to good
Loeb 2010[241]	Prospective	Open	US	152	137	289	1	N/A	N/A	N/A	N/A	N/A	N/A	Poor to fair
Malcolm 2010[58]	Prospective	Open	US	447	135	582	3	59.8	59	N/A	N/A	N/A	N/A	Good
Nadler 2010[47]	Retrospective	Open	US	50	50	100	1	59.8	60	28.6	28.2	6.5	8.5	Good
Stranne 2010[242]	Prospective	Open	Sweden	946	465	1411	N/A	59.8	63	25.8	26.6	7.7	8.3	Good
Truesdale 2010[62]	Retrospective	Open	US	99	217	316	1	59.8	61.7	24.6	23.1	7.04	8.35	Poor to fair
Williams 2010[243]	Prospective	Open	US	604	346	950	1	N/A	N/A	N/A	N/A	N/A	N/A	Fair to good
Yi 2010[244]	Retrospective	Both	South Korea	153	488	641	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Poor to fair

* Study quality was assessed using an appraisal form modified from Hailey et al.,[21] taken from the CADTH HTA[18] on robot-assisted surgery.

Table App 2.2 – Hysterectomy (gynaecology): studies retrieved

First Author / year	Study type	Comparator	Country where study was carried out	# Patients in Robot Arm	# Patients in Comparator Arm	Total # patients in study	# Robotic Surgeons involved in study	Mean age (Robot arm)	Mean age (Comparator arm)	Mean BMI (Robot arm)	Mean BMI (Comparator arm)	Quality*
Bell 2008[75]	Retrospective	Both	US	40	70	110	1	63	70.6	33	31.8	Fair to good
Boggess 2008[90]	Retrospective	Both	US	103	219	322	N/A	61.9	63.3	32.9	32.6	Fair to good
Estape 2009[94]	Retrospective	Both	US	32	31	63	N/A	55	47.9	29.7	28.7	Good
Jung 2010[82]	Prospective	Both	South Korea	28	81	109	2	52.9	50.1	23.4	24.9	Fair to good
Cardenas-Goicoechea 2010[78]	Retrospective	Laparoscopic	US	102	173	275	1	62	59.6	32.3	32.7	Good
Gehrig 2008[245]	Retrospective	Laparoscopic	US	49	32	81	N/A	61.3	61.2	37.5	35	Poor to fair
Nezhat 2009[95]	Retrospective	Laparoscopic	US	26	50	76	N/A	46	47	25.4	26.7	Poor to fair
Payne 2008[85]	Retrospective	Laparoscopic	US	100	100	200	2	43.2	43.5	28.8	28.8	Fair to good
Seamon 2009[86]	Retrospective	Laparoscopic	US	105	76	181	2	59	58	34.2	28.7	Fair to good
Sert 2007[70]	Retrospective	Laparoscopic	Norway	7	8	15	1	41	45	24.6	22.5	Fair to good
Shashaua 2009[74]	Retrospective	Laparoscopic	US	24	44	68	1	44.9	42.2	30.3	30.5	Fair to good
Boggess 2008[76]	Retrospective	Open	US	51	49	100	1	47.4	41.9	28.6	26.1	Poor to fair
Cantrell 2010[93]	Retrospective	Open	US	64	63	127	N/A	N/A	N/A	N/A	N/A	Fair to good
DeNardis 2008[92]	Retrospective	Open	US	56	106	162	N/A	58.9	62.5	28.5	34	Fair to good
Geisler 2010[98]	Retrospective	Open	US	30	30	60	N/A	49	51	34	32	Fair to good
Ko 2008[81]	Retrospective	Open	US	16	32	48	2	42.3	41.7	27.6	26.6	Fair to good
Maggioni 2009[91]	Retrospective	Open	Italy	40	40	80	N/A	44.1	49.8	24.1	23.6	Good

* Study quality was assessed using an appraisal form modified from Hailey et al.,[21] taken from the CADTH HTA[18] on robot-assisted surgery.

First Author / year	Study type	Comparator	Country where study was carried out	# Patients in Robot Arm	# Patients in Comparator Arm	Total # patients in study	# Robotic Surgeons involved in study	Mean age (Robot arm)	Mean age (Comparator arm)	Mean BMI (Robot arm)	Mean BMI (Comparator arm)	Quality*
Seamon 2009[87]	Retrospective	Open	US	109	191	300	2	58	62	39.6	39.9	Fair to good
Veljovich 2008[88]	Retrospective	Open	US	25	131	156	4	59.5	63	27.6	32.2	Poor to fair
Matthews 2010[89]	Retrospective	Both	US	70	274	344	4	51	44.8	N/A	N/A	Poor to fair
Giep 2010[69]	Retrospective	Laparoscopic	US	237	265	502	2	41.5	42.5	30.3	29.9	Fair to good
Holtz 2010[73]	Retrospective	Laparoscopic	US	13	20	33	1	63.5	63.3	35.3	27.8	Fair to good
Lim 2011[79]	Retrospective	Laparoscopic	US	122	122	244	1	62.1	61.6	31	29.9	Fair to good
Nick 2011[246]	Retrospective	Laparoscopic	US	132	285	417	N/A	N/A	N/A	N/A	N/A	Poor
Sarlos 2010[83]	Retrospective	Laparoscopic	Switzerland	40	40	80	2	47	43.6	26	26	Good
Göçmen 2010[71]	Prospective	Open	Turkey	10	12	22	1	55.7	56.4	32.7	30.3	Fair to good
Göçmen 2010[97]	Retrospective	Open	Turkey	8	7	15	N/A	47.8	45.4	33.2	27.8	Poor to fair
Goel 2011[77]	Retrospective	Open	US	59	38	97	1	59.5	66.5	39.3	32.2	Poor to fair
Halliday 2010[80]	Retrospective	Open	Canada	16	24	40	2	49	47	26	25	Fair to good
Lowe 2009[68]	Prospective	Open	US	7	7	14	1	N/A	N/A	N/A	N/A	Poor to fair
Nam 2010[96]	Retrospective	Open	South Korea	32	32	64	N/A	N/A	N/A	N/A	N/A	Fair to good
Nevadunsky 2010[84]	Retrospective	Open	US	66	43	109	2	N/A	N/A	N/A	N/A	Poor to fair
Schreuder 2010[72]	Retrospective	Open	Netherlands	13	14	27	1	N/A	N/A	N/A	N/A	Fair to good

* Study quality was assessed using an appraisal form modified from Hailey et al.,[21] taken from the CADTH HTA[18] on robot-assisted surgery.

Table App 2.3.1 – Nephrectomy HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	Narrative analysis of data	4	2006 – 2008 (2002 - Oct 2008)	NR	6 - 148	RN v LN RN v ON	No clear advantage of RN v ON. RA radical & partial nephrectomy can be safely performed if the surgeon has sufficient experience.
CADTH 2009[18] III-2	Meta-analysis of data	8	2006 – 2009 (up to week 47 of 2009)	'Poor - fair' (1), 'fair – good' (5) 'good quality' (2)	22 - 247	RPN v LPN (8 studies) RPN v OPN (1)	**OT:** Comparable (WMD -8.71 mins, 95% CI -31.77 to 14.34 mins), **LHS:** RPN < LPN (WMD -0.44 days, 95% CI -0.71 to -0.17days), **CR:** Comparable (RR 0.99, 95% CI 0.55 to 1.76), **EBL:** RPN < LPN (-39.99mL, 95% CI -61.11 to -18.87mL), **WIT:** Comparable using pooled estimate (WMD -4 mins, 95% CI -9.46 to 1.46mins)
ASERNIP-S 2009[20] III-2	Narrative analysis of data	4	006 – 2009 (01 Jan 2004 - 20 Feb 2009)	II-3 (1) III-2 (3)	9 - 62	RPN v LN (3) RPN v OPN (1) RAN (radical) v ON (radical) (1)	RPN versus LPN: **OT:** RPN > LPN (1 study, SS), LPN > RPN (1 study, SS). RRN > LRN (1 study, SS) **LHS:** RPN < LPN (2 studies, SS in 1), RRN > LRN (1 study, NSD) **EBL:** Comparable (NSD), TR: RPN < LPN (2 studies, SS in 1), RRN comparable to LRN **C:** RPN > LPN **CR:** RPN > LPN, RRN > LRN PN v ON: **OT:** NSD **TR:** NSD **CR:** NSD **EBL:** RN (radical) < ON (radical) (median, SS), RPN > OPN (NSD) **LHS:** RN < ON (radical) (median, SS), RPN comparable to OPN.

Robot-assisted / laparoscopic / open nephrectomy= **RN / LN / ON**; robot-assisted / laparoscopic / open partial nephrectomy= **RPN / LPN / OPN**; robot-assisted / laparoscopic / open radical nephrectomy= **RRN / LRN / ORN**; operative time=**OT**; estimated blood loss=**EBL**; length of hospital stay=**LHS**; transfusion rate=**TR**; positive surgical margin rate=**PSMR**; warm ischemic time=**WIT**; complication rate=**CR**; conversions=**C**; statistically significant=**SS**; no significant difference=**NSD**; not reported=**NR**;

Table App 2.3.2 – Nephrectomy (urology): individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	WIT (mins)	CR n/N (%)	Study details
Benway BM* 2009[105] III-3	129 RPN 118 LPN	189 v 174 NS	155 v 196 **p=0.03**	2.4 v 2.7 **p<0.0001**	NR	3.9 v 1% NS	19.7 v 28.4 **p<0.0001**	8.5 v 10.2% NSD (PC)	**Study dates:** 2004-2008. **Experience:** 3 high volume surgeons, 3 centres. Conflicts: MSI research director's fund. **Baseline characteristics:** No difference reported.
Deane LA* 2008[107] III-3	11 RPN 12 LPN	228.7 v 289.5 p=0.102 (mean)	115 v 198 p=0.169 (mean)	2 v 3.1 **p=0.039**	0 v 0 (intra-op)	2.1 v 2.9mm **p=0.385** (mean TFM)	32.1 v 35.3 p=0.501 (mean)	1 v 1 (PC)	**Study dates:** Mar 2005-Dec 2006. **Experience:** 2 experienced lap. surgeons, 1 experienced open surgeon (completed >200 RALP). **Conflicts:** Funding or conflict of interest not reported. **Baseline characteristics:** No difference reported.
Wang AJ*, ** 2009[102] III-3	40 RPN 62 LPN	140 v 156 **p =0.04** (mean)	136 vs 173 NS	2.5 v 2.9 **p=0.03**	2 v 1	1 v 1 patient NS	19 v 25 **p =0.03**	15 v 13% (PC)	**Experience:** Single surgeon experience. **Conflicts:** Funding or conflict of interest not reported. **OT:** Defined as incision to specimen extraction. **Baseline characteristics:** No difference reported.
Cho CL 2011[106] III-3	10 RPN 10 LPN	376 v 361 p=0.722	329 v 328 p=0.994	7 v 14 p=0.213	0 v 0 (intra-op)	Margin distance: 2.8 v 2.4mm p=0.728	31 v 40 **p=0.032**	1 v 3 (PC)	**Experience:** No. of surgeons not reported. **Conflicts:** Funding or conflict of interest not reported. **Baseline characteristics:** No difference reported.

Robot-assisted / laparoscopic / open nephrectomy= **RN / LN / ON**; robot-assisted / laparoscopic / open partial nephrectomy= **RPN / LPN / OPN**; operative time=**OT**; estimated blood loss=**EBL**; length of hospital stay=**LHS**; transfusion rate=**TR**; positive surgical margin rate=**PSMR**; warm ischemic time=**WIT**; complication rate=**CR**; post-operative complications=**PC**; no significant difference=**NSD**; not reported=**NR**;

Table App 2.4.1 – Radical cystectomy (urology): RCTs retrieved

First Author/ Year/ Grade	Sample size	Primary end point	Patient exclusion criteria	OT (hr)	EBL (mL)	Return of bowel movement (days)	in-house analgesia usage (mg)	Time to initiation of adjunctive chemotherapy (mean, weeks)	Study details
Nix J[109] 2010 II (RCT)	21 RRC 20 ORC	Lymph node yield	- Patients not considered candidates for either approach, - those not allowing randomization - those with preconceived preference for a specific surgery.	4.20 v 3.52 **p<0.0001**	258 v 575 **p<0.0001**	3.2 v 4.3 **p<0.0008**	89.0 v 147.4 **p<0.0044**	6.7 v 8.8 **p=0.033**	**Study dates:** Apr 2008 to Jan 2009 Conflicts: No funding was received. Baseline differences: No significant differences reported (age, gender, BMI). **Experience:** Both trial arms performed by same primary surgeon who had prior experience of > 75 RRC cases & > 400 ORC cases. Assisted by an experienced surgical team **Results:** Multivariate analysis: cystectomy type - significant predictor for EBL (p=0.0003), days to flatus (p = 0.0044), days to bowel movement (p = 0.0033), OT (p < 0.0001), and in-house analgesic requirement (p = 0.0110) controlling for age, BMI, pathologic stage. **NSD outcomes:** mean LHS RRC < ORC, no. of complications and mean no. of lymph nodes removed were similar. A multivariate analysis predicted a trend towards fewer complications in RRC.

Robot-assisted / open radical cystectomy = **RRC / ORC**; operative time=**OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion rate = **TR**; positive surgical margin rate = **PSMR;** warm ischemic time = **WIT**; complication rate = **CR**.

Table App 2.4.2 – Radical cystectomy (urology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	HTA: Narrative analysis of data	6	2003 – 2008 (2002 - Oct 2008)	NR	NR	NR	RRC is feasible and safe in experienced hands, but that long term outcomes were lacking.
ASERNIP-S 2009[20] III-2	HTA: Narrative analysis of data	4	2007 (01 Jan 2004 - 20 Feb 2009)	III-3 (3, 1 study reports on conversions only) III-2 (1)	14 - 33	RRC v ORC (2) RRC v LRC (1)	**OT:** RRC < LRC (NSD, 1 study), RRC > ORC (SS, 2 studies) **LHS:** RRC < ORC (SS, 2 studies), RRC equivalent to LRC (1 study) **EBL:** RRC < ORC (SS, 2 studies), RRC < LRC (SS, 1 study) **TR:** RRC < LRC (SS, 1 study), RRC comparable to ORC (1 study) **PSMR, C, CR:** (NSD)
Khan MS 2008[110] III-2	Paper: Systematic review	19 + authors own study	1982 - 2007	NR	17 - 33	RRC, LRC, ORC	**TR:** RRC 2% **EBL:** RRC <500ml. Stated that these results better than ORC. In their experience, RRC better than LRC (NSD). **LHS (days):** RRC 5 - 6 (lit. review) but 10 - 12 for authors study (UK). 10 - 12 reported as < national avg. of ORC (UK) by 50%. **PSMR:** 0 (authors study) - 13% (lit. review). **NLNR:** RRC comparable to ORC (RRC: 12 to 19). **OSR, CSR** 95% & 90% respectively at 3.5 yrs follow-up (authors study)
Hemal AK 2009[113] III-2	Paper: Systematic review	14 LRC & 14 RARC studies*** (4 relevant papers with comparators)	2006 – 2007 (relevant papers)	NR	7 – 33 (relevant paper)	RRC v ORC (3) RRC v LRC (1) remaining had no comparators	**OT:** RRC > ORC (2 studies) but RRC < ORC (1 study) **EBL:** RRC < ORC (3 studies) **LHS:** RRC < ORC (1 study) **NLNR:** RRC > ORC (1 study) Major complications slightly less in RRC (1 study). RRC v LRC (1 study): OT similar, mean EBL less, NLNR greater for RRC.
Chade DC 2010[112] III-2	Paper: Systematic review	19	1998 – Mar 2009	NR	10 – 2,289	RRC, LRC, ORC	RRC v LRC: RRC - highest recurrence free survival rate at 1 - 2 yrs (86 - 91% v 83 - 85%). **PSMR:** RRC 0 – 10%; LRC 0- 5%; ORC 4 - 5% **OT (hours):** RRC 3.8 – 8.5 (mean); LRC 4 – 10; ORC 6.4 (median) **LHS (days):** RRC 4 – 11.6 (mean); LRC 5 – 15; ORC 9 (median) **EBL (mL):** RRC 166 – 479 (mean); LRC 200 – 1,000; ORC 1,000
Singh I 2010[114] III-2	Paper: Systematic review	12 (3 relevant studies with comparators)	2003 - 2009	NR	278 cases	RRC v ORC (2) RRC v LRC (1)	RC v LRC: **OT / EBL:** NSD (1 study) **NLNR**: 22 v 16 (1 study, NSD) RRC v LRC: **OT:** 8.4 v 10.6hours (1 study) **EBL:** 1109 v 479mL (1 study) **NLNR:** 20 v 17 (1 study) **CR:** 3 v 4 (1 study)

Robot-assisted / laparoscopic / open radical cystectomy = **RRC / LRC / ORC**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion rate = **TR**; positive surgical margin rate = **PSMR**; warm ischemic time = **WIT**; complication rate = **CR**; overall survival rate=**OSR**; cancer-specific survival rate = **CSR**; number of lymph nodes retrieved = **NLNR**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR;**
*Note: search dates not included. **Note: two studies also included in our retrieved studies.

Table App 2.4.3 – Radical cystectomy (urology): individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Martin AD[116] 2010 III-3	59 RRC ORC (quantity not specified)	NR	NR	NR	NR	NR	NR, OSR reported	**Experience:** 1 surgeon performed most procedures; **Conflicts:** 1 author was proctor, another an investigator for Intuitive **Baseline differences:** No selection bias, higher percentage of patients with stage >pT1 disease & LN+ disease in the RRC compared to ORC group. **Results:** OSR (12, 36 months): 82, 69%; DSR (12, 36 months): 82%, 72%; Results author states "comparable to survival rates for ORC".
Ng CK[117] 2010 III-2	83 RRC 104 ORC	6.25 v 5.95hour; p=0.3 (mean)	460 v 1172, p<0.001	5.5 v 8.0; p<0.0001 (mean)	1.42 v 3.65 units; p<0.0001	7 v 9%; p=0.8 (PMR)	30 days: OCR (41 v 59% p=0.04); MC (10 v 30% p=0.007) 90 days: OCR (48 v 62% p=0.07); MC (17 v 31% p=0.03)	**Experience:** Single surgeon and institute **Conflicts:** Author declared no funding or conflict of interests. **Baseline differences:** No important differences reported **Results:** Complication rate uses modified Clavien classification.
Wang GJ [119] 2008 III-2	33 RRC 21 ORC	390 v 300, p=0.03 Median OT decreased by 112m in last 16 RRC cases.	400 v 750, p=0.002	5 v 8, p= 0.007	0.5 v 2.0units, p=0.007	6 v 14%, p=0.2 (PMR)	21 v 24%, p=0.3	**Study dates:** 2006-2007 Experience: Single surgeon and institute; **Conflicts:** Departmentally funded, no conflict of interest. **Baseline differences:** No important differences reported, more men in RA group & open group had more patients with extravesical disease & nodal metastasis.
Nunez RN [247] 2009 III-3	40 RRC 150 ORC	280 v 252, p=0.01 (mean)	220 v 642, p=0.001 (median)	5 v 10, p=0.001 (median)	14 v 57%, p=0.001	NR	SS lower in RRC group (Clavien system)	**Study dates:** 2004-2008 **Conflicts:** Author declared no funding. **Baseline differences:** No important differences reported. **Note:** Conference abstract.
Richards KA [118] 2010 III-3	35 RRC 35 ORC	530 v 420; p<0.001 (median)	350 v 1000; p<0.001 (median)	7 v 8; p=0.014 (median)	17 v 71%; p<0.001	1 v 3, NSD (PMR)	NSD (Clavien system)	**Study dates:** Apr 2007-Jun 2009 **Conflicts:** Funding or conflict of interest not mentioned **Experience:** Multiple surgeons & single institute, all experienced / 1st 35 surgeries performed at high volume centre by experienced team. **Baseline differences:** No important differences reported **Operative time:** defined as initial incision to final closure of skin.
Davis JW [115] 2011 III-3	11 RRC + RAEPLND 249 ORC	117 for pelvic lymph node dissection (median)	252 for RA portion, 612 for reminder (median)	16 days	4/11 cases	NR	7/11 no complications. 1 complication related to RA surgery	**Study dates:** Oct 2007-Jun 2009 **Conflicts:** No funding or conflict of interest mentioned **Experience:** 1 surgeon (10 RRC's & >300 RAP experience) + 1 second look surgeon, 3 ORC surgeons **Baseline differences:** Did not discuss this.

Robot-assisted / open radical cystectomy = **RRC / ORC**; robot-assisted extended pelvic lymphadenectomy = **RAEPLND**; overall survival rate = **OSR**; disease-specific survival rates = **DSR**; overall complication rate = **OCR**; operation time = **OT**; estimated blood loss = **EBL**; transfusion requirement = **TR**; length of hospital stay = **LHS**; major complications = **MC**; time to resumption of regular diet = **TTRRD;** complication rates = **CR**; positive margin rate = **PMR**; number of lymph nodes removed = **NLNR**; pelvic lymph node dissection = **PLND**; positive lymph node rate = **PLNR**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.5 – Pyeloplasty (urology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	Narrative analysis of data	10	9: 2005 – 2006, discussed 1 later study: 2008 (2002 - Oct 2008)	NR	NR	NR	RP, in qualified hands, appears to have similar results to OP and LP. The learning curve for RP appears to be easier and shorter than for LP.
ASERNIP-S 2009[20] III-2	HTA: Narrative analysis of data	4	2007 (01 Jan 2004 - 20 Feb 2009)	III-3 (3) III-2 (1)	7 - 116	RP v LP	**OT:** RP > LP (2 studies, SS in 1), RP < LP (NSD, 1 study) **EBL:** NSD (2 studies) **LHS:** NSD (2 studies) **SSR & CR:** NSD (3 studies))
Braga LH 2009[120] III-2	Paper: Systematic review & meta-analysis	8	2002-2008 (1992 – 2008)	Low quality (6) High quality (5, lower end) Using Newcastle-Ottawa Scale.	6 - 84	RP v LP for patients with UPJO	**Conflicts:** No funding or conflict of interests. **Meta-analysis:** Weighted mean difference (WMD) used to measure OT and LHS, odds ratio & risk difference used to measure complication and success rates. **LHS:** RP < LP (WMD: -0.5 d; 95% CI: -0.6– -0.4; p < 0.01) **OT:** RP 10min < LP (WMD: -10.4min; 95% CI: -24.6-3; p=0.15)* **CR, SSR:** NSD

Robot-assisted / laparoscopic pyeloplasty = **RP / LP;** operative time = **OT;** estimated blood loss = **EBL;** transfusion requirement = **TR;** length of hospital stay = **LHS;** major complications = **MC;** complication rates = **CR;** surgical success rates = **SSR;** statistically significant = **SS;** no significant difference = **NSD;** not reported = **NR.**
* An editorial comment noted that the relevance of the length of hospital stay finding was negligible.

Table App 2.6.1 – Miscellaneous indications (urology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	Narrative analysis of data	12	2006 – 2008 (2002 - Oct 2008)	NR	NR	NR	Search retrieved: vasovaotomy (2), inguinal herniorrhaphy (2), adrenalectomy (2), prolapse (4), bladder diverticulectomy (1) and ureteral-re-implantation (1) studies. They state that there is limited evidence to show that RA surgery was superior to conventional techniques in these areas.

Not reported=**NR**; Robot-assisted= RA.

Table App 2.6.2 – Miscellaneous indications (urology): Individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Shu T [122] 2008 III-3	8 RAV 8 MSV	71.1 v 73.9 (average)	NR	NR	NR	NR	0 v 0	**Experience:** Number of surgeons or institutes not detailed; **Conflicts:** No funding or conflict of interest mentioned; **Baseline differences:** Not discussed. **Results:** Avg, follow-up time (10.9 v 34.6months). Return to activities comparable between groups.

Robot-assisted varicocelectomies = **RAV;** microscopic subinguinal varicoelectomies=**MSV;** operative time = **OT;** estimated blood loss = **EBL;** length of hospital stay = **LHS;** transfusion requirement = **TR;** positive surgical margin rates = **PSMR;** complication rates = **CR;** not reported = NR.

Table App 2.7.1 – Myomectomy (gynaecology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	HTA: Narrative analysis of data	4 (1 feasibility study 2007, 3 limited case series 2004, 2005, 2007)	2006 – 2008 (2002 - Oct 2008)	NR	NR	NR	RM is feasible and results appear to be similar to the other methods, but that at the time there was no evidence to support the claim that it was superior to other methods. The learning curve for the RA intervention is reported to be shorter and easier than for the laparoscopic intervention.(8)
ASERNIP-S 2009[20] III-2	HTA: Narrative analysis of data	2	2007 - 2008 (01 Jan 2004 - 20 Feb 2009)	III-2 (2)	15 - 35	RM v OM (1 study) RM v LM (1 study)	**OT:** RM > OM, RM > LM (SS in both studies) **EBL:** RM < OM (SS) **LHS:** RM < OM (SS)

Robot-assisted myomectomy = **RM**; open myomectomy = **OM**; laparoscopic myomectomy = **LM**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR;** complication rates = **CR**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.7.2 – Myomectomy (gynaecology): individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Barakat EE 2011[123] III-3	89 RLM 93 SLM 393 OM	181, 155, 126, p<0.001	100, 150, 200 p<0.001 for OM versus RLM & SLM, NSD between RLM and SLM	1, 1, 3, p<0.001 (median)	2.2, 0, 6.4%	NR	0, 2, 1	**Operative time:** defined as incision to closure. **Experience:** Single centre, no. of surgeons not mentioned **Conflicts:** Author declared no conflict of interest. **Baseline differences:** patients in OM group were significantly heavier v LM and RLM. OM group also had significantly higher number of previous operative laparoscopies (tubal ligations and caesarean deliveries). Significantly heavier myomas were reported in the RLM group (once removed). **Results:** HMR: RLM v SLM (223 v 96.55, p=0.001); HMR: RLM v OM (223 v 263, p=0.002).
Ascher-Walsh CJ 2010[124] III-3	75 RLM 75 SLM	RLM > SLM (SS)	RLM < SLM (SS)	RLM < SLM (SS)	NR	NR	PC (NSD)	**Baseline differences:** No differences reported. **Note:** Only the abstract could be retrieved for this study.

Robot-assisted laparoscopic myomectomy = **RLM**; standard myomectomy via laparotomy= **SLM**; open myomectomy= **OM**; heavier myoma removal = **HMR**; estimated blood loss = **EBL**; operative time = **OT**; length of hospital stay = **LHS**; post-operative complications = **PC**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR**; complication rates = **CR**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.8.1 – Tubal re-anastomosis (gynaecology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009[8] III-2	HTA: Narrative analysis of data	4	2000 to 2007 (2002 - Oct 2008)	NR	NR	NR	Surgical results and successful re-anastomosis were encouraging, however, they state that larger series are required to assess post-operative pregnancy rates. **OT:** RA procedure greatly increased OT v open microsurgery. They conclude that RA laparoscopic tubal re-anastomosis is feasible and results appear to be similar to the other methods
ASERNIP-S 2009[20] III-2	HTA: Narrative analysis of data	2	2007 – 2008 (01 Jan 2004 - 20 Feb 2009)	III-3 (1) III-2 (1)	10 - 21	RATA v OTA (2 studies)	**OT:** RTA > OTA (SS, 2 studies) **LHS:** RTA < OTA (SS in 1 study, 4 versus 34.7hrs). Viable pregnancy rate: RTA < OTA (NSD) **CR:** RTA<OTA (1 study, NSD), RTA>OTA (1 study, NSD)

Robot-assisted myomectomy = **RM**; open myomectomy = **OM**; laparoscopic myomectomy = **LM**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR**; complication rates = **CR**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.8.2 – Tubal re-anastomosis (gynaecology): Individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Dharia Patel SP(125) 2008 III-3	18 RTA 10 OTA	201 v 155.3, p=0.001 (mean)	NR	4 v 34.7hrs p=0.0001	NR	NR	Rate of abnormal pregnancy (eptopic: 4 v 1, spontaneous pregnancy: 2 v 1).	**Study dates:** Feb 2003 – Jan 2004 (RTA). **Conflicts:** None stated. **Experience:** For RTA, each case performed by same faculty member and fellow in training, both completed formal training, animate training and one RTA prior to study. **Baseline characteristics:** Some differences with respect to previous surgery were noted. **Results:** Follow-up time of 8.9 months. Return to daily activities (11.1 v 28.1 days). Post-op analgesia (29.3 v 90 tablets, p=0.0001).

Robot-assisted tubal re-anastomosis = **RATA**; open tubal re-anastomosis = **OTA**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR**; complication rates = **CR**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.9.1 – Prolapse surgery (gynaecology): HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results
KCE 2009(8) III-2	HTA: Narrative analysis of data	2 (1 summary of case series, 2007, 1 single case series, 2007)	2006 – 2008 (2002 - Oct 2008)	NR	NR	NR	**Results:** Early results showed that RASC is relatively safe and efficacious and that functional results are similar to the conventional techniques.
ASERNIP-S 2009(20) III-2	HTA: Narrative analysis of data	1	2008 (01 Jan 2004 - 20 Feb 2009)	III-3 (1)	73 (RAS), 105 (OS)	RAS v OS	**OT:** RASC > OSC (SS, 1 study) **EBL:** RASC < OSC (SS, 1 study), **TR:** RASC; V OSC (NSD) **LHS:** RASC < OSC (SS, 1 study) **CR:** RASC > OSC (NSD)

Robot-assisted / laparoscopic sacrocolpopexy = **RASC / LSC**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR**; complication rates = **CR**; post-operative complications = **PC**; statistically significant= **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.9.2 – Prolapse surgery (gynaecology): individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Chan SC 2011(248) III-3	16 RASC 20 LSC	230 v 185 p=0.02	131 v 155 p=0.42	7.5 v 4.3 p=0.05 (median)	NR	NR	IC & PC (NSD)	**Study dates:** Mar 2005 to May2010. **Conflicts:** Author declared no conflict of interest; Single tertiary centre. **Results:** Haemoglobin drop (1.7 v 1.4g; p=0.37); Follow-up (16 v 39month; p<0.001; RASC & LSC had similar results at follow-up)

Robot-assisted / laparoscopic sacrocolpopexy = **RASC / LSC**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR;** complication rates = **CR;** intra-operative complications = **IC**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.10 – Miscellaneous indications (gynaecology): Individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	Complications n/N (%)	Study details
Cervical cancer (locally advanced)								
Lambaudie E 2010[127] III-2	22 RL 20 L 16 CL	210, 267.5, 210; p=0.01 (median)	NR	3, 4.5, 7 p<0.01 (median)	1, 0, 1; NS	NR	22.7, 12.5, 20%; NS (PC) Recurrences: 27.3, 25, 30%; NS Mortality: 9.1, 11.8, 20%, NS	**Experience:** 2 institutions, surgeon's experience in CL, not in RL. **Conflicts:** 2 authors were proctors of Intuitive Surgical. **Results:** RL, L, CL. Median follow-up (11.55, 19.45, 34.6; p<0.001). Baseline differences: None reported. **Operative time:** defined as skin incision to skin closure.
Endometriosis								
Nezhat C 2010[128] III-3	40 RL 38 CL	191 v 159; p=0.045 (mean)	60 v 65 P=0.823	NSD	NR	NR	0 v 0; N/A (IC) 0 v 0; N/A (PC)	**Study dates:** 2008-2009. **Conflicts:** Author collaborated with pioneers of RA surgery. **Experience:** single centre, no. of surgeons not mentioned. **Baseline differences:** Matched study for age, BMI, stage of disease and previous abdominal surgery.
Adnexal mass								
Magrina JF 2009[129] III-3	85 RA 91 LA	83 v 71; p=0.01 (mean) NS for obese group Docking time = 14mins (avg.) Disassembly time = 3mins (avg.)	39 v 41 p=0.65 (mean) SD for **obese group** (39 v 60; p=0.02)	0.15 v 0.28 p=0.26	NR	NR	1 v 2%, NS (IC) 12 v 11%, NS (PC)	**Study dates:** 2003 to 2008. **Conflicts:** 1 author received a proctorship from Intuitive surgical. **Experience:** Same surgeons performed RA and LA; Single centre study. **Baseline differences:** RA surgical group had an increased number of obese patients and higher anaesthetic risk. **Operative time:** defined as skin incision to skin closure.

Robot-assisted laparoscopy = **RL**; adjuvant surgery by laparotomy = **L**; conventional laparoscopy = **CL**; robot-assisted adnexectomy = **RA**; laparoscopic adnexectomy = **LA**; robot-assisted sacrocolpopexy = **RS;** laparoscopic sacrocolpopexy = **LS**; operation time = **OT**; transfusion rate = **TR**; length of hospital stay = **LHS**; complication rate = **CR;** estimated blood loss = **EBL**; intra-operative complications = **IC**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.11.1 – Cardiology: HTAs retrieved

First Author/ Year/ Grade	Study type	No. of studies retrieved	Study years range (search dates)	Quality of studies retrieved	Sample size range	Comparators	Results/conclusions
KCE [8] 2009 III-2	Narrative analysis of data	9* (CABG)	2006 – 2008 (2002 - Oct 2008)	NR	NR	NR	Mini-CABG: promising but very operator dependent. Should be carried out by experienced teams. Role and patient selection for different methods of mini-CABG still need to be determined.
		4** (MVR)	2006	NR	NR	NR	RA totally endoscopic MVR can be performed safely, might allow for similar results as conventional surgery. Lower TR and shorter LHS are indicated. Long-term follow-up required.
		2*** (ELP)	2005 - 2007	NR	NR	NR	RA surgery promising due to difficulties associated with conventional transvenous approach. More definite answers required.
		Miscellaneous 5 (thoracic, vascular surgery)	2006 - 2007	NR	NR	NR	Miscellaneous indications: 1 congenital heart defect, 1 aortofemoral bypass, 1 oesophagectomy, 2 thymectomy study. These studies are small and conclusions can not be drawn from them.
ASERNIP-S[20] 2009 III-2	Narrative analysis of data	4	2005 to 2006 (01 Jan 2004 - 20 Feb 2009)	III-3 (3) III-2 (1)	5 - 341	RA-MVR v open MVR (3 studies) RA-MVR v video assisted endoscopic VAE-MVR (1 study)	**OT:** RA-MVR > open-MVR 2 studies (SS in 1) **EBL:** NSD (1 study) **LHS:** RA-MVR shorter in all studies (SS in 2) **TR:** NSD (1 study), RA-MVR lower (NSD, 1 study) **CR:** RA-MVR higher(2 studies), RA-MVR lower (2 studies)
CADTH 2009[18] III-2			2004 to 2008 (01 Jan 2001 to 14 Jan 2011)	Range: 'poor - fair' to 'high quality'.	50 - 200	Atrial septal repair (2), RA-MVR (3), mini-CABG (1)	Cardiac Procedures v conventional approaches: **OT** RA cardiac procedures longer **LHS:** RA cardiac procedures shorter **TR / CR:** inconsistent findings
CADTH 2011[131] III-2	Narrative analysis of data	6 (1 HTA, 1 systematic review, 4 non-randomised studies)	(up to week 47 of 2009)	NR	NR	Mini-CABG v open chest approach RA-MVR versus open approach	Mini-CABG v open: **OT:** mini- CABG longer (on avg.) **TR:** mini-CABG lower **CR:** mini-CABG fewer **LHS:** mini-CABG shorter MVR: RA procedures, on average, took longer (except of 1 study). **LHS:** RA-MVR shorter **TR:** RA-MVR fewer **PC:** RA-MVR fewer NSD in post-surgery mortality for CABG or MVR v open chest surgeries. Long term clinical benefits data was limited.

*Note: 7 case studies (2000 to 2008), 1 CIGNA Healthcares assessment (2006) and 1 European multi-centre experience study (2007).
**Note: 2 case reports (2006) and 2 comparative studies (2006). ***Note: 1 horizon scan from ASERNIP-S (2005) and 1 systematic review (2007).
Robot-assisted minimally invasive CABG = **mini-CABG**; epicardial lead placement = **ELP**; operative time = **OT**; estimated blood loss = **EBL**; length of hospital stay = **LHS**; transfusion requirement = **TR**; complication rates = **CR**; post-operative complications = **PC**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.11.2 – Cardiology: individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	CR n/N (%)	Study details
Poston RS [133] 2008 III-2	100 matched to 100 sternotomy CABG	5.8 v 4.1hour p<0.001	547 v 1230 p=0.001	3.77 v 6.38 p<0.001 ICU stay: 21.9 v 50.6 p<0.001 IT: 4.80 v 12.24 p<0.001	0.16 v 1.37 units, p<0.001	NR	MACCE: 4 v 26%, p=0.008	**Experience:** 1st year of robot-assisted surgery programme to minimise learning curve bias. All RA surgeries performed by single surgeon, conventional surgery performed by 11 different surgeons. Differences in surgical skill or experience were not accounted for in analysis. **Comparators:** 100 miniCABG (IMA grafting +/- CS) matched to 100 sternotomy CABG (IMA & saphenous veins). **Conflicts:** Not stated. **Baseline characteristics:** Reported no important differences in baseline characteristics.
Kam J.K [132] 2010 III-3	170 RMVR 40 CMVR	239 v 202 p<0.001 CPB & ACC time: 126 v 94 p<0.001 (mean)	NR	6.47 v 8.76 p<0.001 ICU stay: 37 v 45hours, p=0.002	NR	NR	PDMR (comparable) PR (96.3 v 100%, p=0.627) VT (6.17 v 6.61; p=0.412)	**Experience:** **Study dates:** 2005-2008. **Experience:** Single institute, 1 RMVR and 11 CMVR surgeons. 1st year of robot-assisted surgery excluded to eliminate learning curve bias. **Conflicts:** Not stated. **Baseline characteristics:** Tend towards younger patients in the robot-assisted group (not statistically significant) and a statistically significantly higher proportion of severe mitral regurgitation in the robot-assisted surgical group.
Mihaljevic T [134] 2011 III-3	261 RAMVR 114 CS 270 PS 114 RMAT	Median CBT: (42min longer for RAMVR v CS, 39min longer v PS, 11min longer v RMAT; p<0.0001 Median MIT: 26min longer for RAMVR v CS, 26 longer v PS, 16min longer v RMAT; p<0.0001	NR	1.0<CS, 1.6<PS, 0.9<RMAT; p<0.001	NR	NR	Complications similar among matched groups; p>0.1	**Experience:** Single institute; number of surgeons not mentioned, all surgeons highly experienced. **Conflicts:** Author is a consultant for Intuitive Surgical. **Baseline characteristics:** Differences reported in characteristics, as such an adjusted comparison of outcomes was used. **Results:** RAMVR compared to CS, PS, RMAT. CR (9.1, RAMVR; 2.6, PS; 2.6, RMAT).

Minimally invasive coronary artery bypass graft = **mini-CABG**; robot-assisted mitral valve repair = **RAMVR**; conventional MVR = **CMVR**; complete sternotomy = **CS**; partial sternotomy = **PS**; mini-anterolateral thoracotomy = **RMAT**; operation time = **OT**; length of hospital stay = **LHS**; estimated blood loss = **EBL**; transfusion rate = **TR**; intubation time = **IT**; major adverse cardiac/cerebrovascular events = **MACCE**; cardio-pulmonary bypass = **CPB**; aortic cross-clamp = **ACC**; post-operative degrees of mitral regurgitation = **PDMR**; post-operative regurgitation = **PR**; ventilation times = **VT**; myocardial ischemic time = **MIT**; complication rate = **CR**; conversions = **C**; statistically significant = **SS**; no significant difference = **NSD**; not reported = **NR**.

Table App 2.12 – Head and neck disease: Individual studies retrieved

First Author/ Year/ Grade	Sample size	OT (mins)	EBL (mL)	LHS (days)	TR n/N (%)	PSMR n/N (%)	Complications n/N (%)	Study details
Primary or recurrent oropharyngeal carcinoma (early stage)								
Dean NR 2010[137] III-3	15 RP 7 RS 14 OS	NR	NR	RS 5.0 v OS 8.2, p=0.14, RP 1.5 v OS 8.2, p<0.001 (median)	NR	NR	RP, RS, OS: 2, 0, 2	**Study dates:** 2001-2008. **Experience:** Single centre. **Conflicts:** obtained funding (source not identified) but stated they had no financial disclosures. **Baseline differences:** greater proportion of patients in RA primary and open salvage groups underwent resection for tonsillar carcinoma and had advanced stage disease. **Results:** GTD at 6 months (RP, RS, OS: 7, 0, 43%; p=0.06); TTD at 6 months (RP, RS, OS: 0, 0, 7%, p=0.48).
Thyroidectomy								
Lee J 2010[135] III-2	41 RT 43 CT	128.6 v 98.0; p=0.001 (mean)	3.5 v 4.9 p=0.054	2.5 v 3.2day; p=0.196	NR	NR	Post-op pain / LHS (NSD) PC (19.5 v 16.3%; p=0.395)	**Study dates:** Apr to Oct 2009. **Experience:** Single surgeon (not experienced at start). **Conflicts:** None. **Operative time:** skin incision to closure. **Baseline differences:** none noted. **Results:** Hyperesthesia/paresthesia in neck, 1 week (15 v 41; p=0.01), 3 months (4 v 28; p=0.002); Cosmetic satisfaction 3 months, extremely satisfied (24 v 5; p<0.0001); Mean NLND (4.4 v 4.3).
Tae K 2011[136] III-3	41 RAET 167 OT	179 v 131 p<0.001		6.4 v 6.1; p=0.370	NR	NR	NSD (PC)	**Study dates:** Oct 2008-Aug 2009. **Experience:** Single surgeon and institute, inexperienced in RA surgery at start / prospective study with retrospective comparison. **Conflicts:** supported by research fund (Hanyang University) with no conflicts of interest stated. **Baseline differences:** More females, younger cohort (statistically significant) in RA group. **Results:** Post-op (week 1) anterior chest pain score (higher in robot-assisted; p<0.001), NSD at 1,3 months; Mean NLND (4.78 v 9.61; p<0.01); DT (33.5 v 22.9min; p=0.009); Amount of drainage (249 v 152ml; p=0.002); Cosmetic satisfaction (RAET excellent v OT at 1 week, 1,3 months; p<0.001).

Robot-assisted surgery for primary neoplasms (robot-assisted primary) = **RP**; robot-assisted salvage surgery for recurrent disease (robot-assisted salvage) = **RS**; open salvage resection for recurrent disease = **OS**; robot-assisted thyroidectomy = **RT**; conventional thyroidectomy = **CT**; Robot-assisted endoscopic thyroidectomy = **RAET**; open thyroidectomy = **OT**; length of hospital stay = **LHS**; gastrostomy tube dependent = **GTD**; tracheotomy tube dependent = **TTD**; complication rate = **CR**; operation time = **OT**; number of lymph nodes dissected = **NLND**; estimated blood loss = **EBL**; post-operative complications = **PC**; draping time (not included in OT) = **DT**; statistically significant = SS; no significant difference = **NSD**; not reported = **NR**.

Appendix 3.

Meta-analysis of clinical effectiveness studies

Prior to conducting the meta-analyses, data were extracted from the studies identified in the systematic review. For continuous variables the mean and standard deviation were required. A number of studies reported median rather than mean, and range or inter-quartile range rather than standard deviation. The study size and mean were poor predictors of standard deviation so it was necessary to estimate the distribution that would generate the reported mean and range. This was achieved using a log normal distribution and then calculating the standard deviation of that distribution.

Pooled effect estimates were generated using random effects meta-analysis. The Der Simonian-Laird estimator was used to determine study weights. Heterogeneity was assessed using the I^2 statistic. For continuous variables (i.e. operative time, length of stay, blood loss) the mean difference was pooled while for binary outcomes the relative risk was pooled. For binary outcomes a continuity correction of 0.5 was applied to all cells of any study with zero cases.

Meta-analyses were conducted for each effect of interest for a number of study subgroups: all studies excluding abstracts; all studies including abstracts; excluding outliers. For length of stay, the subgroup of non-US studies was also analysed. Potential outliers were identified on the basis of standardised residuals that exceeded ±1.96. Publication bias was assessed using a regression test for funnel plot asymmetry. The alpha level was set at 0.05 for all statistical tests. All calculations were carried out in R 2.12.2[249] using the packages metafor (v. 1.6-0)[250] and meta (v. 1.6-1)[251].

Appendix 4.

Economic evaluation

App 4.1 Introduction

The purpose of this Appendix is to:

- supplement the information provided in Chapter 4
- examine previously published economic analyses of robot-assisted surgeries for prostatectomy and hysterectomy
- describe the economic model for the introduction of robot-assisted prostatectomy and hysterectomy in Ireland.

App 4.2 Review of published economic evaluations

A review of economic evaluation studies comparing robot-assisted surgery to either open or conventional laparoscopic surgery was undertaken. The review was restricted to studies evaluating the cost-effectiveness in prostatectomy and hysterectomy only.

A systematic review approach was taken to identify suitable studies as outlined in Chapter 2. The review used the data gathered in the HTA by the Canadian Agency for Drugs and Technologies in Health (CADTH)[18] and updated the search to January 2011.

App 4.2.1 Prostatectomy

In addition to the 11 studies found in the CADTH review,[158-167;252] a further two studies were identified for prostatectomy.[168;169] One of the additional studies was published as an abstract only; in total four of the 13 studies were published only in abstract form.[160;162;168;252] Abstracts tend to evaluate as poor quality studies due to the limited information provided and because peer review for abstracts is generally less rigorous. One of the abstracts identified in the CADTH review is not readily available and could not be evaluated in this review.[252]

Lotan et al. compared the costs of open, laparoscopic and robot-assisted prostatectomy.[161] Patient characteristics were not reported. Surgical characteristics (e.g. operative time, length of stay) were obtained from a literature review. The analysis was limited to a mature series to remove any bias due to learning curves. Analyses were carried out both with and without the cost of the robot. This accounted for the situation where the robot was donated, but the annual maintenance fee was still incurred. When included, the cost of the robot was amortised over seven years. The average cost per procedure was US$5,554, US$6,041, US$7,280 and US$6,709 for open, laparoscopic, robot-assisted (purchased robot) and robot-assisted (donated robot), respectively.

Joseph et al. published an abstract of a cost comparison of open, laparoscopic and robot-assisted prostatectomy.[160] Average characteristics of the 233 included patients were reported, although no details on outcomes were provided. Limited details of the analyses were provided and although patient time costs were included, it is unclear if the cost of the robot was incorporated. Mean operating room costs were US$1,870, US$3,876 and US$5,410 for open, laparoscopic and robot-assisted surgery, respectively. Although robot-assisted and laparoscopic surgery were reported to have a statistically significant advantage over open surgery in the post-operative period, no details of the analysis were reported.

The average cost of open and robot-assisted prostatectomy were compared by Scales et al.[166] The analysis used the cost model of Lotan et al. with the cost of the robot included and amortised over seven years. Patient characteristics were not reported and no outcomes were included in the analysis. Open surgery was analysed for both a specialist and generalist or community setting. The mean cost per procedure was US$8,146, US$8,734 and US$8,929 for open (generalist setting), open (specialist setting) and robot-assisted surgery (specialist setting), respectively.

Burgess et al. compared the costs and outcomes of open and robot-assisted prostatectomy.[159] Open surgery was split into radical retropubic and radical perineal prostatectomy. This retrospective study did not report the characteristics of the 110 patients included. It was not evident if the cost of the robot was included in the analysis. Unusually, the mean length of stay was comparable across the groups analysed. Total mean cost per procedure was US$29,771, US$31,518 and US$39,315 for radical perineal, radical retropubic and robot-assisted prostatectomy, respectively. The higher costs in the robot-assisted group were driven by the higher operative costs.

Mayer et al. published an abstract comparing the cost of open, laparoscopic and robot-assisted surgery.[162] No patient characteristics were reported and the cost of the robot was not included in the analysis but the cost of maintenance was taken into account. Operative time and cost of hospital stay were assumed to be equivalent for laparoscopic and robot-assisted surgery. Clinical outcomes were not included in the analysis. The mean cost of surgery was GBP£3,701, GBP£4,756 and GBP£6,705 for open, laparoscopic and robot-assisted surgery, respectively.

Mouraviev et al. compared the costs and outcomes of open, robot-assisted and cryosurgical ablation of the prostate.[163] Open was further subdivided into radical retropubic and radical perineal prostatectomy. Mean characteristics were reported for the 452 patients included in the analysis. The cost of the robot was not included in the analysis. The mean total cost of surgery was US$10,704, US$10,536 and US$10,047 for open (radical retropubic), open (radical perineal) and robot-assisted surgery, respectively. Positive margins were highest, percentage patients with a Gleason score over seven was lowest and PSA recurrence was lowest in the robot-assisted prostatectomy cohort.

O'Malley and Jordan published a cost-utility analysis comparing open and robot-assisted prostatectomy.[164] Patient characteristics were not reported. The cost of the robot was incorporated as an initial capital cost followed by 7% interest per annum. Maintenance fees were included, but not incurred in the first year. Utilities were computed based on differences in continence and erectile dysfunction (ED).

Utility data were applied to the median time to return of continence and erectile function. The calculations for utilities are based on reductions in duration of incontinence and ED. The assumption is that outcomes are equivalent with the only difference being the time taken to achieve the outcome. The incremental cost of robot-assisted surgery is reported as AUS$2,264 and the incremental cost per QALY as AUS$24,457. Patient time costs were reported but not included in the analysis.

Steinberg et al. compared the net profit generated by laparoscopic and robot-assisted surgery.[167] Clinical outcomes were not considered and patient characteristics were not reported. Length of stay, blood loss, operative time, room turnover time, and all oncological outcomes were considered equivalent for laparoscopic and robot-assisted surgery. The analysis was conducted with and without the purchase cost of the robot taken into account. When taken into account, the robot capital cost was amortised over five years. In switching from laparoscopic to robot-assisted surgery, to maintain equivalent profit a hospital would have to complete an additional 20 and 78 operations per annum if the robot was donated or purchased, respectively.

As part of a comparison of radical prostatectomy and active surveillance, Ollendorf et al. compared the cost-effectiveness of open and robot-assisted surgery.[165] The economic model used defined patient characteristics. Operative characteristics were obtained from literature review. The perspective of the public payer was taken and the cost of complications and side effects were included. The cost of the robot was not included. The average total discounted costs were US$28,348 and US$26,608 for open and robot-assisted surgery, respectively. The average discounted QALYs were 7.82 and 7.97 for open and robot-assisted surgery, respectively. Robot-assisted surgery was less costly and more effective due to fewer post-surgical visits for complications and side effects.

Bolenz et al. compared the costs of open, laparoscopic and robot-assisted prostatectomy.[158] Characteristics of the retrospective cohort of patients were provided. It was assumed that robot-assisted surgery would be used for 126 cases per annum. The analysis included direct costs only, but also estimated the approximate impact of including the capital and maintenance costs of the robot with the capital cost amortised over seven years. The median direct costs were US$4,437, US$5,687 and US$6,752 for open, laparoscopic and robot-assisted surgery, respectively. Much of the additional cost of robot-assisted surgery stemmed from the cost of the robotic surgical supplies. Taking the cost of the robot and maintenance into account, the cost of robot-assisted surgery would increase by US$2,698 per patient.

Laungani and Shah compared the costs of open and robot-assisted surgery in a single institution.[168] Patient details are not provided and it is not stated whether the initial cost and maintenance fees are included in the analysis. The cost per case was US$16,495 and US$25,593 for open and robot-assisted surgery, respectively. However, the cost per case for robot-assisted surgery decreased over time to US$14,481 per patient. The reduced costs were largely attributed to increased volume with up to 269 operations carried out in a year.

Hohwü et al. compared the cost-effectiveness of open and robot-assisted surgery using a retrospective cohort study.(169) Patient characteristics were reported and the cost of the robot was included as an equivalent annual cost over five years. Costs of treatment for erectile dysfunction and incontinence were included in the model. Both direct and indirect costs were reported, the latter including the cost of absence from work. The average direct cost of surgery was €3,863 and €8,369 for open and robot-assisted surgery, respectively. When absence from work was taken into account, the average indirect cost of surgery was €12,465 and €13,411 for open and robot-assisted surgery, respectively. The incremental cost effectiveness ratio (ICER) per successful operation was €64,343 and €13,514 for direct and indirect cost models, respectively. A successful operation was defined as no residual cancer and urinary continence and sexual function with or without medication.

App 4.2.2 Hysterectomy

In addition to the two studies identified in the CADTH review,[75;83] a further four studies were found for hysterectomy.[73;170-172] Of the additional studies, two were published only as abstracts, so that in total two of the six studies were abstracts.[171;172]

Bell et al. compared the costs of open, laparoscopic and robot-assisted surgery for endometrial cancer staging.[75] Patient characteristics were reported and the capital cost of the robot was included in the analysis, amortised over five years by straight-line depreciation. Results were provided separately for direct and indirect costs. The total average direct costs were US$7,404, US$5,564 and US$6,002 for open, laparoscopic and robot-assisted surgery, respectively. Total average indirect costs were US$5,540, US$2,006 and US$2,210 for open, laparoscopic and robot-assisted surgery, respectively. The higher direct cost of open surgery was largely attributed to the longer average length of stay. The indirect cost differences were mostly influenced by differences in the time to returning to work which was shortest for patients undergoing robot-assisted surgery.

Sarlos et al. compared the operating room costs of laparoscopic and robot-assisted surgery using a matched case-control study.[83] Patient characteristics were reported and the cost of the robot was not included in the analysis. Only costs associated with operating room were included so other costs, such as those associated with length of stay, were not included. The total average cost per patient was €2,151 and €4,067 for laparoscopic and robot-assisted surgery, respectively. The difference in cost was mainly due to the increased material costs relating to the robotic instruments.

Barnett et al. compared the costs of open, laparoscopic and robot-assisted surgery for endometrial cancer staging.[170] Estimates of operative characteristics were drawn from the literature. The cost of the robot was included and amortised over seven years. In addition to a hospital perspective model, a societal model was developed including lost wages and caregiver costs. The base-case model assumed 27 operations per month. In the hospital perspective model including robot cost, the average cost of surgery was US$7,009, US$6,581 and US$8,770 for open, laparoscopic and robot-assisted surgery, respectively. Including the cost of the robot added US$1,292 per case. In the societal perspective model, the average cost of surgery was US$12,847, US$10,128 and US$11,476 for open, laparoscopic and robot-assisted surgery, respectively.

Holtz et al. compared the cost of laparoscopic and robot-assisted surgery for endometrial cancer staging.[73] The study reported the characteristics of the retrospective cohort of 33 patients. The cost of the robot was not included in the analysis. The total hospital costs were US$3,615 and US$5,084 for laparoscopic and robot-assisted surgery, respectively. The main sources of differences in cost of the two approaches were the higher cost of disposable instruments and longer operative time associated with robot-assisted surgery.
Sarlos et al. reported the preliminary results from an RCT comparing laparoscopic and robot-assisted total hysterectomy.[171] Quality of life was recorded, but not reported. Limited details of the analysis are provided and it is assumed that the cost of the robot was not included. The average costs were €1,417 and €3,384 for laparoscopic and robot-assisted surgery, respectively. The results suggest comparability in outcomes, but a longer operative time for robot-assisted surgery that may be influenced by the surgeon's learning curve.

Wright et al. reported a cost comparison of open (abdominal), open (vaginal), laparoscopic and robot-assisted hysterectomy.[172] Costs are based on hospital billing information and it is assumed that the cost of the robot is not included. The average total hospital cost was US$48,720, US$41,143, US$41,436 and US$50,758 for open (abdominal), open (vaginal), laparoscopic and robot-assisted surgery, respectively. Robot-assisted surgery had a much longer average operative time than the other techniques, making a substantial contribution to the increased costs associated with that approach.

Table App 4.1 - Summary of cost-effectiveness and budget impact assessments of robotic assisted prostatectomy

Study	Year	Setting	Full paper	Outcomes	Scenario	Results	Robot purchase cost included
Lotan et al.	2004	US	Yes	Incremental cost	Open	€8,556	Yes
					Laparoscopic	€9,306	
					Robot-assisted	€11,215	
Joseph et al.	2005	US	No	Mean operating room cost	Open	€1,754	Unclear
					Laparoscopic	€3,635	
					Robot-assisted	€5,074	
Scales et al.	2005	US	Yes	Mean cost	Open	€8,191	Yes
					Robot-assisted	€8,374	
Burgess et al.	2006	US	Yes	Mean cost	Open	€28,636	Unclear
					Robot-assisted	€35,720	
Mayer et al.	2007	UK	No	Mean cost	Open	€4,574	No
					Laparoscopic	€5,877	
					Robot-assisted	€8,286	
Mouraviev et al.	2007	US	Yes	Mean cost	Open	€9,725	No
					Robot-assisted	€9,128	
O'Malley and Jordan	2007	Australia	Yes	Incremental cost	Robot-assisted v open	€2,122	Yes
				ICER per QALY	Robot-assisted v open	€22,918	
Steinberg et al.	2008	US	Yes	Additional procedures required for equivalent profit	Robot-assisted v laparoscopic	78	Yes
Ollendorf et al.	2009	US	Yes	Mean cost	Open	€24,203	No
					Robot-assisted	€22,717	
Bolenz et al.	2010	US	Yes	Median cost	Open	€3,727	Yes
					Laparoscopic	€4,777	
					Robot-assisted	€7,938	
Laungani and Shah	2010	US	No	Mean cost	Open	€13,856	Unclear
					Robot-assisted (initial)	€21,498	
					Robot-assisted (high volume)	€12,164	
Hohwü et al.	2011	Denmark	Yes	Mean cost	Open	€2,936	Yes
					Robot-assisted	€6,360	
				ICER per QALY	Robot-assisted v open	€48,901	

Costs inflated to 2010 prices using local consumer price indices and then transferred to Ireland using Purchasing Power Parity Index
ICER = incremental cost effectiveness ratio

Table App 4.2 - Summary of cost-effectiveness and budget impact assessments of robotic assisted hysterectomies

Study	Year	Setting	Full paper	Outcomes	Scenario	Results	Robot purchase cost included
Bell et al.	2008	US	Yes	Mean cost	Open	€6,299	Yes
					Laparoscopic	€4,734	
					Robot-assisted	€5,106	
Sarlos et al.	2010	Switzerland	Yes	Mean cost	Laparoscopic	€3,097	No
					Robot-assisted	€5,856	
Barnett et al.	2010	US	Yes	Mean cost	Open	€5,888	Yes
					Laparoscopic	€5,528	
					Robot-assisted	€8,452	
Holtz et al.	2010	US	Yes	Mean cost	Laparoscopic	€3,037	No
					Robot-assisted	€4,271	
Sarlos et al. b	2010	Switzerland	No	Mean cost	Laparoscopic	€2,040	Unclear
					Robot-assisted	€4,873	
Wright et al.	2010	US	No	Mean cost	Open	€40,925	No
					Laparoscopic	€34,806	
					Robot-assisted	€42,637	

Costs inflated to 2010 prices using local consumer price indices and then transferred to Ireland using Purchasing Power Parity Index

App 4.3 Details of the economic evaluation

The economic evaluation uses a probabilistic model to simulate the impact on costs and outcomes of introducing robot-assisted surgery compared to the current standard of care. The assessment of clinical effectiveness found evidence to support economic modelling for prostatectomy and hysterectomy. For prostatectomy there is evidence of differences in outcomes and hence a cost-utility analysis was feasible. For hysterectomy there was no evidence of differences in outcomes so a cost-minimisation was the most appropriate method of evaluation. Finally, a third model combining a mix of prostatectomy and hysterectomy was developed using a cost-minimisation approach.

For all three models a patient cohort is modelled for each year of the robot lifespan. The cohort is characterised by the age and, in the case of prostatectomy, the pathological stage and life expectancy, of each patient. For both the current standard of care and for robot-assisted surgery, each patient is given operative characteristics (e.g., operative time, length of stay, number of units transfused). In the case of prostatectomy the outcomes for sexual function, urinary function and positive surgical margin are also simulated along with the implications for further treatment (i.e., continence pads, PDE5 inhibitors, adjuvant radiotherapy). The operative characteristics and outcomes are used to compute the total incremental cost of robot-assisted surgery for the cohort.

The process of modelling a cohort over the robot lifespan generates the data to compute the average incremental cost for a single simulation. The key model parameters are expressed as distributions rather than point estimates to account for the uncertainty around their values. The model runs repeated simulations to capture the effect of variation in the model parameters. Each of the three models is a variation of the same basic structure but with parameters specific to the indication being modelled. The following text outlines the steps in the basic model:

- For each simulation a robot lifespan is simulated along with the initial and steady state volumes.
- In the simulation the model generates a patient cohort for each year of the robot lifespan.
- Each patient cohort is given ages and, in the case of prostatectomy, tumour stage.
- For the current standard of care an operative time, length of stay and number of blood transfusions is simulated for each patient.
- For robot-assisted surgery an operative time, length of stay and number of blood transfusions is simulated for each patient.
- For prostatectomy, positive surgical margin, urinary function and sexual function outcomes are also simulated for each patient under the current standard of care and also for robot-assisted surgery.
- The costs of care are computed for the cohort for both the current standard of care and for robot-assisted surgery.
- The incremental costs, budget impact and, in the case of prostatectomy, incremental cost effectiveness are recorded for each year of the simulation.
- The costs are summed for each simulation with discounting applied for calculating the incremental cost and ICER.
- The median, 2.5th and 97.5th percentiles are computed across all simulations to give the point estimate, lower bound and upper bound, respectively, for each output (i.e. incremental cost, budget impact and ICER).

The model was developed an executed in R 2.13.0.(249)

App 4.4 Economic model parameters

The economic model requires a range of input parameters that describe the characteristics of the patients undergoing treatment, the operative characteristics, the clinical effectiveness and the costs associated with surgery. The purpose of this section is to detail the assumptions around the key parameters.

App 4.4.1 Target population

Two target populations are relevant to this study: men requiring radical prostatectomy; and women requiring hysterectomy that cannot be completed vaginally. The age distribution of patients was obtained from the Hospital In-Patient Enquiry system.[174]

Key assumptions:

- the age distribution of patients undergoing prostatectomy and hysterectomy will remain unchanged over the next ten years
- patients over 70 are not excluded from the analysis although the distributions have been selected to minimize the number of over 70s in line with the observed data from HIPE

For men undergoing radical prostatectomy, the probability of a positive surgical margin is dependent on the pathological status. Based on the analysis of clinical effectiveness studies approximately three quarters of patients are pT2 with the remainder being pT3.

Key assumption:

- the proportion of prostatectomy patients who are pathological status pT2 will not change markedly in the next ten years

App 4.4.2 Volume of operations

The volume of patients that can be treated each year is constrained by logistical issues. The time taken to complete robot-assisted surgery is assumed to decrease with increasing surgeon and team experience. Based on the opinion of the Expert Advisory Group, it is assumed that this translates into increasing volumes until a steady state is reached within 3 to 5 years.

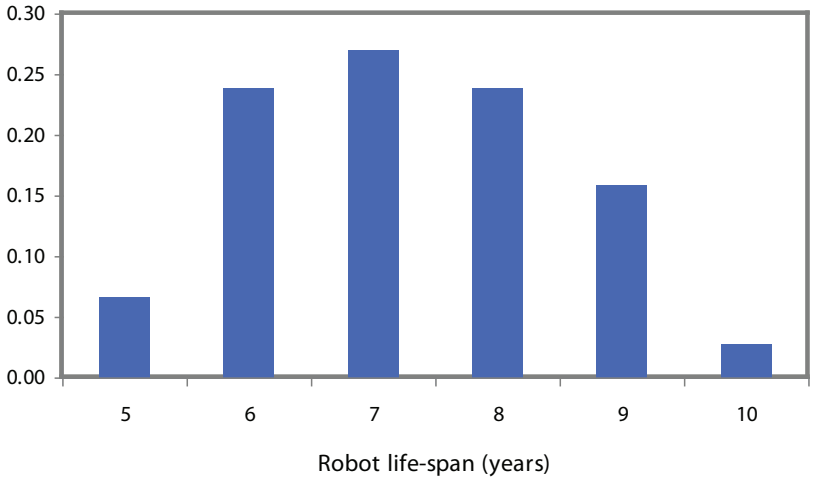
Key assumptions:

- In all three models the volume of operations in year one will be 100 (95% CI: 75 – 125)
- In the prostatectomy alone model the steady state volume is 200 (95% CI: 200 – 250) operations per annum
- In the hysterectomy alone and combined models the steady state volume is 300 (95% CI: 225 – 375) operations per annum
- The rate of increase of operations per annum from initial to steady state is approximately 50 cases
- In the prostatectomy alone model steady state is generally reached in the third year
- In the hysterectomy alone and combined models steady state is generally reached in the third year

App 4.4.2 Time horizon

The evaluation is restricted to operations taking place during the lifespan of the robot. The median robot lifespan is 7 years with a range of 5 – 10 years.

Figure App 4.1 Probability of different robot lifespans



App 4.4.3 Efficacy and effectiveness

The data on the efficacy and effectiveness of robot-assisted prostatectomy and hysterectomy has been derived from a systematic review of the relevant studies (see Chapter 3).

Key assumptions:

- The pooled mean differences for operative time derived from international literature are applicable to the Irish setting
- Data on length of stay derived from US and Asian studies are not applicable to the Irish setting and only European studies are appropriate to derived pooled mean differences
- Probability of transfusion is a more relevant parameter than estimated blood loss and that where blood loss is clinically significant a transfusion will occur
- The data for hysterectomy have been generated by a weighted pooling of data for radical, total with node staging and total simple hysterectomy. The prevalence of these three types of surgery in non-vaginal hysterectomy is approximately in the ratio of 4:26:70 in Ireland.

App 4.4.4 Safety

While differences in complication rates were observed it was unclear if they were in more or less severe complications. As rates of complications tended to be low and studies tended to have small numbers of participants, the studies were underpowered for analyses of subgroups of complications. Hence there were insufficient data to determine if the differing rates of complications could be taken as evidence of difference in patient outcomes.

Differences in conversion rates for robot-assisted and laparoscopic surgery have been found in the literature. The rates of conversion from robot-assisted and conventional laparoscopic to open have been incorporated into the model.

Key assumptions:

- Any differences in peri-operative complications do not lead to differences in patient outcomes or costs.
- Robot-assisted surgery converts to open rather than laparoscopic surgery.
- When surgery converts from robot-assisted to open, operative time is equal to on average half the operative time for robot surgery plus normal operative time for open surgery.
- When surgery converts from robot-assisted to open, the outcomes from open surgery apply.
- The conversion rates for hysterectomy have been generated by a weighted pooling of data for radical, total with node staging and total simple hysterectomy. The prevalence of these three types of surgery in non-vaginal hysterectomy is approximately in the ratio of 4:26:70 in Ireland.

App 4.4.5 Resource use and costs

Only direct costs relevant to the publicly-funded health and social care system are included in the evaluation. For all models this includes: robot capital and maintenance costs, theatre staff costs, theatre equipment costs, anaesthetic costs, blood transfusion costs, sterilisation costs, hospital stay costs, and incineration costs. The capital cost of the robot is annualised using straight-line depreciation over the time horizon. There is no maintenance cost in the first year after purchase of the robot. For the prostatectomy model costs are also included for continence pads, PDE5 inhibitors and adjuvant radiotherapy. Prices are current with staff costs taken from the mid-point of published pay scales. Location and theatre allowances are included. Transfer payments (VAT) are excluded.

Table App 4.3 – Breakdown of costs

Item	Cost (€)	VAT rate
Robot purchase	1.45 million	21%
Additional robot capital equipment	4,600	21%
Annual robot maintenance fee	150,000	13.5%
Equipment costs per prostatectomy:		
Open	380	21%
Laparoscopic	813	21%
Robot-assisted	2,402	21%
Equipment costs per hysterectomy:		
Open	345	21%
Laparoscopic	707	21%
Robot-assisted	2,458	21%
Theatre staff (per hour)	850	
Anaesthetic maintenance vapours (per hour)	60	
Waste incineration (per tonne)	1800	13.5%
Per diem:		
Prostatectomy	731	
Hysterectomy	534	
Unit of RBC for transfusion	248	
Central Sterile Supply Department (per hour)	97	
Adjuvant radiotherapy (per session)	283	
Continence pads (each)	1.15	21%
PDE5 inhibitors (per pack)	28.85	21%

Key assumptions:

- It takes an additional 55 minutes to sterilize equipment for the robot after a procedure.
- A sharps bin weighs on average 6.2kg after an open operation and 8.25kg after a laparoscopic or robot-assisted operation.
- With the exception of theatre staff, Central Sterile Supply Department and the robot itself, all other costs may vary by ±20% each year.

App 4.4.6 Outcomes

For the economic evaluation of prostatectomy alone, the outcomes of positive surgical margin, sexual function and urinary continence are estimated. The presence of a positive surgical margin results in a probability of requiring adjuvant radiotherapy in preference to active surveillance.

Key assumptions regarding functional outcomes:

- The pooled relative risks for surgical outcomes derived from international literature are applicable to the Irish setting
- A patient can only regain urinary or sexual function post-operatively if they were pre-operatively functional
- There is no correlation between regaining urinary and sexual function. That is, it is assumed in the model that a patient regaining urinary function is no more likely to regain sexual function than a patient who does not regain sexual function.
- It is assumed that a patient who loses urinary function will use on average one pad a day.
- For patients who have sexual function following prostatectomy, it is assumed that 23% (95% CI: 4% - 58%) do so with the aid of PDE5 inhibitors.
- Of patients requiring either continence pads or PDE5 inhibitors, it is assumed that 50% (95% CI: 21% - 79%) will be eligible for, and avail of those provided through the publicly-funded healthcare system.
- Patient acquiring PDE5 inhibitors through the publicly-funded healthcare system will be entitled to one packet per month.
- The inconvenience of erectile dysfunction and hence the loss of utility persists on average for 4 years (95% CI: 1–7).
- The utility gain for urinary function is assumed to extend on average to a point halfway between 4 years post-operatively and life-expectancy. The average prostatectomy patient has a life expectancy of 21 years. The mid-point between 4 years post-operative and life-expectancy is 12.5 years post-operative.
- Where both urinary incontinence and erectile dysfunction are experienced, the combined loss of utility applies for on average 4 years (95% CI: 1–7) after which the loss of utility for urinary incontinence continues on average to a point halfway between 4 years and life expectancy.
- The utility of combined urinary incontinence and erectile dysfunction is always less than the utility of urinary continence alone. This applies where a patient transfers from combined loss of function to loss of urinary function.

Key assumptions regarding positive surgical margins:

- Only patients with a positive surgical margin will be considered for adjuvant radiotherapy.
- Courses of adjuvant radiotherapy typically comprise 33, 35 or 45 sessions with equal probability.

The median and confidence bounds for each of the main parameters along with the type of distribution used is listed for the three models in the following tables (Tables App 4.4 – App 4.6).

Table App 4.4 - Parameter values for prostatectomy model

Parameter	Distribution (median & 95% CI)			
	Universal	**Open**	**Robot**	**Laparoscopic**
Robot lifespan (years)	7 (5- 10			
Annual volume of operations				
Year 1	99 (74 - 124)			
Year 2	164 (131 - 206)			
Year 3 onwards	199 (146 - 249)			
Patient age (years)	gamma			
	58 (47 - 71)			
Laparoscopic surgery	beta			
	0.07 (0.04 - 0.11)			
Probability of being pT2	beta			
	0.75 (0.70 - 0.80)			
Utility for loss of urinary function	beta			
	0.90 (0.57 - 1.00)			
Utility for loss of sexual function	beta			
	0.93 (0.68 - 1.00)			
Utility for loss of urinary and sexual function	beta			
	0.87 (0.47 - 1.00)			
Probability of pre-operative urinary function	beta			
	0.80 (0.63 - 0.93)			
Probability of pre-operative sexual function	beta			
	0.80 (0.63 - 0.93)			
Proportion of patients with post-operative sexual function requiring PDE5 inhibitors	beta			
	0.23 (0.04 - 0.58)			
Proportion patients eligible for State-provided continence pads and PDE5 inhibitors	beta			
	0.50 (0.21 - 0.79)			
Operative time (minutes)		log normal	open + normal	robot + normal
		190 (134 - 272)	227 (167 - 310)	203 (137 - 289)
Length of stay (days)		gamma	open + normal	robot + normal
		9 (4 - 16)	7 (2 - 14)	7 (2 - 15)
Probability of blood transfusion		beta	beta	beta
		0.20 (0.13 - 0.29)	0.02 (0.01 - 0.04)	0.05 (0.03 - 0.08)
Probability of conversion to open			beta	beta
			0.005 (0.002 - 0.011)	0.013 (0.003 - 0.035)
Probability of PSM (pT2)		beta	beta	beta
		0.15 (0.11 - 0.19)	0.11 (0.09 - 0.13)	0.14 (0.10 - 0.18)
Probability of PSM (pT3)		beta	beta	beta
		0.42 (0.35 - 0.50)	0.43 (0.36 - 0.51)	0.32 (0.18 - 0.48)
Probability of sexual function at 12 months		beta		
		0.40 (0.30 - 0.51)		
Relative risk of sexual function at 12 months			log normal	log normal
			1.55 (1.21 - 1.99)	1.68 (0.84 - 3.34)
Probability of continence at 12 months		beta		
		0.88 (0.83 - 0.92)		
Relative risk of continence at 12 months			log normal	log normal
			1.06 (1.01 - 1.11)	1.09 (1.03 - 1.16)

Note: 'open + normal' denotes a normal distribution was added to the distribution estimated for open surgery.

Table App 4.5 - Parameter values for hysterectomy model

Parameter	Distribution (median & 95% CI)			
	Universal	**Open**	**Robot**	**Laparoscopic**
Robot lifespan (years)	7 (5- 10			
Annual volume of operations				
Year 1	99 (74 - 124)			
Year 2	158 (131 - 187)			
Year 3	216 (185 - 253)			
Year 4	269 (221 - 311)			
Year 5 onwards	297 (223 - 374)			
Patient age (years)	gamma			
	49 (31 - 74)			
Laparoscopic surgery	beta			
	0.08 (0.06 - 0.09)			
Operative time (minutes)		log normal	open + normal	robot + normal
		108 (67 - 176)	172 (117 - 246)	160 (94 - 240)
Length of stay (days)		log normal	open + normal	robot + normal
		8 (3 - 18)	6 (1 - 16)	6 (1 - 17)
Probability of blood transfusion		beta	beta	beta
		0.09 (0.04 - 0.16)	0.01 (0.00 - 0.04)	0.03 (0.01 - 0.07)
Probability of conversion to open			beta	beta
			0.028 (0.015 - 0.047)	0.054 (0.024 - 0.102)

Note: 'open + normal' denotes a normal distribution was added to the distribution estimated for open surgery. s

Table App 4.6 - Parameter values for the combined prostatectomy and hysterectomy model

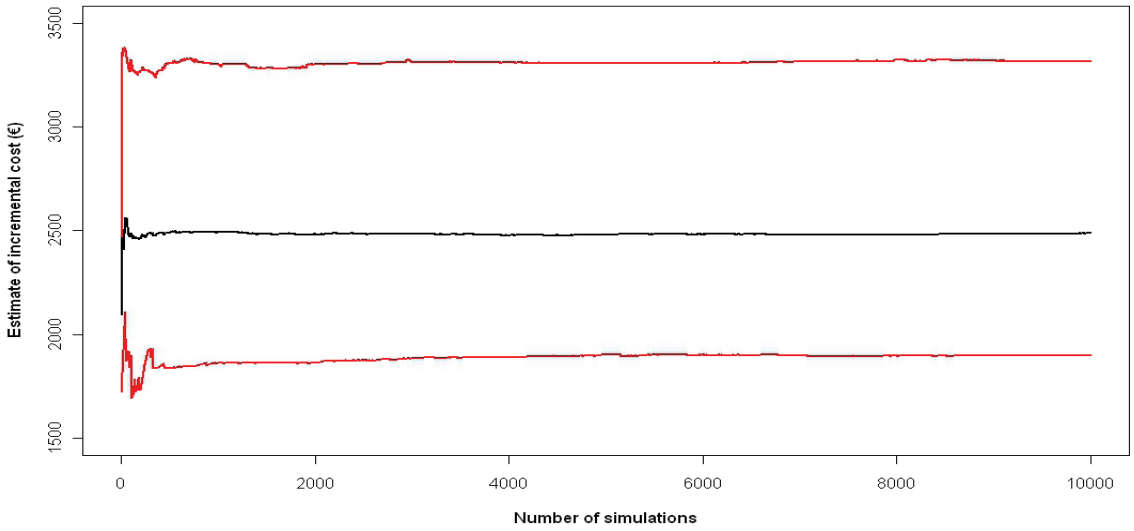
Parameter	Distribution (median & 95% CI)		
	Hysterectomy	**Prostatectomy**	**Combined**
Robot lifespan (years)	7 (6 - 9)		
Annual volume of operations			
Year 1	80 (59 - 101)	20 (14 - 27)	99 (74 - 124)
Year 2	127 (105 - 152)	32 (24 - 42)	158 (131 - 187)
Year 3	174 (147 - 206)	43 (33 - 57)	215 (185 - 253)
Year 4	217 (176 - 254)	54 (40 - 70)	268 (221 - 310)
Year 5 onwards	240 (177 - 303)	60 (41 - 82)	297 (222 - 372)

App 4.5 Model convergence

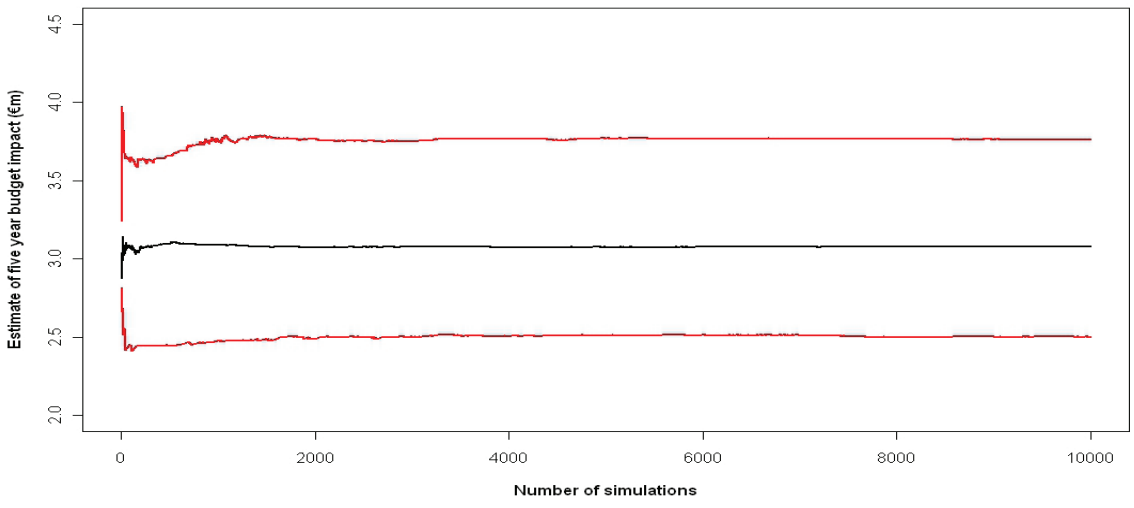
As the economic models were fully probabilistic with many parameters defined by wide distributions, it was important to ensure that sufficient simulations were used to obtained stable estimates of the main outputs. Each of the three models was run for 10,000 simulations. The outputs of incremental cost, five-year budget impact and, in the case of Model 1, ICER were assessed to determine how many simulations were required for the model to converge on a stable result (see Figures App 4.2, App 4.3 and App 4.4). With the exception of the ICER in Model 1, all outputs converged on a stable result within 5,000 simulations. The point estimate for the ICER in Model 1 converged on a stable result within 3,000 simulations but the estimate of the upper bound was not stable until after 6,000 iterations.

Figure App 4.2 - Model convergence: prostatectomy model

a) Incremental cost



b) Budget impact



c) ICER

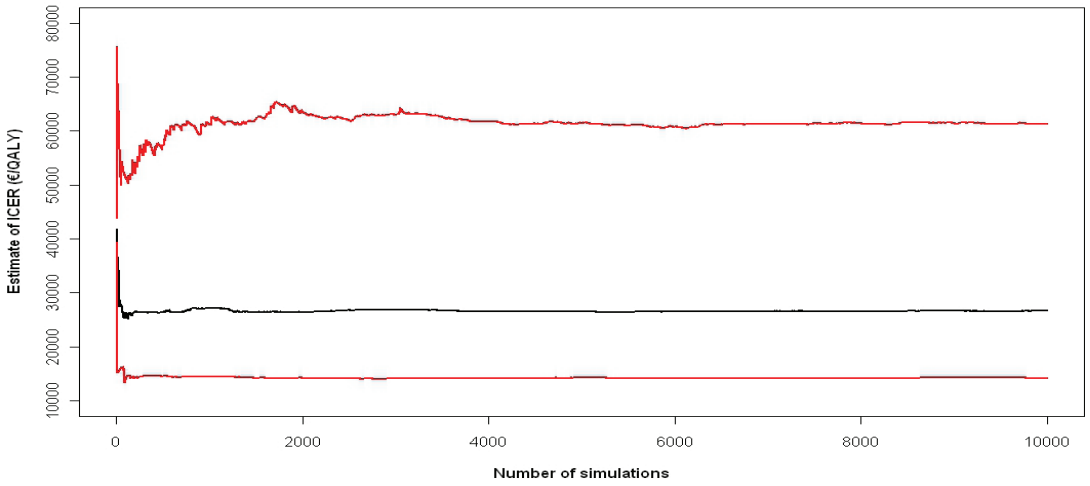
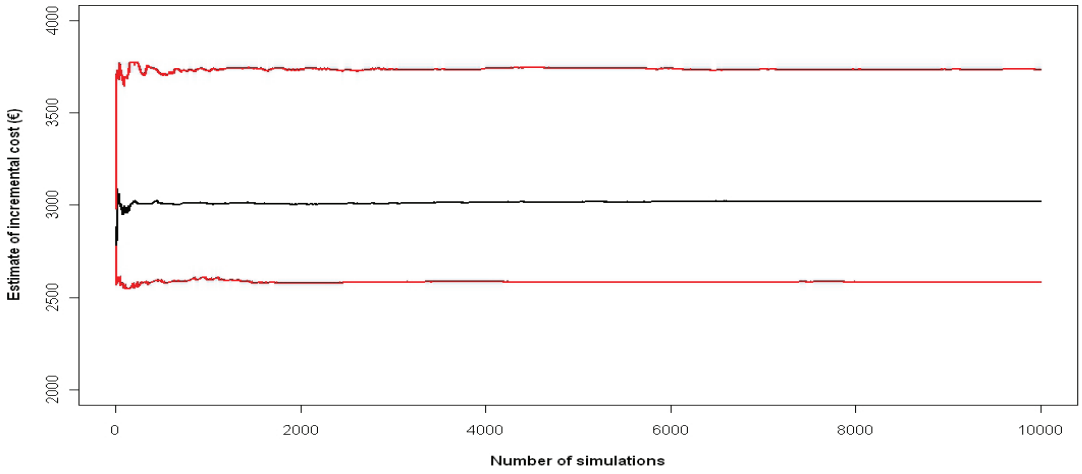


Figure App 4.3 - Model convergence: hysterectomy model

a) Incremental cost



b) Budget impact

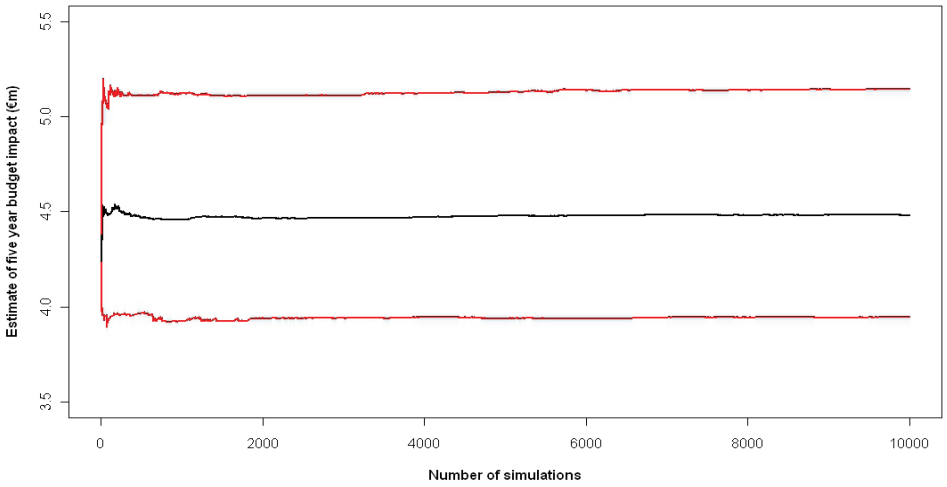
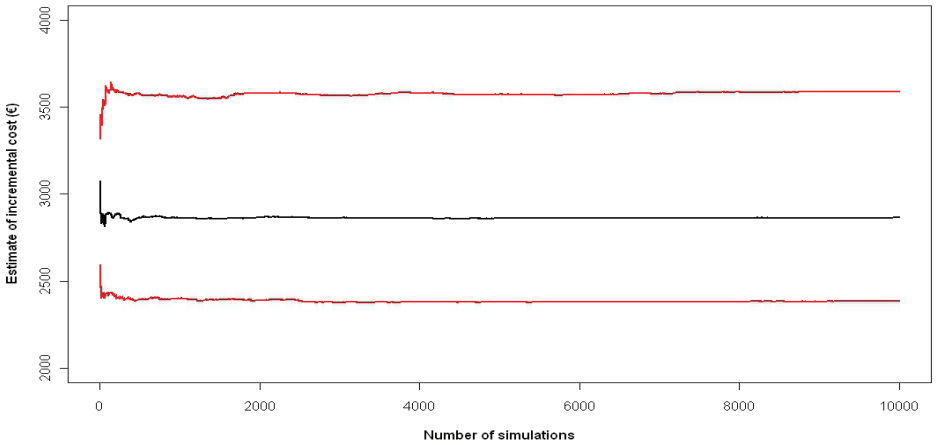
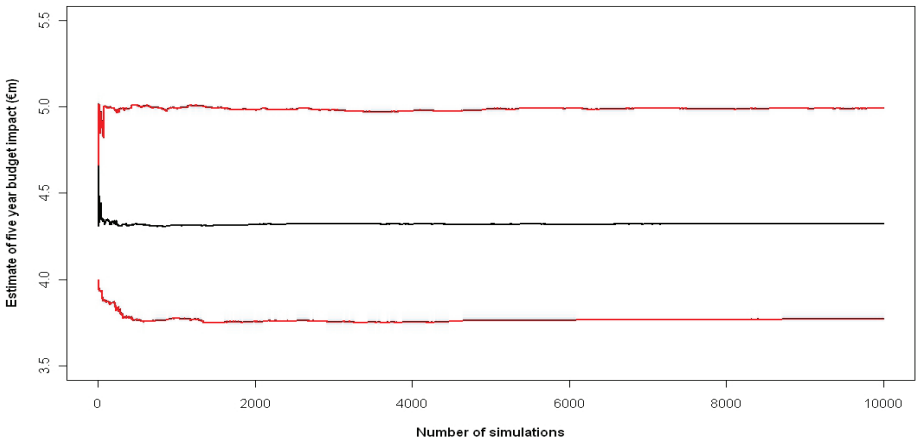


Figure App 4.4 - Model convergence: combined prostatectomy and hysterectomy model

a) Incremental cost



b) Budget impact



Appendix 5.

Published information in relation to training in robotic surgery

Post-fellowship surgeons with proficiency in open or laparoscopic procedures require a structured training programme to become competent in robot-assisted surgery.[185] Such programmes commence with a pre-clinical phase. This phase is primarily provided by the technology manufacturer, Intuitive Surgical Inc., although in the US a 'mini-residency' programme has been initiated in one organisation.[12] The pre-clinical programme includes familiarisation with the equipment, online tutorials, dry lab experience, wet lab experience with animals or cadavers together with training to deal with emergencies and troubleshooting. The robot workstation can be used as both a console controlling the robotic system and also as a simulator environment to rehearse specific procedures.[7] Additionally, training may also include the use of a second console that allows the trainee to view the surgery as per the primary surgeon and to assist during a case.[202;209]

In the second phase of training, the clinical phase, the trainee operates under the supervision of a surgeon trainer (preceptor). A preceptor is an experienced surgeon that scrubs in, supervises the procedure that the trainee is undertaking and retains primary responsibility for the wellbeing of the patient. The preceptor provides performance feedback to the trainee and assists in new skills-transfer using an active hands-on approach.[12] A second form of supervision is through a proctor – defined as an observer responsible for the assessment of the skills and knowledge of the trainee. In contrast to preceptoring, the trainee retains overall responsibility for the care of the patient. The proctor may report the findings to the department head or the medical staff at the institution and provides recommendations based on the findings.[12]

The importance of proctoring as an essential mechanism for institutional credentialing and as a prerequisite for granting unrestricted privileges on the robot has been highlighted by the American Society of Urologic Robotic Surgeons.[12] Surgeons who have performed as few as 20 procedures may currently be nominated as eligible proctors by the manufacturers. For competency to be assured, the development of appropriate guidelines and oversight for the nomination of proctors is recommended.[12]

Designating the number of surgeries required for proficiency is difficult as it depends on the surgeon, their professional experience, the procedure type and the complexities of the case. Specifically, the learning curve will differ depending on baseline experience in minimally invasive surgery. Fully trained and competent laparoscopic surgeons need just to add knowledge of the robot technology to existing clinical skills. Substantial learning is required for those with little or no experience in minimally invasive surgery however.[7;7] As a basic premise, it is recommended that designating competency should be based on demonstration of proficiency and safety in executing basic robotic skills and procedural tasks, rather than being based on a set number of completed cases.[185] A number of specific surgeon training recommendations and guidelines have been published, and a summary of these is included in the table below.

As with any technology, there is an ongoing requirement for surgeons to maintain and update their skills inline with system and equipment updates. Formal training for advanced robot-assisted surgical skills with structured interactive sessions are recommended.[185] It has been proposed that ongoing credentialing should take place,[7] with suggestions that this should include a minimum number of robot-assisted surgery procedures per year to avoid the loss of expertise and to ensure surgical competency and patient safety.[184;209;253]

Table App 5.1

Author / year / type	Preclinical Phase	Clinical Phase
Lee JY Literature search (2011)[185]	Background information: • Understanding disease pathophysiology • Basic laparoscopy understanding (physiology, technique, complications) Robot familiarization: • Introduction to components & functionality of robot relevant to the model to be used Lab experience: • Dry lab practice (e.g. models, virtual reality simulators) • Wet lab practice (e.g. pig or cadaveric lab sessions)	Procedure experience: • Procedure specific familiarization (observation (videos, live cases), bedside assistant) • Console time (using a graduated, step-wise approach)
SAGES-MIRA Guidelines (2007)[7]	Background information: • Initiate mentoring by providing information, skill training, technology familiarisation Identify proctor with: • Substantial practical experience in clinical applications (reported results & review) Individuals should have: • Specialty specific experience, expertise in technology Training duration: • Reflect technology complexity, specific procedure, experience of student Robot familiarization: • Technology, device function, altered functional status, basic troubleshooting, other technical issues, device parameters & limitations understanding Lab experience: • Hands on experience: non clinical simulation - system set up, connections, operation, troubleshooting • Initial skill training: techniques to complete intended procedure	Procedure experience: • Live cases: procedure prep, system set up, patient positioning, review of case selection and intra-operative technical aspects • Clinical simulation: complete key components using appropriate model, use advanced simulation tools when available. Residency programs: • Specialty training programs - exposure to therapeutic robotic interventions as part of their curriculum.
Baus Guidelines (2006)[184]	Background information: • BAUS, UK (training in laparoscopy)* Lab experience: • Dry lab practice, develop facilities to practice • Wet lab practice (animal-based) Identify proor.	Procedure experience: • View live procedures or demonstrations • Attend high-volume centre • Practice procedure with mentor • Carry out several procedures independently observed by experienced surgeon • Audit results • Submit results to BAUS • Carry out > 12 marker cases per year

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