Health Technology Assessment 2012; Vol. 16: No. 41
ISSN 1366-5278

Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer

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November 2012
10.3310/hta16410

Health Technology Assessment
NIHR HTA programme
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Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer

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Declared competing interests of authors: none

Published November 2012
DOI: 10.3310/hta16410

This report should be referenced as follows:

Ramsay C, Pickard R, Robertson C, Close A, Vale L, Armstrong N, *et al*. Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer. *Health Technol Assess* 2012;**16**(41).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE, *Science Citation Index Expanded* (*SciSearch*®) and *Current Contents*®/ Clinical Medicine.

NIHR Health Technology Assessment programme

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 09/14/02. The contractual start date was in March 2011. The draft report began editorial review in July 2011 and was accepted for publication in February 2012. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design.The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

ISSN 2046-4932 (DVD)

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by Charlesworth Press.

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Abstract

Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer

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Background: Complete surgical removal of the prostate, radical prostatectomy, is the most frequently used treatment option for men with localised prostate cancer. The use of laparoscopic (keyhole) and robot-assisted surgery has improved operative safety but the comparative effectiveness and cost-effectiveness of these options remains uncertain.
Objective: This study aimed to determine the relative clinical effectiveness and cost-effectiveness of robotic radical prostatectomy compared with laparoscopic radical prostatectomy in the treatment of localised prostate cancer within the UK NHS.
Data sources: MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, BIOSIS, Science Citation Index and Cochrane Central Register of Controlled Trials were searched from January 1995 until October 2010 for primary studies. Conference abstracts from meetings of the European, American and British Urological Associations were also searched. Costs were obtained from NHS sources and the manufacturer of the robotic system. Economic model parameters and distributions not obtained in the systematic review were derived from other literature sources and an advisory expert panel.
Review methods: Evidence was considered from randomised controlled trials (RCTs) and non-randomised comparative studies of men with clinically localised prostate cancer (cT1 or cT2); outcome measures included adverse events, cancer related, functional, patient

driven and descriptors of care. Two reviewers abstracted data and assessed the risk of bias of the included studies. For meta-analyses, a Bayesian indirect mixed-treatment comparison was used. Cost-effectiveness was assessed using a discrete-event simulation model.

Results: The searches identified 2722 potentially relevant titles and abstracts, from which 914 reports were selected for full-text eligibility screening. Of these, data were included from 19,064 patients across one RCT and 57 non-randomised comparative studies, with very few studies considered at low risk of bias. The results of this study, although associated with some uncertainty, demonstrated that the outcomes were generally better for robotic than for laparoscopic surgery for major adverse events such as blood transfusion and organ injury rates and for rate of failure to remove the cancer (positive margin) (odds ratio 0.69; 95% credible interval 0.51 to 0.96; probability outcome favours robotic prostatectomy = 0.987). The predicted probability of a positive margin was 17.6% following robotic prostatectomy compared with 23.6% for laparoscopic prostatectomy. Restriction of the meta-analysis to studies at low risk of bias did not change the direction of effect but did decrease the precision of the effect size. There was no evidence of differences in cancer-related, patient-driven or dysfunction outcomes. The results of the economic evaluation suggested that when the difference in positive margins is equivalent to the estimates in the meta-analysis of all included studies, robotic radical prostatectomy was on average associated with an incremental cost per quality-adjusted life-year that is less than threshold values typically adopted by the NHS (£30,000) and becomes further reduced when the surgical capacity is high.

Limitations: The main limitations were the quantity and quality of the data available on cancer-related outcomes and dysfunction.

Conclusions: This study demonstrated that robotic prostatectomy had lower perioperative morbidity and a reduced risk of a positive surgical margin compared with laparoscopic prostatectomy although there was considerable uncertainty. Robotic prostatectomy will always be more costly to the NHS because of the fixed capital and maintenance charges for the robotic system. Our modelling showed that this excess cost can be reduced if capital costs of equipment are minimised and by maintaining a high case volume for each robotic system of at least 100–150 procedures per year. This finding was primarily driven by a difference in positive margin rate. There is a need for further research to establish how positive margin rates impact on long-term outcomes.

Funding: The National Institute for Health Research Health Technology Assessment programme.

Contents

List of abbreviations

ASA	American Society of Anesthesiologists
AUS	artificial urinary sphincter
BAUS	British Association of Urological Surgeons
CDSR	Cochrane Database of Systematic Reviews
CEAC	cost-effectiveness acceptability curve
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
COMET	Core Outcome Measures in Effectiveness Trials
CrI	central credible interval (for Bayesian analysis)
cT	preoperative clinical classification of tumour stage
DARE	Database of Abstracts of Reviews of Effects
EQ-5D	European Quality of Life-5 Dimensions
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30
EPIC-UISS-SFSS	Expanded Prostate Cancer Index Composite urinary incontinence and sexual function subscales
HRG	Healthcare Resource Group
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
ICIQ-UI	International Consultation of Incontinence Questionnaire
ICS	International Continence Society
IIEF-5	International Index of Erectile Function-5
I-PSS	International Prostate Symptom Score
ISD	Information Services Division (Scotland)
ISUP	International Society of Urological Pathology
LHRH	luteinising hormone-releasing hormone
log-OR	logarithm of the odds ratio
MAPS	men after prostate surgery trial
NICE	National Institute for Health and Clinical Excellence
NIH	National Institutes of Health
NIHR	National Institute for Health Research
OPCS	Office of Population Census and Surveys
OR	odds ratio
PSA	prostate-specific antigen
pT	postoperative pathological classification of tumour stage
QALY	quality-adjusted life-year
RCT	randomised controlled trial
SD	standard deviation
SF-12	Short Form questionnaire-12 items
SF-36	Short Form questionnaire-36 items
SHIM	Sexual Health Inventory for Men
TRUS	transrectal ultrasound
UCLA-PCI	University of California Los Angeles – Prostate Cancer Index

UICC	Union for International Cancer Control
VAS	visual analogue scale
WHO	World Health Organization

All abbreviations that have been used in this report are listed here unless the abbreviation is well known, such as NHS, or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Men diagnosed with cancer of the prostate, a sex gland located at the base of the bladder in the pelvis, have different treatment options depending on the severity of disease. One option is complete removal of the prostate, radical prostatectomy, which approximately 5000 men in the UK undergo each year. A keyhole surgical technique of radical prostatectomy either by standard laparoscopy or with the aid of robotic technology does appear to offer advantages in terms of reduced blood loss and quicker return to activity over the traditional open surgical approach. Advocates of the robotic system claim greater precision in dissection and more rapid gaining of surgeon competence than with the laparoscopic approach but the robotic system is costly. This review was designed to help inform decisions regarding the commissioning and use of robotic and laparoscopic surgery for men with localised prostate cancer in the NHS. The study aimed to:

- describe clinical care pathways in a UK NHS context
- determine the relative clinical effectiveness and safety of each procedure
- perform a systematic review of existing economic evaluations of each procedure
- determine which procedure is most likely to be cost-effective for implementation in the NHS
- determine the influence of the learning curve on estimates of effectiveness, safety and cost-effectiveness
- identify future research needs.

Methods

Clinical effectiveness review

MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, BIOSIS, Science Citation Index and Cochrane Central Register of Controlled Trials were searched from 1995 onwards for primary studies. Conference abstracts from meetings of the European, American and British Urological Associations were also searched, websites consulted and reference lists scanned. Evidence was considered from randomised controlled trials (RCTs) and non-randomised comparative studies and, for estimates of learning curve effects only, case series. Participants were men with clinically localised prostate cancer (preoperative clinical classification of tumour stage: cT1 or cT2) undergoing radical prostatectomy. Robotic radical prostatectomy was considered as the intervention and laparoscopic radical prostatectomy as the comparator. Outcome measures were adverse events, cancer-related outcomes, functional outcomes, patient-driven outcomes and descriptors of care. Two reviewers abstracted data and assessed the risk of bias of the included studies. For meta-analyses, a Bayesian indirect mixed-treatment comparison was used.

Cost-effectiveness

A systematic review of economic evaluations comparing the two forms of surgery was attempted. It was anticipated that this would be insufficient for decision-making and consequently a modelling exercise was planned. A discrete-event simulation model was produced reflecting the likely care pathways. Parameter estimates were derived from the systematic review of clinical effectiveness, a review of previous economic evaluations, other literature, the expert advisory group and other UK sources. The outputs of the model were costs and quality-adjusted life-years (QALYs) for each procedure, incremental costs and QALYs, and incremental cost per QALY for a 10-year time horizon. Both costs and QALYs were discounted at the rate recommended

by the UK Treasury of 3.5%. Probabilistic sensitivity analysis was performed to explore the uncertainty surrounding parameter estimates. This was combined with deterministic sensitivity analysis around variables believed to be key determinants of cost-effectiveness, including cost of the robotic system, number of procedures performed, positive margin rates and risk of biochemical recurrence.

Results

Clinical effectiveness

The searches identified 2722 potentially relevant titles and abstracts, from which 914 reports were selected for full-text eligibility screening. From these, data were included from 19,064 patients across one RCT and 57 non-randomised comparative reports. Few of these were considered to have a low risk of bias. The results, although associated with some uncertainty, demonstrated that robotic surgery was associated with a lower risk of major adverse events such as organ injury, and lower rates of surgical margins positive for cancer [odds ratio (OR) 0.69; 95% credible interval 0.51 to 0.96; probability outcome favours robotic prostatectomy = 0.987]. The predicted probability of a positive margin was 17.6% following robotic prostatectomy compared with 23.6% for laparoscopic prostatectomy. Restriction of the meta-analysis to studies at low risk of bias did not change the direction of effect, but did decrease the precision of the effect size (odds ratio 0.73; 95% credible interval 0.29 to 1.75). The available data suggested no evidence of a difference in the proportion of men suffering urinary incontinence at 12 months (OR 0.55; 95% credible interval 0.09 to 2.84; probability outcome favours robotic prostatectomy = 0.783). There were insufficient data to draw any conclusions on the likely size of a differential effect on rates of cancer-related, patient-driven or erectile dysfunction outcomes. The data provided no evidence that learning contributed differently to positive margin rates between the two procedures ($p = 0.755$).

Cost-effectiveness

In the base-case analysis (10-year time horizon) the incremental cost per QALY for robotic prostatectomy was < £30,000 provided that the number of procedures performed per year with each robotic system was > 150 [when the number of procedures per year was 100, the incremental cost-effectiveness ratio (ICER) was £47,822]. The probabilistic sensitivity analysis showed that the two procedures had a roughly equal likelihood of being considered cost-effective when the number of procedures per year was 150. When a lifetime time horizon was adopted the costs and QALYs for both procedures increased but the increase in QALYs more than compensated for the increase in cost of the robotic system and hence the incremental cost per QALY was < £30,000 for all of the scenarios considered. This includes a scenario in which the number of procedures performed per year was 50 and for which the most costly robotic equipment was used.

The results of the economic evaluation suggested that when the difference in positive margin rate estimated by meta-analysis of all included studies was used (base case), robotic radical prostatectomy was on average associated with an incremental cost per QALY that was less than the threshold value typically adopted by the NHS (£30,000) when the number of cases performed per year was ≥ 150. Only when optimistic assumptions were made for the positive margin rate (OR = 0.506) did the incremental cost per QALY for robotic prostatectomy fall below £30,000 for a throughput of 100 cases per year (when only 50 cases per year are performed the incremental cost per QALY was > £66,000).

In the base-case analysis, biochemical recurrence rates were assumed to be the same between treatments. A sensitivity analysis using the point estimate for the OR of differential rates between the treatments (0.89) resulted in a slight reduction in the incremental cost per QALY for all surgical capacity scenarios. In contrast to using the point estimate, doubling the chance

of biochemical recurrence in line with the absolute rates documented in the meta-analysis further reduced the incremental cost per QALY such that it was < £30,000 when the number of procedures performed using the robotic system was ≥ 100 cases per year.

Strengths and limitations

The main limitations were the low quantity and poor quality of the data available on cancer-related outcomes and long-term adverse events of urinary and sexual dysfunction. Many published studies were poorly reported or lacked sufficient detail and much of the information available was unsuitable for meta-analysis. The paucity of data had implications for the economic evaluation. In particular, the limited data meant that there was insufficient evidence to assume that there was any difference between interventions for a number of parameters, a particular issue for biochemical recurrence. The impact of these assumptions was explored in sensitivity analyses.

Conclusions

The results of this study should be interpreted with caution because of uncertainty but they do demonstrate that robotic prostatectomy has advantages in terms of reducing both perioperative morbidity and the risk of a positive surgical margin. Although direct cancer outcome data were lacking, use of the differential margin rate in our model suggests that use of robotic prostatectomy may be associated with improved overall survival. There were no data to infer whether use of robotic surgery resulted in a lower risk of incontinence or sexual dysfunction, although this was modelled.

Robotic prostatectomy will always be more costly to the NHS because of the fixed capital and maintenance charges for the robotic system. Our modelling shows that this excess cost per case might be reduced by commercial negotiation and by maintaining a high throughput of cases in each centre of at least 100–150 procedures per year. The cost-effectiveness of robotic prostatectomy was predominantly driven by the difference in positive margin rate. Uncertainties remain concerning the potential for bias in the estimates and how positive margin rates impact on long-term outcomes; therefore, a degree of caution is warranted in the interpretation of the results.

Recommendations for further research

- Well-designed prospective cohort studies directly comparing robotic and laparoscopic prostatectomy are required. Ideally such studies would be multicentre with long-term follow-up and would include independent assessment of prespecified measures of prostate cancer-specific survival, as well as independent recording of learning curve, urinary and sexual function and health-related quality of life.
- Further evidence on the relationship between positive margin rates and long-term outcomes.
- Research to elicit the short- and long-term postoperative health-state valuations (e.g. utility values) associated with prostatectomy and the contribution of different adverse consequences of surgery as perceived by men.
- Agreed definitions of outcomes in urology and measures for recording them. This would require consensus work in partnership with governing bodies.
- Research into strategies to improve the evaluation and potential dissemination of costly new technologies in the UK NHS.

Funding

- Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1

Background

Description of the underlying health problem

The decision about which treatment is best for a man diagnosed with cancer of the prostate, a sex gland located at the base of the bladder in the pelvis, presents an abundance of different but interrelated aspects that have been the focus of a number of previous Health Technology Assessments (HTAs) worldwide.[1–3] The present review was tasked with determining whether, for the UK NHS, complete removal of the prostate (radical prostatectomy) is best achieved using laparoscopic (keyhole) surgery or robotic surgery.

To understand the need for the review it is first necessary to consider changes in the characteristics of men diagnosed with prostate cancer over the last 30 years (see *Evolution of prostate cancer diagnosis*) and the resultant evolution of the technique of radical prostatectomy during that time period (see *Development of radical prostatectomy*). The technologies to be considered will then be described (see *Description of the interventions*) followed by an outline of the current demand for their use in the NHS (see *Current use in the UK NHS*).

Evolution of prostate cancer diagnosis

The discovery of prostate-specific antigen (PSA) in 1979 as an organ-specific serum marker of prostate cancer, followed by its introduction as a commercially available laboratory test in 1986, transformed the way that prostate cancer was diagnosed and managed worldwide.[4] Before PSA testing, men were generally diagnosed with prostate cancer following an abnormal digital rectal examination, with worsening urinary symptoms or with symptoms of metastatic disease such as bone pain. This meant that approximately 70% had locally advanced or metastatic disease on presentation.[5] Although complete removal of the prostate (radical prostatectomy) was a treatment option for locally advanced disease, most men progressed to metastasis when only palliative treatment such as androgen ablation (castration) could be offered, resulting in 5-year survival rates of < 50%.[6] The advent of PSA testing allied to systematic biopsy of the prostate gland changed this situation dramatically. It was realised that men with a serum PSA raised above a threshold value, originally set at 4 ng/ml[7] and more recently in the UK at age-specific values of between 3 and 5 ng/ml,[8] were more likely to have prostate cancer, which, if present, was usually at a preclinical stage without symptoms and was not detectable on digital rectal examination. Autopsy studies had previously showed that small foci of prostate cancer were common in men older than 45 years and that this prevalence increased with age. It was therefore not surprising that widespread adoption of PSA testing resulted in a substantial increase in the number of men diagnosed with prostate cancer during the 1980s and 1990s[9] (*Figure 1*). Areas of the world that adopted PSA testing have subsequently experienced falling mortality rates for prostate cancer, but whether this is due to more successful radical treatment or a mixture of length and lead-time bias remains uncertain.[11]

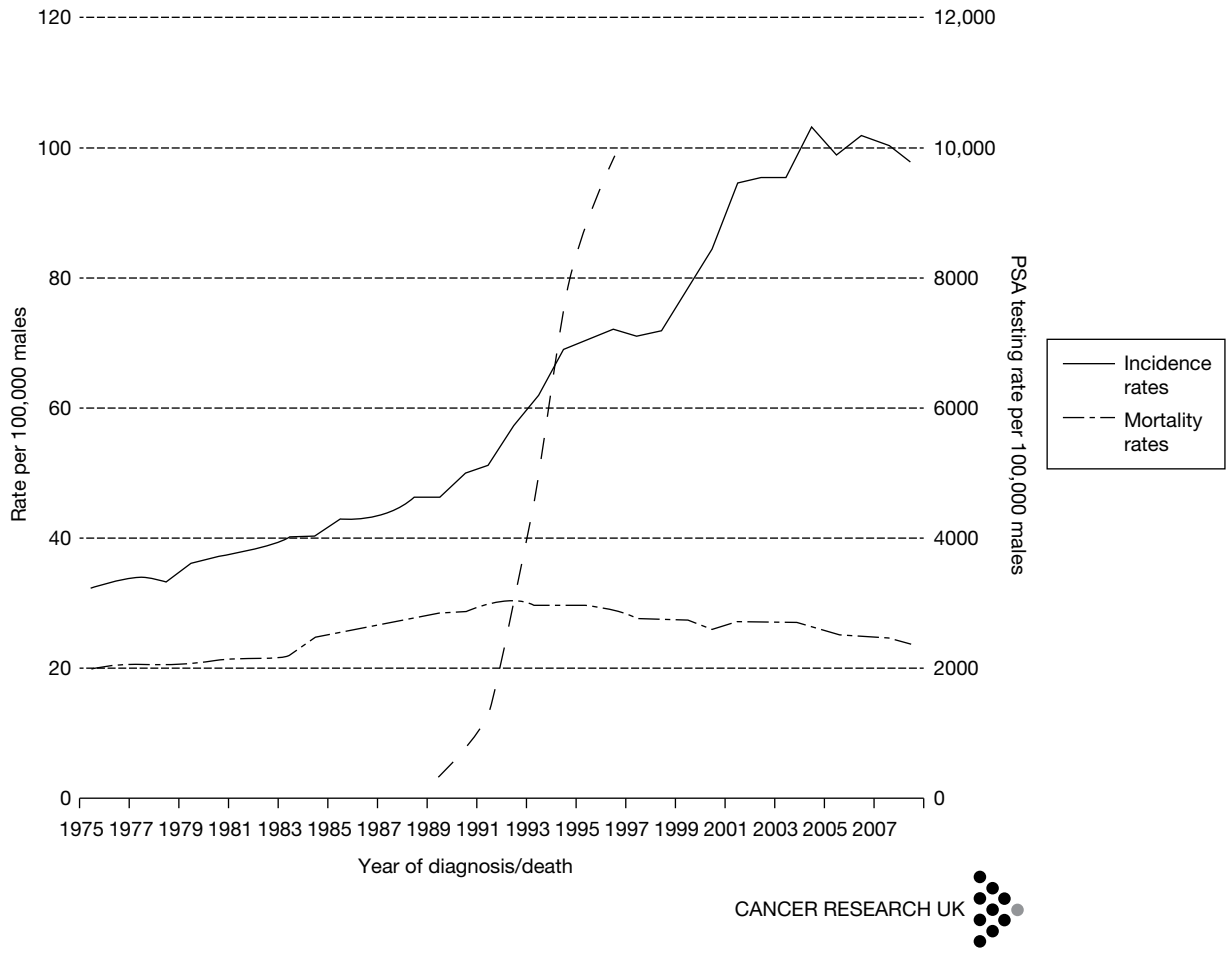

FIGURE 1 Change in rates of PSA testing and prostate cancer diagnosis in the UK.[10] Adapted with the permission of Cancer Research UK.

Development of radical prostatectomy

This sudden rise in incidence of localised prostate cancer inevitably led to an increased demand for curative treatments. The initial focus was on open radical prostatectomy, a surgical operation to completely remove the prostate together with its surrounding thin layers of connective tissue through a lower abdominal incision.[12] This procedure was historically associated with excessive blood loss, complete loss of erectile function and a high rate of urinary incontinence together with an appreciable mortality.[13] Rapid expansion of the number of predominantly asymptomatic men requiring treatment for PSA-detected cancer stimulated development of surgical techniques to reduce the morbidity and mortality of open radical prostatectomy while achieving long-term cancer cure. It was realised that routine use of specific manoeuvres to prevent blood loss together with precise identification and preservation of the nerves and blood vessels that supply the erectile tissue of the penis and urinary sphincter allowed the operation to be performed within an acceptable margin of safety without compromising cancer cure.[14,15] These techniques were further refined by many surgeon innovators, establishing the three main principles of radical prostatectomy termed the '*trifecta*': to cure the cancer, to preserve continence and to preserve erectile function. Despite these developments, the outcome of open radical prostatectomy remains less than ideal, with 20% of men requiring a blood transfusion, 7% having long-term urinary incontinence and 40% suffering erectile dysfunction after surgery, although surgeons who perform larger numbers of cases tend to have better results.[16–18] The risk of these longer-term

adverse effects is an important part of counselling for men having to face treatment choices for PSA-detected localised prostate cancer given that most will have normal urinary and sexual function before intervention. Surgeons and technology researchers have therefore continued to seek ways to reduce the functional disturbance of the procedure but maintain its disease-curing potential, leading to the development during the last decade of first laparoscopic prostatectomy,[19] and subsequently robotic prostatectomy, to enhance the accuracy of surgical dissection and further reduce blood loss.[20] Although not the prime focus of this review, it must be noted that the technique of open prostatectomy also continues to evolve with the same aim of minimising harms. Large high-volume single-institution series, particularly from the USA, suggest that open prostatectomy remains an option for men considering surgery for localised prostate cancer.[21]

Description of the interventions

Technical description

Laparoscopic prostatectomy

Experience in gall bladder and kidney surgery highlighted the advantages of a laparoscopic approach to intra-abdominal organ removal. Insufflation of the abdominal cavity and use of endoscopic lens and digital camera systems for image magnification greatly enhanced surgical view, aiding accurate dissection, and reduced bleeding. Technological development in instrument design and the use of differing energy sources for haemostasis added further potential benefits over open surgery. Appreciation of these advantages led to the first series of men undergoing laparoscopic radical prostatectomy being reported in 1997.[22]

For standard laparoscopic radical prostatectomy the patient is anaesthetised and positioned supine on the operating table with legs abducted. Following skin cleansing and draping, the abdomen is punctured with a trocar at the umbilicus under vision using a Hassan technique and a pneumoperitoneum induced with CO_2 gas, which is then maintained throughout the operation at a pressure of 10–12 mmHg. A telescopic camera is then inserted though the insufflation port (10 mm diameter) and a further three 5-mm ports and one 12-mm port are inserted in a specific configuration to allow ergonomic access to the pelvis without instrument clashes (*Figure 2*). The operating table is then adjusted with the patient in a 45° head-down position. The principal operating surgeon then proceeds with dissection of the prostate under televisual control using long narrow instruments such as a diathermy knife, scissors, graspers and needle holders passed through the ports while one or two assistant surgeons maintain the magnified view projected on two television screens by manipulating the telescopic camera and removing blood and fluid by suction.[23] Alternatively, the camera can be operated by a single active robotic manipulator arm that is controlled through voice commands from the operating surgeon.[24] Generally, blood loss is prevented by securing visible blood vessels with clips, diathermy and the use of other energy devices such as ultrasound. By considering preoperative findings and direct inspection of the prostate the surgeon will decide whether to preserve one or both neurovascular bundles attached to the posterolateral surface of the prostate that supply the urinary sphincter and penile erectile tissue. Once the prostate is dissected free it is placed in a retrieval bag within the abdomen and the continuity between the bladder and urethra restored by anastomosis using up to six interrupted sutures or by single continuous suture; a urinary catheter is then placed. One of the 12-mm ports is widened slightly to allow retrieval of the excised prostate, which is sent for pathological examination, haemostasis is then confirmed and the port sites closed with sutures. Anaesthesia is then reversed and the patient transferred to the recovery area for initial observation. The procedure typically takes 3.5–4 hours of operating theatre time. Increasing experience with the technique has demonstrated that it does result in reduced blood loss and earlier return to full activity compared with open prostatectomy, but any reduction in rates of erectile dysfunction and incontinence remains uncertain.[25,26]

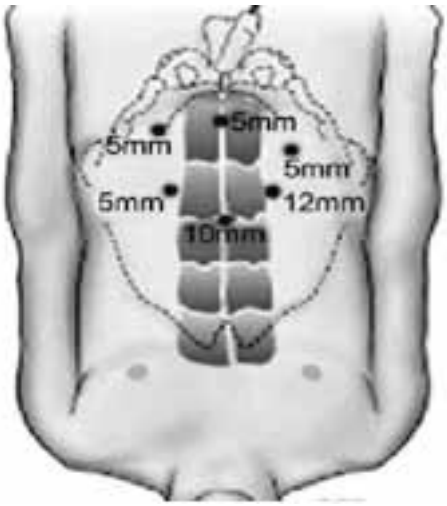

FIGURE 2 Configuration of differently sized abdominal port sites through which instruments are introduced for laparoscopic prostatectomy.[23] Reproduced with permission from the *International Brazilian Journal of Urology*.

Robotic prostatectomy

A surgical robot can be defined as a powered device with artificial sensing that can be programmed or externally controlled by a surgeon to position and manipulate instruments to undertake surgical tasks. The key surgical benefits of robotic technology are to tirelessly make precise repetitive movements to move, locate and hold tools and to respond quickly to changes in commands. Robots are intended to assist rather than replace the surgeon, who retains control at all times. They can be broadly classified into three groups: passive, active and master–slave telemanipulators.[27,28] Early positive experience with passive devices, such as frames to accurately position instruments during brain surgery, and active devices programmed to respond to voice- or pedal-activated commands, such as extra 'arms' to position the endoscopic camera during standard laparoscopic surgery, led to the design of master–slave surgical manipulators. Here, the surgeon sits at a master console in the operating theatre separate from the patient and remotely controls arms that position and operate the camera and tools inserted into the patient through ports. The control mechanism can be through a joystick, pedals or, more appropriately for surgery, gloved handles that mimic the movements of the slave manipulator. The technology allows the scaling of motion whereby the relatively gross hand movements of the surgeon are translated to micromotions of the robotic arms. This is further enhanced by 'wrists' built into the instruments that allow six degrees of freedom of movement, which more closely approximates the range of movements possible by the human hand during open prostatectomy, rather than the more limited four degrees of freedom possible with standard laparoscopic instruments. An advanced camera lens system allows three-dimensional vision and 10–15× magnification to be transmitted to the master console. Such master–slave telemanipulators were initially developed from previous US military designs by two commercial companies and used for coronary artery bypass surgery,[29] but a subsequent commercial merger resulted in a single company, Intuitive Surgical Incorporated (Sunnyvale, CA, USA), which developed the da Vinci® system for wider clinical use.[30]

The advantages of the multi-armed robotic telemanipulator system in terms of improved dexterity of operation of laparoscopic instruments by increasing articulation and scaling together with the three-dimensional magnified image all set in an ergonomic platform encouraged a number of centres, particularly in the USA, to apply this system to radical prostatectomy. It was also thought that the greater scope for telemedicine mentoring and the ability of the robot to scale surgeon movements and hence reduce unwanted movements such as tremor would widen the group of surgeons who could achieve competency at keyhole prostatectomy.[31,32]

The initial preparation for robotic prostatectomy is identical to that for the standard laparoscopic procedure. The operating theatre is required to be of a minimum size to accommodate the extra equipment, although this is now standard for newer hospital facilities, including those within the UK NHS. Once the ports (generally six) are placed and the patient tilted in a 45° head-down position, the robot is then 'docked' to the patient, which generally takes 15–20 minutes. The docking requires the attachment of one robotic 'slave' arm to the telescopic camera while the other two (for the three-arm model) or three (for the four-arm model) are attached to the operating instruments that will be manipulated remotely by the lead surgeon. The arms are housed on a cart that is positioned adjacent to the patient. The assistant surgeon generally operates the suction device or retracting instruments through the remaining ports. The operating surgeon sits at a teleconsole within the operating theatre linked to the robot by cable, although more remote wireless locations are possible (*Figure 3*).[33] The console comprises a three-dimensional display monitor for the camera-fed operative view, 'master' arms linked to the 'slave' arms, which allow the surgeon to direct and operate the instruments, camera-positioning controls, foot pedals controlling diathermy for haemostasis and finally a central processing unit to regulate the system. Additional controls can adjust the display, the offset angle of the telescopic camera lens and the ratio of the scaling of surgeon's movements to instrument movements. The procedure typically takes 3.5–4.5 hours of operating theatre time. Robotic prostatectomy also results in reduced blood loss and quicker return to full activity but again the hoped-for reduction in rates of incontinence and erectile dysfunction as a result of improved vision remains uncertain.[34] A deficiency of the robotic technique is the lack of transmission of the feel of the tissues from the remote instruments; reproduction of this haptic sense is a key aim of future development.

It should be noted that the robotic technology within the da Vinci system continues to evolve and advancements tend to be added by Intuitive Surgical as options to the basic platform at extra cost. Currently, purchasers of the system can choose to have a fourth robotic arm, reducing the number of surgical assistants required, more advanced image transmission and an additional console to allow mentoring of surgeons under training (similar to dual controls for a motor car).

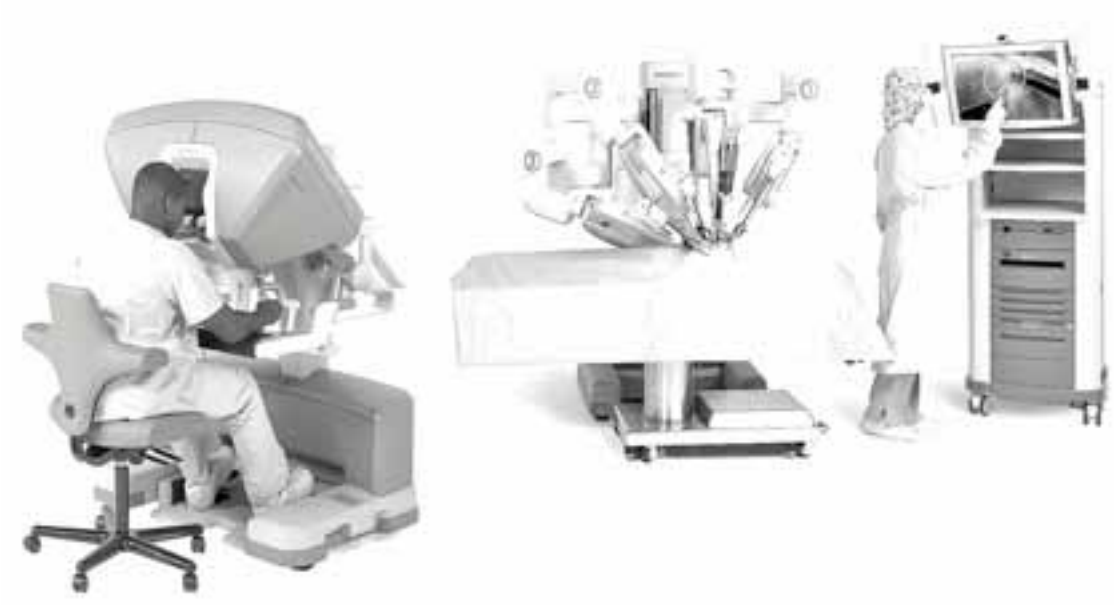

FIGURE 3 da Vinci surgical robot system showing, from left to right, surgeon at remote console; three-armed (labelled 1–3) telemanipulator for docking to patient; and assistant adjusting room monitor. ©[2011] Intuitive Surgical, Inc. Reproduced with permission from ©2010 Intuitive Surgical, Inc.

Current use in the UK NHS

Requirement for radical treatment of prostate cancer in the UK NHS

In the UK prostate cancer is generally detected by PSA testing of men complaining of lower urinary tract symptoms, although the numbers of asymptomatic men requesting a PSA test to assess their risk of having or developing prostate cancer is increasing, particularly among more affluent socioeconomic groups in the south of England.[35] For men with a serum PSA above a diagnostic threshold currently set in the UK at 3 ng/ml for men in their 50s, 4 ng/ml for those in their 60s and 5 ng/ml for those in their 70s, prostate biopsy is recommended.[8,36] Biopsy involves obtaining 10–12 cores of prostate tissue measuring 10×2 mm by transrectal ultrasound (TRUS)-guided needle biopsy as an outpatient procedure under local anaesthetic. This procedure is uncomfortable and is often associated with mild adverse effects such as bleeding and urinary tract infection (30–80%); more severe adverse effects such as systemic sepsis are uncommon (< 1%).[37]

At present, approximately 25% of men with PSA levels above threshold will have cancer detected on biopsy,[38] with 37,051 men being registered with the diagnosis in the UK during 2008.[11] Following diagnosis a treatment decision has to be made, which will involve consideration of the PSA level, the clinical stage of the cancer categorised on the tumour, node, metastasis (TNM) staging system,[39] the aggressiveness of the cancer classified by grading the degree of disruption of the normal glandular architecture of the prostate seen on microscopic examination using the Gleason score[40] and person factors such as life expectancy and treatment preference.[12,41,42] For men with apparent localised disease confined to the prostate gland (preoperative clinical classification of tumour stage cT1 and cT2, N0, M0), radical treatment by either surgery or radiation is an option, together with active surveillance programmes, with deferred treatment for men with a Gleason score ≤ 6.[43] Current evidence suggests that any benefit to the individual receiving radical treatment for prostate cancer takes at least 10 years to accrue and therefore these options are best used for men whose comorbidity and age suggests a life expectancy of > 10 years.[44] Finally, evidence is increasing that more aggressive cancers, categorised by a Gleason score of ≥ 8 out of 10 and a PSA of > 20 ng/ml, are likely to already have developed metastases and therefore such patients are considerably less likely to benefit from radical treatment alone.[45] The typical man who undergoes radical prostatectomy therefore is generally fit [American Society of Anesthesiologists (ASA) grade 0–2] and aged < 70 years and has tumour characteristics suggesting low or intermediate risk of disease progression according to the D'Amico risk classification system (*Table 1*).[46]

Estimated demand for radical prostatectomy

Assuming that 45% of men diagnosed with prostate cancer in the UK are aged < 70 years[11] and that the disease is localised to the prostate in 86% of cases,[47] approximately 14,000 men would have the option of radical treatment each year. Health episode statistics recorded for NHS England[48] show that approximately 4000 (28% of the estimated total) men underwent radical prostatectomy in the year 2009–10, this being a similar proportion to that seen for men diagnosed with cancer in the control arm of the European Randomised Study of Screening for Prostate Cancer [946/3402 (28%)].[49] [It is noted that there is a discrepancy between differing NHS datasets in the numbers of men coded as having a radical prostatectomy in NHS England in the financial year 2009–10: 4100 using the Office of Population Census and Surveys (OPCS) four-character procedure codes compared with 4703 using Healthcare Resource Group (HRG) codes.] The remaining men chose alterative treatment options such as implantation of radioactive seeds (brachytherapy, 15%), external beam radiotherapy (40%) or decided on an active surveillance

TABLE 1 Risk of biochemical recurrence signified by a rising PSA level after radical treatment stratified according to tumour characteristics[43]

Group	PSA (ng/ml)		Gleason score (0–10)[a]		Clinical stage[a]
Low risk	< 10	and	≤ 6	and	cT1–cT2a
Intermediate risk	10–20	or	7	or	cT2b–cT2c
High risk	> 20	or	8–10	or	cT3–cT4

a For full explanation see *Chapter 2, Preoperative characteristics of men undergoing radical prostatectomy.*

protocol (17%). Demographic trends in terms of the increasing number of men at risk together with an anticipated continued rise in the use of PSA testing in the UK suggest that the demand for prostatectomy and other options to treat localised prostate cancer will increase over the next 10 years. Using the hypothetical scenario of increased 'on demand' use of PSA testing up to the rate currently practised in the USA would give an estimated figure of 7000 men per year,[50] and this would rise further to an estimated 11,000 men per year with the hypothetical scenario of a national programme of PSA screening.[49,50]

Current use of technologies in UK NHS

Under the NHS Cancer Plan pelvic cancer surgery, including radical prostatectomy, is concentrated within 60 UK cancer centres, of which approximately 20 perform at least some procedures laparoscopically [personal communication from expert panel members (D Neal, C Eden, R Kodelburg, N Soomro, A McNeil), 2010]. In 2010, 16 had access to a da Vinci robotic system, although most robotic systems in the UK were installed in 2009–10 and were not yet fully operational at the time of carrying out this review (*Figure 4*).[30,51] NHS England reference cost data recorded 1816 laparoscopic/robotic procedures in the year 2009–10, suggesting that these options were used for 46% of all radical prostatectomies.[52] Our own survey of cancer units known to be carrying out laparoscopic and robotic radical prostatectomies suggests a current 50 : 50 split between laparoscopic and robotic techniques, meaning that approximately 23% of radical prostatectomies carried out in the UK at present are performed using the robotic technique. Other areas of the world have experienced a greater uptake of robotic prostatectomy, for example in the USA it was estimated that 43% of all radical prostatectomies were performed using the robotic technique in the year 2006–7 and approximately 70% in 2008.[17,53,54]

Current costs for the UK NHS

NHS reference costs for England for the financial year 2009–10 published by the UK government's Department of Health show an average tariff for open radical prostatectomy (HRG code LB21Z) of £4614 with 2897 procedures claimed by NHS hospitals giving a total annual cost of £1,336,758. For laparoscopic and robotic prostatectomy (HRG code LB22Z), the average tariff was £5257, with 1816 procedures claimed, giving a total annual cost of £9,546,712. (It is noted that there is a discrepancy between differing NHS datasets in the numbers of men coded as having a radical prostatectomy in NHS England in the financial year 2009–10: 4100 using OPCS four-character procedure codes compared with 4703 using HRG codes.) These data suggest a grand total tariff-based cost to the English NHS of £10,883,470 for the year 2009–10. Both an increase in the number of radical prostatectomies required and an increase in the proportion of procedures carried out using a laparoscopic or robotic technique would substantially increase the cost to the NHS. For example, a scenario of increased use of PSA testing leading to a demand for 7000 procedures per year that were all carried out laparoscopically or robotically would increase the tariff-based cost by 240% to £36,799,000.

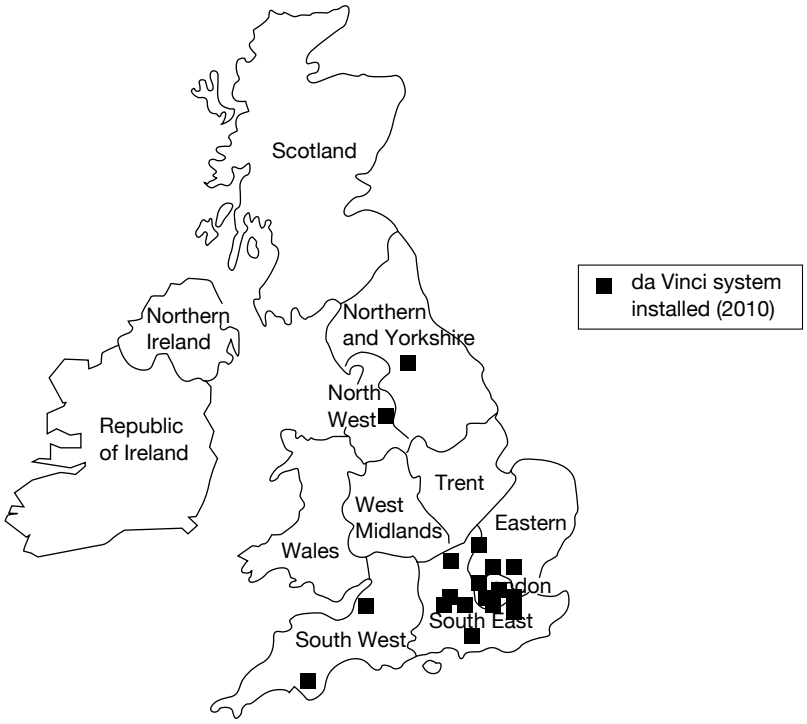

FIGURE 4 UK sites with an installed da Vinci robotic surgical system in 2010.

Summary

Policy-makers within the UK NHS are therefore faced with the need to plan service provision for the increasing number of men diagnosed with localised prostate cancer who decide on radical prostatectomy as their preferred treatment option. A keyhole technique of radical prostatectomy either by standard laparoscopy or with the aid of robotic technology does appear to offer advantages in terms of reduced morbidity over the traditional open surgical approach. Advocates of the robotic system claim greater precision in dissection and more rapid gaining of surgeon competence for the procedure but this comes at a substantially greater equipment cost. This review has therefore been designed to help inform decisions regarding the commissioning and use of robotic surgery for men with localised prostate cancer in the NHS.

Aim of the review

This study aimed to determine the relative clinical effectiveness and cost-effectiveness of robotic prostatectomy compared with laparoscopic prostatectomy in the treatment of localised prostate cancer within the UK NHS (the full study protocol is available at www.hta.ac.uk/2169). The specific objectives of the study were to:

1. describe clinical care pathways for laparoscopic and robotic prostatectomy in a UK context
2. determine the relative clinical effectiveness and safety of each procedure
3. determine the influence of the learning curve on estimates of effectiveness and safety
4. perform a systematic review of existing economic evaluations of each procedure
5. determine which procedure is most likely to be cost-effective for implementation in the NHS
6. identify future research needs.

Chapter 2

Description of the care pathway

Introduction

The described care pathway (*Figure 5*) was constructed using available evidence and consensus building through two meetings of the expert panel convened for this review. Although it is primarily constructed to plan the systematic assembly of evidence and design the mathematical model that will estimate effectiveness and cost-effectiveness, the pathway is consistent with previously published clinical pathways of care.[43,45,51,55,56] This chapter will describe each component of the pathway.

Preoperative characteristics of men undergoing radical prostatectomy

Patient characteristics

The population of patients considered for this review are men with localised prostate cancer undergoing radical prostatectomy at designated pelvic cancer surgical treatment centres within the UK NHS. The patient variables that define this population include age and comorbidity that together determine an estimated life expectancy of at least 10 years. The great majority of such men are able to undergo radical prostatectomy by either standard laparoscopic or robotic techniques; the few exceptions suited only to the open approach are those with poor respiratory reserve, morbid obesity or previous extensive pelvic surgery.

Disease factors are focused on the estimated risk of developing recurrent disease from metastases not identified at preoperative assessment or because of failure to completely remove localised disease. The approximate magnitude of this risk for an individual man diagnosed with prostate cancer can be calculated using a nomogram developed from linear regression models, the most commonly used version being hosted by the Memorial Sloan Kettering Cancer Institute in web-based form.[57] These models use the preoperative disease factors of age, PSA, clinical tumour stage, Gleason grade and number of needle biopsy cores positive for cancer.

Preoperative level of prostate-specific antigen

The preoperative serum PSA level is an independent statistically significant predictor of future recurrence but on its own is limited in reliability and predictive value. For prognostic purposes the value is defined in groupings corresponding to low (< 10 ng/ml), intermediate (10–20 ng/ml) and high (> 20 ng/ml) risk of disease progression.

Staging of prostate cancer

The stage of an individual's cancer is categorised according to the Union for International Cancer Control (UICC) 2009 classification (*Table 2*).[39] Preoperatively this is determined by clinical assessment using digital rectal examination and imaging with the allocated tumour stage (T) given the prefix 'c', for example cT1. Following prostatectomy, pathological examination of the prostate and, in some cases, adjacent lymph nodes may result in a change in the staging as

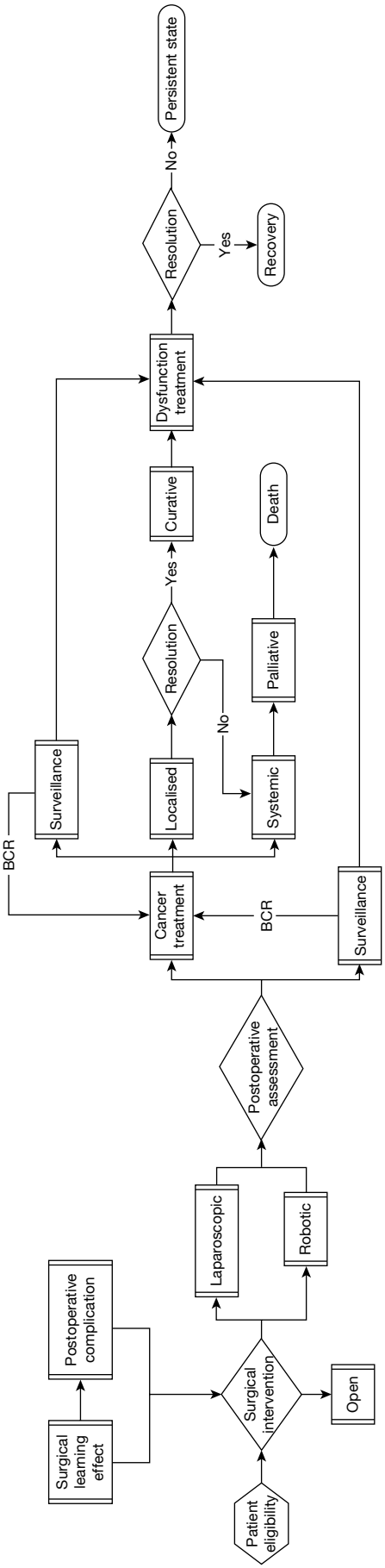

FIGURE 5 Summary flow chart showing complete care pathway used to frame the systematic review questions and the health economic model. BCR, biochemical (PSA) recurrence.

TABLE 2 Prostate cancer staging according to the UICC 2009 classification

Stage	Substage	Description
T0		No evidence of cancer found on complete pathological examination of the prostate
T1		Clinically unapparent tumour, not detected by digital rectal examination nor visible by imaging
	T1a	Incidental histological finding; ≤ 5% of tissue resected during TURP
	T1b	Incidental histological finding; > 5% of tissue resected during TURP
	T1c	Tumour identified by needle biopsy
T2		Confined within the prostate
	T2a	Tumour involves half of the lobe or less
	T2b	Tumour involves more than half of one lobe but not both lobes
	T2c	Tumour involves both lobes
T3		Tumour extends through the prostate capsule but has not spread to other organs
	T3a	Extracapsular extension (unilateral or bilateral) including bladder neck[a]
	T3b	Tumour invades seminal vesicle(s)
T4		Tumour is fixed or invades adjacent structures other than seminal vesicles
	T4a	Tumour invades external sphincter and/or rectum
	T4b	Tumour invades levator muscles and/or is fixed to pelvic wall

TURP, transurethral resection of the prostate.
a Categorised as T4a in the UICC 2002 classification.

more accurate information concerning the size of the tumour and whether it has breached the external surface of the prostate will be available. To indicate this more accurate evaluation, the T stage assigned following pathological examination of the whole prostate is given the prefix 'p', for example pT2a. Rarely, no tumour will be found on pathological examination of the prostate following radical prostatectomy for biopsy-proven cancer; this is designated pT0.

Gleason grading

The qualitative low-magnification microscopic histological description of prostate cancer first suggested by Gleason[58] remains an essential aspect of prognostic categorisation although there have been substantial modifications over the subsequent years.[40] The classification grades individual areas of prostate cancer according to the degree of disruption of normal glandular architecture, with grade 1 indicating minimal disruption, grade 5 complete loss of normal glandular arrangement and grades 2, 3 and 4 intermediate between these two extremes. Standard practice consists of identifying the first and second most prevalent patterns within a set of biopsy cores, which give the primary and secondary Gleason grades (each rated 1–5). These are then added together to give the overall Gleason sum score (2–10). Recent consensus tends to limit the use of grades 1 and 2 and therefore scores generally range between 6 and 10.[59] Any tertiary higher disease areas are also reported irrespective of their extent. Higher individual grade and total sum score indicate more aggressive disease with the primary grade being more predictive. For example, an individual whose tumour is categorised as Gleason score 4 + 3 = 7 will tend to have a worse prognosis than an individual with a Gleason score of 3 + 4 = 7.[60] Recent consensus mandates that pathological reporting of prostate cancer using the Gleason grading system should include the most prevalent pattern (primary grade), the second most prevalent pattern (secondary grade) and the presence of any areas that are assigned a higher grade than that assigned to either the primary or secondary patterns (tertiary grade). For needle biopsies the Gleason score is obtained by summing the higher of the secondary or tertiary grades. For radical prostatectomy specimens the Gleason score is obtained by summing the primary and secondary grades, any higher-grade tertiary pattern being stated separately if it occupies < 5% of the tumour.

Cancer extent

There is some evidence that the tumour extent on needle core biopsy estimated by measuring the number of cores positive for cancer, the percentage of needle core tissue affected by cancer and the length in millimetres of the core segments with cancer present is also an independent prognostic factor predictive of future disease progression.[61] Similarly, the total volume of cancer identified by pathological examination of the whole prostate after radical prostatectomy has been assessed as a possible predictive factor for recurrence but was found not to be independently significant on multivariate analysis.[62] These pathological measures of cancer extent have not been included in our care pathway given the current uncertainty of the evidence base.

Summary

Variables collected preoperatively for men undergoing radical prostatectomy including age, tumour stage, Gleason score and tumour volume can predict the risk of disease progression at some time after surgery, with stage and Gleason sum score being most useful. It is therefore important that studies comparing treatments, such as this review, include an assessment of whether or not the patient groups undergoing each procedure are balanced for these variables.

Perioperative care

Introduction

For the purposes of this review it is assumed that the procedures being considered will be carried out in hospitals that have the necessary resources in terms of staff, facilities and NHS cancer plan approval to carry out either laparoscopic prostatectomy or robotic prostatectomy on a routine basis. This will comprise operating theatre and recovery facilities including critical care and standard urology wards, the required clinical and technical expertise including surgeons, anaesthetists, theatre nursing team, pathologists and technicians, and continued care including outpatient review, repeat imaging and facilities for further treatment for adverse events or cancer progression. The procedures have been described in *Chapter 1*.[30,63] For the safe conduct of both procedures it is important that all members of the operating theatre team have had specific training in the performance of the procedures, this being particularly crucial from a technical point of view for the robotic procedure.

Surgeon learning curve

Both laparoscopic and robotic prostatectomy are currently being implemented in the UK NHS, requiring the training of surgeons to perform the procedures. The performance of repeated tasks tends to improve with experience and this improvement is characteristically rapid at first and then slower as a steady state expert level is reached, leading to the use of the term 'learning curve' to describe the process. Learning of surgical procedures can be additionally influenced by the previous experience of the surgeon or surgical team, case-mix selection, use of multiple outcomes defining 'success' and continued development of the technology.[64] The learning curve effect is often crudely quantified by the number of procedures required to reach competence or the reducing time taken to perform the procedure; in open prostatectomy, for example, experience-related changes in performance may continue even after 250 procedures.[18] As use of laparoscopic prostatectomy increased it was realised that the procedure was difficult to master, requiring a high number of training procedures to achieve competence, and that the skills required did not translate directly from those used in open surgery.[65] This is a particular problem in countries such as the UK, where few centres undertake more than 50 cases per year, the suggested volume required for training and maintenance of competency.[66] Findings from individual case series suggest that robotic prostatectomy reduces the number of cases required for competence, enabling the surgeon to reach an expert level quicker, and that previous experience

of laparoscopic prostatectomy is not essential.[67] In addition, it is possible that some surgeons who are unable to master the laparoscopic technique can take advantage of the greater movement control offered by the robotic system to become competent in robotic prostatectomy. Any evaluation of effectiveness and safety of the prostatectomy procedures must therefore balance the relative effects of the learning curves.

Pelvic lymphadenectomy

Men whose disease is characterised preoperatively as intermediate or high risk (see *Table 1*) may be advised to undergo pelvic lymphadenectomy as part of their laparoscopic or robotic radical prostatectomy in order to detect occult lymph node metastases. The lymphadenectomy is performed as the first part of the radical prostatectomy procedure using a standard dissection template and the package of lymph nodes is removed separately from the prostate for subsequent pathological examination. The prostatectomy would be aborted only if there was gross visible lymph node enlargement, which, given preoperative imaging, is a very rare circumstance. For the purposes of this evaluation we chose, in consultation with the expert panel, to assume that all men with intermediate- or high-risk disease undergoing laparoscopic or robotic prostatectomy would also have a pelvic lymphadenectomy. This is in line with current guidance but we do acknowledge the controversy in this area.[45]

Hospital stay

Men are generally admitted to hospital either on the day of surgery or the evening before. A rectal enema is administered to clear the lower bowel. Just before surgery prophylactic antibiotics are given according to local policy and venous thrombosis/embolism prophylaxis also commenced. After surgery the patient is routinely nursed on a standard ward in the UK although specific comorbidities or intraoperative complications may require a period in a critical care area. In the UK, men are typically discharged home after 3 days with an indwelling catheter although this can be reduced by managed care programmes. They then return to the ward after a further 7–14 days according to local protocol as a day patient for urinary catheter removal and voiding check.

Perioperative adverse events

General

Although men undergoing this surgery generally do not have concurrent comorbidity that is a persistent threat to their health a proportion will be expected to suffer adverse events associated with major surgery and prolonged anaesthesia such as cardiac ischaemia, pulmonary embolism and prolonged loss of bowel function (ileus). In addition, specific complications include urinary and bloodstream infection, inadvertent injury to adjacent organs, particularly rectal perforation, excessive blood loss requiring transfusion and prolonged urinary or lymphatic leakage from abdominal drains. The adverse effect of these complications in terms of their severity and requirement for additional interventions and hospital stay can be summarised according to the Clavien–Dindo system (*Table 3*).[68,69]

Bladder neck contracture

An additional specific short-term complication is fibrosis and contracture of the sutured join between the top of the urethra and bladder outlet, the vesico-urethral anastomosis, termed bladder neck contracture or bladder neck stenosis. This will become noticeable after removal of the draining catheter with the narrowing of the urine channel, resulting in voiding problems reported by the patient over the next 3–6 weeks according to the severity of contracture. It is treated by endoscopic incision of the narrowed area, which requires an additional short hospital stay and a 7-day period of catheterisation. For most men the problem is cured by a single incision although for some this may need to be repeated once or twice.[70]

TABLE 3 Abbreviated Clavien–Dindo classification of surgical complications

Grade	Definition	Exclusions
Grade 0	No deviation from planned postoperative course considering procedure and pre-existing comorbidity	
Grade I	Any deviation from the normal postoperative course without the need for specific pharmacological treatment or surgical, endoscopic and radiological interventions	
Grade II	Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Includes blood transfusions and total parenteral nutrition	Treatments listed under grade I
Grade IIIa	Requiring surgical, endoscopic or radiological intervention not under general anaesthesia	
Grade IIIb	Requiring surgical, endoscopic or radiological intervention under general anaesthesia	
Grade IVa	Life-threatening complication affecting single organ system requiring IC/ICU management	TIA
Grade IVb	Life-threatening complication affecting more than one organ system requiring IC/ICU management	TIA
Grade V	Death of a patient	

IC, intensive care; ICU, intensive care unit; TIA, transient ischaemic attack.

Pathological examination of the prostate

Careful and thorough microscopic examination of the removed prostate by an experienced pathologist is required to determine the true extent of the disease and to identify whether or not the surgery may have been unable to remove all of the contained cancer (positive margin), whether or not the cancer has spread outside the prostate (extraprostatic extension) and, if lymphadenectomy has been performed, the presence of lymph node metastatic disease. In addition, a more comprehensive assessment of the Gleason patterns within the cancer is possible.[71] This examination will recategorise the disease according to stage and, if appropriate, lymph node status (pT and pN) and postoperative Gleason sum score, which will allow more accurate estimation of prognosis according to available post-radical prostatectomy prognostic nomograms[57] and inform whether early additional (adjuvant) treatment should be advised. The crucial nature of this examination has led to regular international plenary meetings of expert pathologists who have made consensus recommendations guiding best practice for specimen collection, processing, examination and analysis in order to promote consistency in pathologist reporting of radical prostatectomy specimens.[59,72]

Surveillance following radical prostatectomy

Follow-up schedule

Men who have undergone radical prostatectomy are generally seen by the operating team as outpatients 6 weeks after their surgery and then 3-monthly for the first year and 6-monthly for the next 4 years. At each follow-up consultation serum PSA is checked for evidence of tumour recurrence and a qualitative assessment made for continence and desired sexual function. If further assessment or treatment is required for any of these aspects then the pathway of care will be changed accordingly (see *Figure 5*).

Detection of persistent or recurrent disease

The risk of disease recurrence is higher if one or more of the following disease factors are present: preoperative PSA > 20 ng/ml, pathological Gleason score > 7, pathological extraprostatic disease (pT3/pT4), pathological positive margin or positive lymph nodes (pN1/pN2). If positive lymph nodes are found or the likelihood of disease persistence or recurrence is otherwise deemed to be very high then immediate adjunctive treatment may be offered. For the majority of men, however, PSA surveillance is started according to a standard schedule, for example that defined in the preceding paragraph. Following removal of the prostate, serum PSA (half-life 2.2 days) levels

will rapidly fall to an undetectable level, defined as values less than the sensitivity of the assay. Generally, ultrasensitive PSA assays are used for men following radical prostatectomy giving postoperative values of < 0.01 ng/ml. Definitions of the threshold of PSA rise that signifies cancer recurrence vary but generally the finding of two successive PSA readings > 0.2 ng/ml is used, this being denoted biochemical recurrence.[73,74] Once biochemical recurrence occurs a decision will be made with the patient whether to continue surveillance or commence adjuvant treatment. This decision will be informed by tests such as magnetic resonance imaging and radionuclide bone scanning designed to demonstrate the site of recurrence as being in the prostatic bed (localised) or as lymph node or bony metastases (systemic).

Adjuvant treatment

For purely localised recurrence radical radiotherapy is recommended as defined in the RADICALS trial protocol.[75] The treatment consists of delivery of up to 66 Gy of radiation divided into daily doses over 4–6 weeks. It is uncertain whether or not the addition of short-term androgen deprivation is beneficial for presumed localised disease, a research question that RADICALS is designed to address. For men with likely systemic recurrence, long-term, typically life-long, androgen deprivation therapy (medical castration) most commonly achieved with a luteinising hormone-releasing hormone (LHRH) agonist is recommended. This consists of 3-monthly subdermal injections of a depot preparation of the chosen drug. Alternatively, some men may choose surgical castration, removing both testicles (bilateral orchiectomy). The use of long-term androgen deprivation therapy or bilateral orchiectomy for metastatic disease is thought to be palliative because at some point the disease will lose androgen dependency (castrate-resistant prostate cancer). The duration from start of therapy to escape from androgen control, signified by a further substantial rise in PSA values, varies according to the aggressiveness and extent of disease, with a median time of approximately 12 months. Side effects of androgen deprivation therapy include hormonal changes leading to hot flushes, gynaecomastia and altered fat distribution together with osteoporosis. Men with castrate-resistant prostate cancer have a median survival of approximately 18 months and further treatment is usually palliative with symptom control and use of corticosteroid drugs to improve well-being. The chemotherapeutic agent docetaxel does have some activity, extending survival by 3 months on average, but is suited only to men with good performance status.[76]

Urinary incontinence

Recovery of continence following radical prostatectomy can take up to 12 months although most men will regain continence by 6 months. In general, therefore, men suffering urinary incontinence will be advised to use containment devices such as absorbent pads or penile sheath drainage for the initial 12 months. If bothersome leakage persists beyond this time then the main treatment options will be surgical implantation of an artificial urinary sphincter (AUS) or continued use of containment devices. For the purposes of this evaluation we used the individual definition of urinary incontinence given in each study without attempting to separate out differing definitions or categorisation of severity. A recently reported randomised controlled trial (RCT) of pelvic floor muscle therapy following radical prostatectomy demonstrated that the rate of urinary incontinence beyond 12 months using patient-reported measures and data collection independent of the clinical team was higher than that given by most of the studies used in our meta-analysis.[77]

Erectile dysfunction

For men who were sexually active before surgery, approximately 40% will experience worsening of their sexual function and in particular difficulty initiating and sustaining penile erection sufficient for desired sexual activity. This is particularly dependent on preservation of one or both neurovascular bundles at the time of radical prostatectomy. Similar to urinary incontinence full recovery can take up to 12–18 months following surgery. For men with persistent and

bothersome erectile dysfunction, treatment options will include drug treatment taken on an as-required basis, a vacuum constriction device or penile implant surgery. Most men will first trial an oral phosphodiesterase type V inhibitor, with a suggested prescribing frequency of one treatment per week according to NHS guidance. The next option will be alprostadil (Carerject®, Pfizer) given as an intraurethral pellet or an intracavernosal injection with suggested NHS prescribing frequency again of one treatment per week. For men who achieve satisfactory restoration of sexual activity with these drugs their use will continue long term. If drug treatments are unsuccessful men may trial a vacuum constriction device or consider surgical implantation of a penile prosthesis. The proportion of men pursuing these last two options is small as most will accept their loss of sexual function in the longer term. In addition, it should be noted that, although this outcome is an important aspect determining treatment selection for many men with localised prostate cancer, the definition of any deterioration is not standardised and collection of data concerning sexual function before and after surgery is generally poor. Most studies do not separately categorise those men who were sexually active before surgery and who underwent deliberate nerve-sparing surgery with the aim of preserving sexual function.

Chapter 3

Methods of the systematic review of clinical effectiveness

Methods

Comprehensive electronic searches were conducted to identify reports of published studies. Highly sensitive search strategies were designed including appropriate subject headings and text word terms, interventions under consideration and specific study designs. There was no language restriction but searches were restricted to years from 1995 onwards, reflecting the time of introduction of the techniques. MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, BIOSIS, Science Citation Index and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for primary studies while the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effects (DARE) and the HTA database were searched for reports of evidence syntheses. Reference lists of all included studies were scanned to identify additional potentially relevant reports. The expert panel provided details of any additional potentially relevant reports.

Conference abstracts from meetings of the European, American and British Urological Associations were searched. Ongoing studies were identified through searching Current Controlled Trials, ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry and the National Institutes of Health (NIH) Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER). Websites of manufacturers, professional organisations, regulatory bodies and the HTA were checked to identify unpublished reports. Full details of the search strategies used are detailed in *Appendix 2*.

Inclusion and exclusion criteria

Types of study

Evidence was considered from RCTs, non-randomised comparative studies and, for estimates of learning curve effects only, case series. For estimating learning curve effects robotic or laparoscopic arms of comparative studies were treated as separate case series. Conference abstracts and non-English-language reports were included only if they were of comparative studies.

Types of participants

The types of participants considered were men with clinically localised prostate cancer (cT1 or cT2), defined as cancer confined to the prostate gland and considered curable by radical removal of the prostate. Studies were included if ≥ 90% of the included men fulfilled this definition.

Types of interventions and comparators

Robotic radical prostatectomy was considered as the intervention and laparoscopic radical prostatectomy as the comparator. Open radical prostatectomy was also considered in studies comparing open radical prostatectomy with robotic radical prostatectomy and/or laparoscopic radical prostatectomy so that such studies could be included in a mixed-treatment comparison

model (see *Data analysis*) assessing the relative effectiveness of robotic and laparoscopic radical prostatectomy.

Types of outcome measures

The following types of outcome measures were considered:

- complications and adverse events including blood transfusion, anastomotic leak, bladder neck contracture, wound infection, organ injury, ileus, deep-vein thrombosis and pulmonary embolism
- cancer related:
  - rate of positive margin in resected specimen
  - biochemical (PSA) recurrence
  - need for further cancer treatment
  - disease-free survival, defined as absence of clinically detectable disease
  - survival
  - mortality
- functional:
  - recovery of sexual (penile erection) function, quantified where possible by validated scores such as the International Index of Erectile Function-5 (IIEF-5)
  - urinary continence, defined as use of one thin pad or less per day and/or as assessed on a validated symptom score
- patient driven
  - pain, quantified on a validated pain score, and analgesic requirements
  - productivity (time to return to full activity)
  - generic and disease-specific quality of life, measured through validated scores
- descriptors of care
  - equipment failure
  - conversion to open procedure
  - operative time
  - duration of catheterisation
  - hospital stay
  - learning curve.

Exclusion criteria

The following types of report were excluded:

- studies of men with metastatic disease
- case series of open radical prostatectomy.

Data extraction strategy

Three reviewers independently screened titles and abstracts of all identified items. Full-text copies of all potentially relevant reports were obtained and independently assessed by two reviewers to determine whether or not they met the inclusion criteria. Three reviewers extracted details of study design, methods, participants, interventions and outcomes onto a data extraction form (see *Appendix 3*). Each reviewer's data extraction was independently checked by a second reviewer for errors or inconsistencies. Any disagreements were resolved through consensus or arbitration by a third party. For studies reporting adverse events, two surgeons categorised each complication using the Clavien–Dindo classification of surgical complications[68] (see *Table 3*) with a third surgeon acting as arbiter in cases of disagreement about classification.

Quality assessment strategy

Risk of bias

A modified version of the Cochrane risk of bias tool[78] was adapted to include potential topic-specific confounders, which were identified through discussions with members of our project advisory group and our knowledge of existing literature. The topic-specific confounders related to specific outcomes are shown in the modified risk of bias tool (see *Appendix 4*). Three sets of two reviewers independently assessed the risk of bias of included full-text studies, with the exception of non-English publications and conference abstracts. Any differences in assessment or issues of uncertainty were resolved by discussion and consensus between the reviewers. The risk of bias assessment was summarised at the study level using judgements incorporating individual outcomes as well as study-level risk of bias domains. Individual outcomes were categorised as high risk of bias, low risk of bias or unclear risk of bias. The categories were weighted to reflect higher disagreement between the two clear categories of low and high risk with lower weighting for disagreement between either high- or low-risk and unclear judgements. Any disagreements were resolved by consensus or arbitration by a third party. The kappa statistic was used to assess inter-rater agreement between assessors of the risk of bias in each study, with 0–0.2 as slight agreement, 0.21–0.4 as fair agreement, 0.41–0.6 as moderate agreement, 0.61–0.8 as substantial agreement and 0.81–1 as perfect agreement.[79] If there was a sufficient number of low risk of bias studies, a meta-analysis would be performed restricted to only these studies (see *Data analysis*).

Determination of surgical margin status

Various protocols are described for the standardisation of processing and reporting of radical prostatectomy specimens, to identify pathological factors that could accurately predict patient outcome.[59,80–82] Variations in the protocols employed may potentially affect the determination of surgical margin status. Details of the methods described for the handling, processing and reporting of radical prostatectomy specimens were tabulated and summarised (see *Table 7*). The categories for the tabulations were derived from the findings of a recent international consensus conference on handling and staging of radical prostatectomy specimens, which convened following a web-based survey of members of the International Society of Urological Pathology (ISUP) with the intention to promote consistency in pathological reporting and the collection of appropriate prognostic information.[83,84] If there was a sufficient number of studies, a meta-analysis would be performed restricted to only the studies that reported all criteria (see *Data analysis*).

Data analysis

Data from each study were tabulated and summarised for each procedure in a form appropriate for the mixed-treatment comparison model. The lack of RCT evidence precluded undertaking a standard two-group meta-analysis; therefore, an indirect comparison (cross design) approach allowing inclusion of non-randomised comparative data was adopted[85] within a mixed-treatment comparison framework. The models implemented were based on mixed-treatment comparison models developed by Lu and Ades.[86] The main parameters in the models for dichotomous outcomes are the logarithm of the odds ratios (log-ORs) of each procedure compared with the reference procedure open surgery. A random-effects model was adopted that incorporated an adjustment for the correlation between arms in studies that compared all three procedures. The model parameters were estimated within Bayesian methodology with the use of WinBUGS software version 1.4.3 (MRC Biostatistics Unit, Cambridge, UK).

For continuous data for duration of operation, a similar model was constructed using means and standard errors instead of log-ORs and standard errors. This was carried out only in studies that compared robotic with laparoscopic procedures directly. Some assumptions were made because of the inconsistent reporting of duration of operation. If a median was reported but no mean the median was used as a substitute for the mean. Furthermore, if the standard deviation (SD) was not reported, imputation was conducted using the method proposed by Marinho and colleagues.[87] In this method, a linear regression of log (standard deviation) on log (mean) for all studies that reported a mean and standard deviation is first undertaken. The resultant predictive formula is then used to impute standard deviations for studies missing this value given the reported mean. This was conducted for each radical prostatectomy procedure separately.

Odds ratios (ORs) and associated 95% central credible intervals (CrIs) were estimated between laparoscopic surgery (the base case) and robotic surgery; if the OR is > 1 the calculated odds of a particular event are higher for robotic surgery than for laparoscopic radical prostatectomy, whereas if the OR is < 1 the calculated odds of a particular event are higher for laparoscopic radical prostatectomy. The CrI will show the degree of uncertainty around these calculated values. The statistical probability of the OR being different from 1, and hence the probability that robotic radical prostatectomy was better or worse than laparoscopic radical prostatectomy for specific outcomes, was calculated (this is sometimes called the 'Bayesian *p*-value' and is the proportion of the samples in the simulation in which the OR was < 1). In this report we have assumed that a probability equal to 0.95 is 'statistically significant'. Finally, an individual estimate of the probability of the event occurring for each type of radical prostatectomy was calculated. These estimates were calculated from the model by using a prior distribution for the probability of an event when using the reference treatment (which was open radical prostatectomy) and combining that with the OR between each type of surgery and open surgery. The prior distribution for the event rate for open surgery was estimated using the data for open surgery in the included studies only and by applying a normal distribution to the log-OR of the probability of each outcome, with its mean and variance being estimated from a standard Bayesian random-effects model.

When there were a sufficient number of studies, the heterogeneity of effects was explored by repeating the analyses including only data from studies assessed at low risk of bias. In addition, for surgical margins, if there was a sufficient number of studies, the heterogeneity of effects was explored by repeating the analysis including only data from studies that reported all key pathological data (see *Quality assessment strategy*).

Vague prior distributions were used on the necessary parameters: the log-ORs of intervention procedures compared with open surgery, the individual study event rates and the random-effects standard deviation. For most outcomes a burn-in period of 20,000 iterations was adequate to achieve convergence and a further 100,000 samples were taken for each outcome.

Assessment of learning curves

The approach developed by members of our project team to estimate the learning effects on key outcomes was used.[88] In this approach, the expertise of the participating surgeons or centres described in each included study was first categorised according to previous experience (number of previous radical prostatectomies undertaken using open, laparoscopic or robotic techniques) and according to occurrence of the key outcomes of positive surgical margin rate. Positive margin rate was then plotted against previous experience to describe learning curve effects in the included studies. Data on the three key features of learning (starting level, rate of learning and expert level) were extracted where possible and a random-effects meta-analysis performed to

estimate the pooled effect of the key features together with an appropriate measure of uncertainty [95% confidence interval (CI)].

The robustness of the above approach was assessed by extending the inclusion criteria to include case series of laparoscopic and robotic radical prostatectomy that included > 200 men. Positive surgical margin rates for the first and last cases were abstracted from each included case series (together with any other parameters used in the studies to assess learning). A test for a logarithmic shape of learning was undertaken using a linear least-squares regression (using the natural logarithm of procedure number as the independent variable and the natural logarithm of the positive surgical margin rate as the dependent variable). A dummy variable for robotic compared with laparoscopic case series was included in the analysis to test for any difference in rate of learning between the two radical procedures and the associated 95% CI was calculated.

Chapter 4

Clinical effectiveness of robotic compared with laparoscopic techniques

Quantity and quality of evidence

Number of studies identified

The searches identified 2722 potentially relevant titles and abstracts (*Figure 6*), from which 914 reports were selected for full-text eligibility screening. Of these, 58 reports (54 studies) were included and 856 reports were excluded with reasons for exclusion detailed in *Figure 6*. We attempted to obtain further details for 69 of the 80 (86%) reports that were excluded because of lack of clear information on the number of patients for each baseline clinical stage and which had contact details available. Nineteen replies were obtained. Only one of these 19 reports[89] was subsequently deemed eligible for inclusion, but confirmation of this was received too late for it to be included in the review. *Appendices 5* and *6* give the bibliographic details of the included and excluded studies respectively.

Number and type of included studies

The searches identified one RCT of laparoscopic versus open radical prostatectomy[90] and 57 non-randomised comparative reports of 53 studies from 40 different clinical institutions: eight robotic versus laparoscopic prostatectomy;[91–98] four robotic versus laparoscopic versus open prostatectomy [three primary,[99–101] one secondary[102] (earlier report of the same study but containing unique data)]; 18 robotic versus open prostatectomy (16 primary,[103–118] two secondary[119,120]) and 27 laparoscopic versus open prostatectomy (26 primary,[121–146] and one secondary[147]). There were three conference abstracts: two comparing robotic versus laparoscopic prostatectomy[94,97] and one comparing robotic versus laparoscopic versus open prostatectomy.[102]

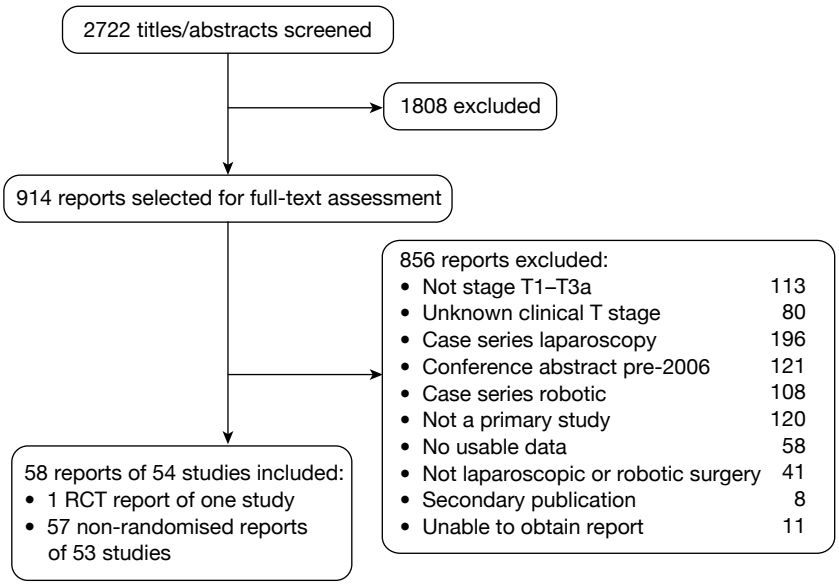

FIGURE 6 Flow chart of the number of potentially relevant reports of identified studies and the numbers subsequently included and excluded from the clinical effectiveness review.

Four studies were considered to include potential patient overlap: the study conducted by Menon and colleagues[95] was a comparison of 40 laparoscopic and 40 robotic prostatectomies performed between 23 October 2000 and 22 October 2001; Tewari and colleagues[116] report an extension of this work but compared 100 open and 200 robot operations between October 1999 and December 2002. As these studies included different comparators, they were treated as separate studies but the potential for overlap of robotic prostatectomy patients was noted. Similarly, Joseph and colleagues[94] report a comparison including 800 laparoscopic cases from the Henri Mondor hospital, France, and 745 robotic cases from the University of Rochester, USA, between 2002 and 2006. An earlier publication[93] analysed the last 50 cases from a series of 70 laparoscopic and 200 robotic cases from the University of Rochester (dates not given). The studies were treated as separate. Similar affiliated institution details of first authors were noted for seven studies: those by Anastasiadis[122] and Salomon,[140] Ficarra[106] and Fracalanza,[107] and Greco,[129] Jurczok[131] and Fornara.[127] These studies report overlapping treatment dates and similar procedures but it is unclear whether or not they include patient overlap as details of the institutions where the men were treated are not clearly given within the reported text. Similarly, we noted similar author institution details for another seven studies: those by Malcolm,[110] Ball[99] and Soderdahl,[142] Trabulsi[98] and Brown,[125] and Loeb[109] and Wagner[146] although these involved different comparison groups and were treated as separate studies.

The 57 non-randomised comparative reports (of 53 studies) included 28 prospective and 17 retrospective reports. Three studies[92,112,114] included a mixture of prospective and retrospective data and eight[96,97,100,119,123,132,134,138] did not report the method of data collection. The method of data collection was uncertain in the study by Kim and colleagues[132] because of a limited translation of the full-text version. *Table 4* provides further details of the number and type of included studies.

The RCT conducted by Guazzoni and colleagues[90] comparing laparoscopic with open prostatectomy was set in Italy. Half of the included non-randomised studies were conducted in the USA (28/57, 49%). The remaining studies were conducted in France,[91,94–96,101,122,140] Italy,[106,107,114,123,129,134] Germany,[127,131,137] Japan,[135,136,144] Canada;[121,130] there was one study from each of Australia,[105] Austria,[139] Brazil,[141] Chile,[133] Croatia,[143] Republic of Korea,[132] Spain,[138] Sweden[104] and Taiwan, Province of China.[113] Of the non-randomised comparative studies comparing robotic with laparoscopic radical prostatectomy, three primary full-text studies[92,93,98] and one conference abstract[97] were set in the USA, one conference abstract was set in both the USA and France[94] and three studies were set in France.[91,95,96] Of the non-randomised comparative studies comparing robotic, laparoscopic and open radical prostatectomy, two primary studies[99,100] and one secondary report[102] were set in the USA and one study was set in France.[101] Of the non-randomised comparative studies comparing robotic and open radical prostatectomy, 10 primary studies[103,108–112,115–118] and two secondary reports[119,120] were set in the USA, one study was set in Australia,[105] three primary studies[106,107,114] were set in Italy, one study was set in Sweden[104] and one was set in Taiwan, Province of China.[113] Of the non-randomised comparative studies comparing laparoscopic and open radical prostatectomy, seven primary studies[124–126,128,142,145,146] and one secondary report[147] were set in the USA, three primary studies[127,131,137] were set in Germany, three primary studies[135,136,144] were set in Japan, three primary studies[123,129,134] were set in Italy, two primary studies[122,140] were set in France and one study each was set in Austria,[139] Brazil,[141] Canada,[121] Chile,[133] Croatia,[143] Republic of Korea[132] and Spain.[138]

The four full-text publications that required translation paired with their original language were Fornara and Zacharias[127] (German), Kim[132] (Korean), Soric[143] (Croatian) and Raventos Busquets and colleagues[138] (Spanish).

TABLE 4 Number and type of included studies

Comparison	Study report	Data collection	Number of reports
Robotic vs laparoscopic	RCT		0
	Non-randomised comparative	Prospective	2
		Retrospective	3
		Both	1
		Not reported	2
	Total		8
Robotic vs laparoscopic vs open	RCT		0
	Non-randomised comparative	Prospective	1
		Retrospective	1
		Not reported	2
	Total		4
Robotic vs open	RCT		0
	Non-randomised comparative	Prospective	8
		Retrospective	6
		Both	2
		Not reported	2
	Total		18
Laparoscopic vs open	RCT	Prospective	1
	Non-randomised comparative	Prospective	15
		Retrospective	7
		Unclear	1
		Not reported	4
	Total		28

Characteristics of patients

The 58 reports included 21,126 men at enrolment. Excluding secondary reports and following exclusions because of ineligibility or participant dropout, the final study analyses included 19,064 men, of whom 6768 underwent robotic radical prostatectomy, 4952 underwent laparoscopic radical prostatectomy and 7344 underwent open radical prostatectomy. The demographic and disease characteristics of these included men are summarised in *Table 5*.

All studies reported age with a median (interquartile range) of 62 (60–64) years and a total range of 35–84 years.

Baseline clinical tumour staging data were reported for all studies except that conducted by Bolenz and colleagues;[100] however, clinical staging data for this study were available from an earlier report in abstract form.[102] Eight reports[107,111,120,126,139,141,143,147] did not report specific baseline clinical stage, simply reporting their inclusion criterion as '≤ cT1–T2', and one[109] did not report clinical stage by procedure. The baseline clinical tumour staging was similar between the laparoscopic and robotic radical prostatectomy patients with 68% and 69%, respectively, categorised as T1.

Less than half of the included reports (23/58, 40%)[91,98,99,101,103,105–108,110,115,117–121,125,128,135,136,142,145,146] gave detailed biopsy Gleason scores for men undergoing prostatectomy in the format we required: numbers of men categorised as Gleason score ≤ 6, 7 or ≥ 8. Seven studies[90,95,97,111,126,139,141] and one secondary report[147] did not report biopsy Gleason grades or score. Over one-third

TABLE 5 Summary description of the individual patient characteristics for the included studies, where data were combinable, from the information reported by the study authors

Variable	Robotic	Laparoscopic	Open
n	6768	4952	7344
Age (years), median	60.7	61.9	63
Interquartile range (years)	59.8–62	60.0–63.65	60.5–64.8
Clinical stage, *n* (%)			
cT1	4380 (64.7)	3257 (65.8)	3956 (53.9)
cT2	1743 (25.8)	1312 (26.5)	2194 (29.9)
cT3	58 (0.9)	26 (0.5)	148 (2.0)
cT4	1 (0.01)	8 (0.2)	0 (0)
Missing/unknown[a]	586 (8.7)	349 (7.0)	1046 (14.2)
Preoperative Gleason score, *n* (%)			
≤ 6	2179 (32.2)	989 (20.0)	2389 (32.5)
7	949 (14.0)	429 (8.7)	1574 (21.4)
8–10	198 (2.9)	54 (1.1)	333 (4.5)
Missing/unknown[a]	3442 (50.9)	3480 (70.3)	3048 (41.5)
Preoperative PSA (ng/ml), median	6.3	7.2	7.9
Interquartile range (ng/ml)	5.4–7.1	6.3–8.6	6.0–9.3
Postoperative whole prostate radical prostatectomy Gleason score, *n* (%)			
≤ 6	1200 (17.7)	485 (9.8)	1666 (22.7)
7	1110 (16.4)	415 (8.4)	1634 (22.2)
8–10	161 (2.4)	49 (1.0)	379 (5.2)
Missing/unknown[a]	4297 (63.5)	4003 (80.8)	3665 (49.9)
Pathological tumour stage, *n* (%)			
pT0	7 (0.1)	6 (0.1)	22 (0.3)
pT1	0 (0)	29 (0.6)	25 (0.3)
pT2	2060 (30.4)	2373 (47.9)	4246 (57.8)
pT3	571 (8.4)	669 (13.5)	1368 (18.6)
pT3/4[b]	23 (0.3)	45 (0.9)	76 (1.0)
pT4	7 (0.1)	17 (0.3)	33 (0.4)
Missing/unknown[a]	4203 (62.1)	1710 (34.5)	1574 (21.4)

a Either because of missing/unsuitable or non-reported data.
b pT stage as reported by Ball and colleagues[99] and Soderdahl and colleagues.[142] Authors did not differentiate between pT3 and pT4.

of the included reports (21/58, 36%) reported either mean[93–95,113,122–124,129,130,132,139,140,143,144] or median[104,114,127,131,133,134,137] scores. The remaining reports presented details using different scoring formats[90,92,102,138,141] or did not present separately by procedure.[100] Two-thirds of men undergoing both laparoscopic and robotic radical prostatectomy had a Gleason score ≤ 6.

Fifty reports[90,91,93–101,103–109,112–119,122–125,127–146] gave preoperative PSA values, with the majority (38/50, 76%) reporting mean PSA for each group of men. Nine studies[106–108,131,134,141,142,144,145] reported median group PSA values, whereas two studies[135,136] reported mean and median PSA and one study[119] reported PSA range only. Combining the median and mean PSA values across all of the studies demonstrated slightly lower levels of preoperative PSA in the robotic than in the laparoscopic procedures: 6.3 ng/ml and 7.2 ng/ml respectively. Three studies[92,121,126] reported the number of men in each group falling into varying ranges of PSA values but as the ranges were inconsistent we were unable to include these data in the summary.

The postoperative Gleason sum score following pathological examination of the prostate was similar between the robotic and laparoscopic patients with 50% of the men in both groups with combinable Gleason information having a Gleason score ≤ 6. Pathological staging assigned following consideration of the operative finding during surgery and pathological examination of the removed prostate was similar between the robotic and laparoscopic patients with 78% of the men with combinable staging information in both groups categorised as pT2. There was a trend towards worse disease characteristics in men undergoing open prostatectomy with 55% having a post-prostatectomy Gleason score > 6 and 30% categorised as pT2 or higher.

Twenty-nine primary reports[90–93,96,99,100,106,108,110–113,118,122,123,125,126,128,129,132,135–137,139,142,144–146] and two secondary reports[102,119] reported the use of nerve-sparing techniques.

Overview of types of outcomes reported

The numbers and types of included studies reporting our main considered outcomes are summarised below.

Efficacy

Thirty-nine studies (67%)[90,94–98,101,103,105–109,112–116,118,122,123,125–127,129–134,137–141,143–146] reported data on the rate of positive surgical margins in the excised prostate specimen.

Thirteen studies (22%)[95,101,103,108,109,112,113,115,116,123,133,137,140] reported the rate of biochemical recurrence, but the time points at which this was censored, the definition of biochemical recurrence and the threshold values of PSA used varied between studies.

The need for and outcome of further treatment for prostate cancer recurrence was reported by one study. Dahl and colleagues[126] reported information on the numbers of men requiring further cancer treatment consisting of salvage external beam radiation therapy, androgen deprivation therapy or both for cohorts of men undergoing laparoscopic or open prostatectomy.

Eight studies[90,111,116,130,135–137,139] reported quality-of-life data using validated measures.

Safety

The majority of reports (45/58, 78%) included data on perioperative adverse events.

Thirteen primary reports[93,94,99,103,109,110,130,135,136,141,142,144,145] and one secondary report[147] did not report perioperative safety outcomes.

Four studies[104,105,126,140] reported deaths within 30 days postoperatively because of surgical complications.

Postoperative incontinence and sexual dysfunction

Twenty-one studies (36%)[91,93,97,99,106,108,110,113,114,116,123,126,128–130,133,135–137,142,146] provided data on urinary incontinence postoperatively. Three other studies[112,122,139] reported continence data in a form that could not be converted to the numbers of incontinent men, which was our required format for meta-analysis. Two studies also reported data that we were unable to use because of presentation in graph format rather than numbers of incontinent men[105] or because of presentation of immature data.[95] The study conducted by Carlsson and colleagues[104] reported the number of patients requiring additional surgery for urinary incontinence between 30 days and 15 months after radical prostatectomy.

Nineteen studies (33%)[93,99,106,108,110,112–114,116,122,123,126,128,129,133,135,136,142,146] provided data on sexual function following prostatectomy.

Risk of bias

Overall assessment of risk of bias

Forty-eight reports from 28 individual author-affiliated institutes were assessed for risk of bias. The secondary reports by Dahl and colleagues[147] and Chan and colleagues[119] contained unique outcomes not included in the associated primary studies[103,126] and we therefore conducted risk of bias assessment for both reports. Twenty-four reports (50%)[92,93,95,96,98,104–108,112,113,115,116,124,126,130,134,136,139,142,144,146,147] were judged to be at high overall risk of bias, 13 (27%)[90,99–101,103,117,118,122,128,129,137,141,145] were low risk and 11 (23%)[109,111,114,119,121,123,125,131,135,140] were judged unclear. Analysis of inter-rater agreement for overall assessment of risk of bias gave a kappa = 0.34 and a weighted kappa = 0.35, indicating moderate agreement.

Only the RCT conducted by Guazzoni and colleagues[90] was judged to be at low risk of bias for sequence generation and the study by Touijer and colleagues[145] was judged to be at low risk for allocation concealment. All other studies were high risk or unclear for these two key domains.

Risk of bias for reported outcomes

The risk of bias assessments for our chosen main outcomes of efficacy (predominantly surgical margins status), urinary incontinence and erectile dysfunction and perioperative adverse events are summarised in *Figures 7–10* respectively.

Efficacy

Thirty-seven reports[90,93,95,96,98,101,103,105–109,112–118,122–126,128–131,134,137,139–141,144–147] were assessed for risk of bias for efficacy outcomes. Of these, 30 (81%)[90,95,96,98,101,103,106,108,113–118,122–126,128,129,131,137,139–141,144–147] were considered to be at low risk of bias for confounding factors.

Urinary dysfunction

Twenty-three studies[93,95,99,105,106,108,110,112–114,116,122,123,126,128–130,135–137,139,142,146] were assessed for risk of bias for reporting of urinary incontinence outcomes. Of these, 10 (43%)[99,108,110,114,116,122,126,128,129,146] were considered to be at low risk of bias for confounding factors.

Erectile dysfunction

Twenty studies[93,95,99,106,108,110,112–114,116,122,123,126,128,129,135–137,142,146] were assessed for risk of bias for reporting of erectile dysfunction. Of these, nine studies (39%)[99,110,114,122,126,128,129,135,137] were considered to be at low risk of bias for confounding.

Perioperative safety

Thirty-five studies[90,92,93,95,96,98,100,101,104–108,111–117,119,121–126,128,129,131,134,137,139,140,146] were assessed for risk of bias for reporting of perioperative adverse events. Of these, 11 (31%) were judged to be at low risk of bias for confounding factors.[90,96,100,106,114,116,122,124–126,131]

Assessment of effectiveness

Data concerning outcomes included in the meta-analysis are detailed in *Tables 6–16*. A detailed description of all outcomes abstracted from the included studies is given in tables contained in *Appendix 9*.

Positive margins

Meta-analysis of data from the 37 included studies[90,94–98,101,103,105–109,112–116,118,122,123,125,127,129–134,137,139–141,143,144,146,147] that reported positive surgical margin rates (*Table 6*) showed a statistically significant improvement for robotic compared with laparoscopic prostatectomy (OR 0.69; 95% CrI 0.51 to 0.96; probability outcome favours robotic prostatectomy = 0.987). The probability

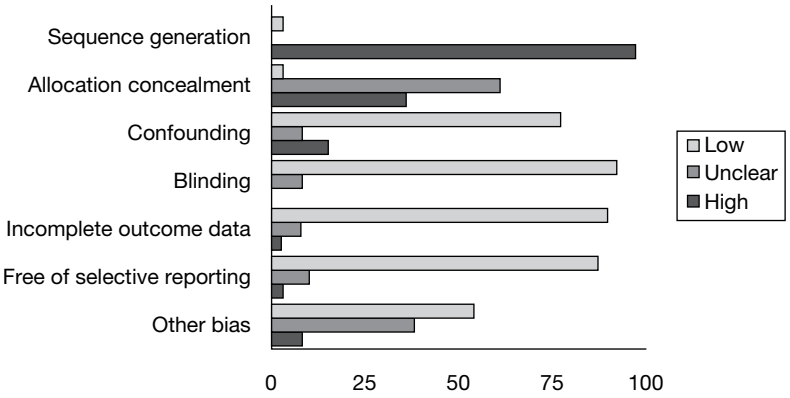

FIGURE 7 Summary of risk of bias assessment for reports of efficacy ($n = 37$).

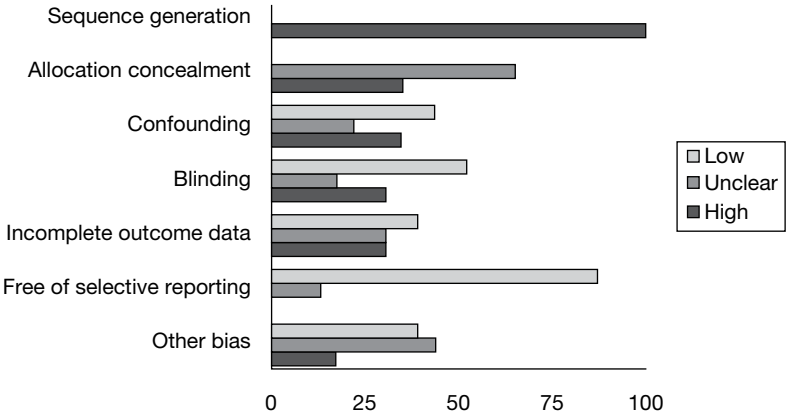

FIGURE 8 Summary of risk of bias assessment for reports of urinary dysfunction ($n = 23$).

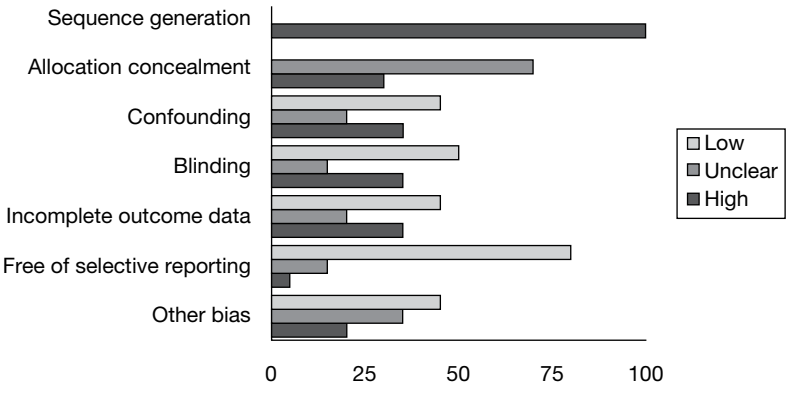

FIGURE 9 Summary of risk of bias assessment for reports of erectile dysfunction ($n = 20$).

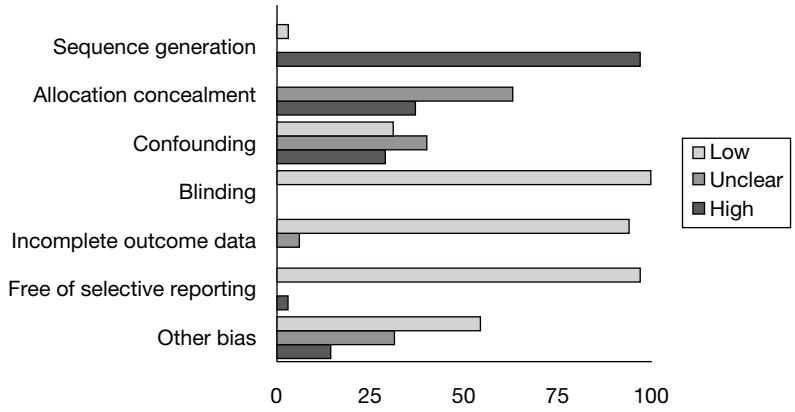

FIGURE 10 Summary of risk of bias assessment for reports of perioperative safety ($n = 35$).

of a positive margin predicted by the mixed-treatment comparison model was 17.0% following robotic prostatectomy compared with 23.6% following laparoscopic prostatectomy. Restriction of the meta-analysis to studies at low risk of bias did not change the direction of effect but did decrease the precision of the effect size (OR 0.73; 95% CrI 0.29 to 1.75), with the probability that the event rate was lower for robotic prostatectomy being no longer statistically significant ($p = 0.782$).

Pathological examination of the prostate

Details of the methods described for the handling, processing and pathologist reporting of radical prostatectomy specimens were given in 24 included study reports[90,94,96,98,101,103,105,106,109,112,114,116,118,122,123,134,137–141,144] and are summarised in *Table 7*. In 10 (42%) of these studies reference was made to a published standardised protocol for examination of radical prostatectomy specimens: four studies gave one of three alternative references for the Stanford protocols[148–150] and one[122] specified the Stanford protocol without citing a relevant reference; the remaining studies referenced other protocols published from various centres.[82,151–153]

Concerning established key features of quality-assured pathological examination, 19 (79%) studies described preliminary dyeing of the surface of the prostate to accurately identify the location of the surgical margin. The accepted definition of a positive margin in terms of tumour cells touching or in contact with the dyed prostate surface was specified by 18 (75%) studies; alternative descriptions used were 'an extension of tumour at the surface of incision'[141] and 'a malignant margin is considered a positive margin',[138] but these studies did not comment on whether or not the specimen was dyed before sectioning. One study defined margin positivity following robotic prostatectomy as 'cancer seen in the intra-operative distal biopsies'[116] whereas a further study reported use of 'frozen section to control for negative margins'.[139] Concerning the methods used to prepare microscope slides (sections) for examination of the prostate gland, the recommended technique of embedding the whole gland for sectioning was specified by nine (38%) studies[98,105,106,109,118,123,134,137,140] whereas one (4%) specified systematic partial sampling[103] and the sampling method was not specified or unclear in the remaining 14 (58%) studies.[90,94,96,101,112,114,116,122,138,141,144,145,147] Section thickness was specified within the recommended range of 2–6 mm in 11 (46%) studies.

The recommended technique of examining sagittal sections from both the apical and the basal slices of the prostate was specified by six (25%) studies.[98,103,105,123,134,144] Of the remainder, one study[147] used radial sections, two studies[137,140] used sagittal sections for the apex only and two studies[137,140] used shave margins for both apex and base. No information was given or practice was unclear in the remaining 13 (54%) studies.[90,94,96,101,106,112,114,116,118,122,138,139,141]

TABLE 6 Positive margins

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
[a]Anastasiadis 2003[122]		61/230 (26.5)	20/70 (28.6)
Artibani 2003[123]		21/71 (29.6)	12/50 (24.0)
Barocas 2010[103]	281/1413 (19.9)		148/491 (30.1)
Brown 2004[125]		10/59 (16.9)	12/60 (20.0)
Dahl 2006[147]		43/286 (15.0)	124/714 (17.4)
Doumerc 2010[105]	45/212 (21.2)		84/502 (16.7)
[a]Drouin 2009[101]	12/71 (16.9)	16/85 (18.8)	15/83 (18.1)
Ficarra 2009[106]	35/103 (34.0)		21/105 (20.0)
Fornara 2004[127]		5/32 (15.6)	7/32 (21.9)
Fracalanza 2008[107]	10/35 (28.6)		6/26 (23.1)
[a]Greco 2010[129]		12/150 (8.0)	17/150 (11.3)
[a]Guazzoni 2006[90]		16/60 (26.7)	13/60 (21.7)
Jacobsen 2007[130]		22/67 (32.8)	60/148 (40.5)
Joseph 2007[94]	99/754 (13.1)	246/800 (30.8)	
Jurczok 2007[131]		63/163 (38.7)	104/240 (43.3)
Kim 2007[132]		11/30 (36.7)	11/45 (24.4)
Krambeck 2009[108]	46/294 (15.6)		100/588 (17.0)
Lama 2009[133]		16/56 (28.6)	21/59 (35.6)
Loeb 2010[109]	22/152 (14.5)		25/137 (18.2)
Martorana 2004[134]		12/50 (24.0)	13/50 (26.0)
Menon 2002[95]	7/40 (17.5)	10/40 (25.0)	
Nadler 2010[112]	5/50 (10.0)		12/50 (24.0)
Ou 2009[113]	15/30 (50.0)		6/30 (20.0)
Poulakis 2007[137]		15/72 (20.8)	16/70 (22.9)
Remzi 2005[139]		10/39 (25.6)	8/41 (19.5)
Rocco 2009[114]	26/120 (21.7)		60/240 (25.0)
Rozet 2007[96]	26/133 (19.5)	21/133 (15.8)	
Salomon 2002[140]		32/155 (20.6)	30/151 (19.9)
Schroeck 2008[115]	106/362 (29.3)		122/435 (28.0)
Silva 2007[141]		22/90 (24.4)	37/89 (41.6)
Soric 2004[143]		6/26 (23.1)	3/26 (11.5)
Sundaram 2004[97]	2/10 (20.0)	2/10 (20.0)	
Terakawa 2008[144]		54/137 (39.4)	52/220 (23.6)
Tewari 2003[116]	18/200 (9.0)		23/100 (23.0)
Trabulsi 2008[98]	3/50 (6.0)	35/190 (18.4)	
Wagner 2007[146]		7/75 (9.3)	14/75 (18.7)
[a]White 2009[118]	11/50 (22.0)		18/50 (36.0)
Predicted probability of event	0.176	0.236	0.238
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.69 (0.51 to 0.96); 0.987	
	Low-risk studies only	0.73 (0.29 to 1.75); 0.782	

a Study included in the low risk of bias meta-analysis.

The site of positive margin was specified in six (24%) studies;[98,118,134,141,144,147] in four studies[118,134,141,147] locations were defined, with some variation in terminology, as apex, base or bladder neck, lateral or posterolateral and multiple and in two further studies[98,144] as apex, base, anterior or posterior and apex, base or other. No study gave the extent in millimetres of positive margins in the results.

TABLE 7 Description of pathology methods used to examine the removed prostate for cancer foci

Study	Gland inked	Positive margin	Embedding	Blocks	Slice thickness	Apex slice sections	Base slice sections	Location of positive margin	Review	Other details	Method reference
Anastasiadis 2003[122]	NS	NS	NS	NS	NS	NS	NS	NS	One pathologist		Stanford protocol unreferenced[a]
Artibani 2003[123]	Inked	Defined for RRP[b]	Complete	Whole mounts	RRP 2–3 mm, LRP 4–6 mm	Sagittal	Sagittal	NS	Two pathologists	Unreferenced protocol for LRP	McNeal 1990[149]
Barocas 2010[103]	Inked	Defined[b]	Systematic sample	NS	3 mm	Sagittal	Sagittal	NS	NS		Srigley 2006[82]
Dahl 2006[147]	Inked	Defined[b]	NS	NS	NS	Radial	Radial	Classified[c]	Urological pathologists		
Doumerc 2010[105]	Inked	Defined[b]	Complete	Small blocks	NS	Sagittal	Sagittal	NS	One urological pathologist		
Drouin 2009[101]	Inked	Defined[b]	NS	NS	NS	NS	NS	NS	NS		
Ficarra 2009[106]	NS	NS	Complete	Whole mounts	4 mm	NS	NS	NS	NS		
Guazzoni 2006[90]	Inked	Defined[b]	NS	NS	NS	NS	NS	NS	NS		
Joseph 2007[94]	Inked	Defined[b]	NS	NS	NS	NS	NS	NS	NS		
Loeb 2010[109]	Inked	Defined[b,d]	Complete	NS	2–3 mm	Sagittal	1-mm shave	NS	One urological pathologist		
Martorana 2004[134]	Inked	Defined[b]	Complete	NS	2–3 mm	Sagittal	Sagittal	Classified[e]	One pathologist		McNeal 1990[149]
Nadler 2010[112]	Inked	Defined[b]	NS	NS	NS	NS	NS	NS	One pathologist		

Study	Gland inked	Positive margin	Embedding	Blocks	Slice thickness	Apex slice sections	Base slice sections	Location of positive margin	Review	Other details	Method reference
Poulakis 2007[137]	Inked	Defined[a]	Complete	Small blocks	3 mm	Shave	Shave	NS	One pathologist		Humphrey 1993[148]
Raventos Busquets 2007[138]	NS	Defined[e]	NS	NS	NS	NS	NS	NS	NS		
Remzi 2005[139]	NS	NS[f]	NS	NS	NS	NS	NS	NS	NS		
Rocco 2009[114]	Inked	Defined[a]	NS	NS	NS	NS	NS	NS	NS		
Rozet 2007[96]	Inked	Defined[a]	NS	NS	NS	NS	NS	NS[g]	NS	Apex commonest +ve site[g]	
Salomon 2002[140]	Inked	NS	Complete	Small blocks	3 mm	Shave	Shave	NS	One pathologist		Stamey 1988[150]
Silva 2007[141]	NS	Defined[h]	NS	NS	NS	NS	NS	Classified[b]	Pathology services		
Terakawa 2008[144]	Inked	Defined[a]	NS	Whole mount	3 mm	Parasagittal sections	Parasagittal sections	Classified[i]	One pathologist		
Tewari 2003[116]	Inked	Defined[a,j]	NS	NS	5 mm	NS	NS	NS	NS		Ohori 1995[152]
Touijer 2007[145]	Inked	Defined[a]	NS	NS	3–4 mm	Parasagittal sections	NS	NS	One GU pathologist		
Trabulsi 2008[98]	Inked	Defined[a]	Complete	Whole mount	NS	Parasagittal sections	Parasagittal sections	Classified[k]	Multidisciplinary conference review		Brown 2003[151]
White 2009[118]	Inked	Defined[a]	Complete	Whole mount	2–3 mm	NS	NS	Classified[b]	NS		True 1994[153]

LRP, laparoscopic radical prostatectomy; NS, not stated; RRP, radical retropubic open prostatectomy.

a Tumour cells touch the ink, tumour at the inked surface or inked to determine margin.
b Apex, base/bladder neck, lateral/posterolateral, multiple.
c Any tumour on the bladder neck slice is positive.
d Apex, posterolateral, basal and bladder neck.
e Malignant margin is considered positive margin.
f Frozen section to control for negative margins.
g Apex commonest positive site.
h An extension of tumour at the surface of incision.
i Apex, base, anterior, posterior.
j For robot-assisted laparoscopic prostatectomy, margin positive if cancer seen in intraoperative distal biopsies.
k Apex, base, other.

DOI: 10.3310/hta16410

Given that no studies reported the same methodology for ascertainment of positive margin status it was not possible to undertake a meta-analysis restricted to studies using appropriate methodology.

In summary, these studies showed variation in the pathology protocols employed, which may have affected the determination of positive margin status and thereby increased the risk of bias in the results.

Biochemical recurrence

Biochemical recurrence rates up to 1 year following radical prostatectomy were reported in six studies (*Table 8*).[108,113,115,123,133,137] There was no evidence of a difference in the rates of biochemical recurrence calculated by the mixed-treatment comparison model between robotic and laparoscopic prostatectomy (OR 0.89; 95% CrI 0.24 to 3.34; probability outcome favours robotic prostatectomy = 0.588). Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were at high risk.

Urinary incontinence

The 22 studies that reported urinary incontinence used a variety of measures at different time points. Measures included observed urinary leakage,[93] pad use,[91,97,108,112–114,116,122,128,129,137,139,146] fluid volume voiding diary[130] and validated questionnaire scores [University of California Los Angeles – Prostate Cancer Index (UCLA-PCI)[99,110,135,136,142] and International Consultation of Incontinence Questionnaire (ICIQ-UI)[106]]. Artibani and colleagues[123] measured both urinary leakage and pad use. The study conducted by Lama and colleagues[133] did not give a definition of incontinence. The results from the 10 studies[106,108,113,114,126,128–130,133,146] that reported urinary incontinence at a standard time point of 12 months following prostatectomy are given in *Table 9*. There was no evidence of a difference in the rates of urinary incontinence between robotic and laparoscopic prostatectomy (OR 0.55; 95% CrI 0.09 to 2.84; probability outcome favours robotic prostatectomy = 0.783). Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were at high risk.

The study conducted by Carlsson and colleages[104] reported 7/1253 (0.6%) patients requiring further postoperative surgery for incontinence between 30 days and 15 months after their initial robotic operation compared with 11/485 (2.2%) requiring further postoperative surgery for incontinence after undergoing an open radical prostatectomy.

TABLE 8 Biochemical recurrence within 12 months

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		12/63 (19.0)	5/44 (11.4)
Krambeck 2009[108]	14/248 (5.6)		32/492 (6.5)
Lama 2009[133]		6/56 (10.7%)	7/59 (11.9)
Ou 2009[113]	6/30 (20.0)		5/30 (16.7)
Poulakis 2007[137]		17/204 (8.3)	11/70 (15.7)
Schroeck 2008[115]	29/362 (8.0)		54/435 (12.4)
Predicted probability of event	0.087	0.097	0.110
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.89 (0.24 to 3.34); 0.588	
	Low-risk studies only	Not estimable	

TABLE 9 Urinary incontinence at 12 months

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Dahl 2009[126]		17/78 (21.8)	9/72 (12.5)
Ficarra 2009[106]	3/103 (3.0)		12/105 (11.4)
Ghavamian 2006[128]		7/70 (10.0)	8/65 (12.3)
Greco 2010[129]		4/150 (2.7)	13/150 (8.7)
Jacobsen 2007[130]		10/57 (17.5)	19/148 (12.8)
Krambeck 2009[108]	20/244 (8.2)		30/476 (6.3)
Lama 2009[133]		0/56	2/59 (3.4)
Ou 2009[113]	0/30		1/30 (3.3)
Rocco 2009[114]	2/79 (2.5)		26/217 (12.0)
Wagner 2007[146]		24/67 (35.8)	35/66 (53.0)
Predicted probability of event	0.045	0.079	0.109
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.55 (0.09 to 2.84); 0.783	
	Low-risk studies only	Not estimable	

Erectile dysfunction

As described in *Overview of type of outcomes reported*, a total of 19 studies provided data on sexual function. The time point following surgery when the outcome was assessed and the measure used to quantify the outcome varied between studies. Erectile dysfunction was variously defined as the inability to achieve and maintain a spontaneous or drug-assisted erection suitable for sexual intercourse[93,108,113,114,116,122,123,126,129] or by validated symptom questionnaire scores [UCLA-PCI,[99,110,135,136,142] IIEF-5[106,128] Expanded Prostate Cancer Index Composite, sexual function subscale (EPIC-SFSS)[146] and Sexual Health Inventory for Men (SHIM)[112]]. The study conducted by Lama and colleagues[133] did not report a definition of erectile dysfunction. Given the diversity of definitions and types of data (continuous and dichotomous) it was not possible to collate data from individual studies into a form suited to meta-analysis. Of the two studies directly comparing robotic and laparoscopic prostatectomy that reported erectile dysfunction, one[99] showed earlier recovery of sexual function following the robotic prostatectomy procedure, with 35% compared with 21% returning to baseline functioning at 3 months post surgery and 43% compared with 25% returning to baseline functioning at 6 months, and the other[93] favoured laparoscopic prostatectomy (46% required drug aid vs 36% at 3 months in the robotic and laparoscopic groups, respectively).

Quality of life

Quality of life following prostatectomy as measured by validated patient-reported questionnaires was reported in 10 studies: European Quality of Life-5 Dimensions (EQ-5D) visual analogue scale (VAS); [90,116,139] Short Form questionnaire-36 items (SF-36);[135,136] Short Form questionnaire-12 items (SF-12);[111] European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30);[137] the quality-of-life item contained within the International Prostate Symptom Score (I-PSS);[130] the International Continence Society (ICS)[91] and the Expanded Prostate Cancer Index Composite urinary incontinence and sexual function subscales (EPIC-UISS-SFSS).[146] Full details are given in *Appendix 9*. Quality-of-life measurements following robotic prostatectomy were reported by two studies[111,116] with a maximum observation period of 6 weeks. The data were insufficient to enable us to assess any difference in quality of life following robotic or laparoscopic prostatectomy. Three studies[135–137] reported that preoperative physical functioning level was not achieved in all patients by 6 months postoperatively but the clinical significance of the differences was unclear.

Pain

There were no direct comparative studies of robotic and laparoscopic procedures reporting pain. It was therefore not possible to report any difference in pain between the procedures either postoperatively or in the long term.

Need for further cancer treatment

Dahl and colleagues[126] was the only report that included information on the numbers of men requiring further treatment for cancer persistence or recurrence, with rates of 5/104 (5%) for laparoscopic prostatectomy and 2/102 (2%) for open prostatectomy.

Death

Four studies[104,105,126,140] reported deaths resulting from complications in the 30-day postoperative period. These included two fatal cardiac arrests[104,126] and one cerebrovascular accident[105] following open prostatectomy. Salomon and colleagues[140] also reported one death due to pulmonary embolism following laparoscopic prostatectomy. Five studies[92,95,96,137,154] involving 1600 men specifically reported no postoperative deaths. Drouin and colleagues[101] reported one death due to prostate cancer 5 years after open prostatectomy and four deaths due to cardiovascular complications without specifying which procedure these men had received. Krambeck and colleagues[108] reported all-cause mortality rates of 4/248 (1.6%) for men undergoing robotic prostatectomy and 4/492 (0.8%) after open prostatectomy at a median follow-up time of 1.3 years.

Perioperative adverse events

Data on the perioperative adverse events of blood transfusion, anastomotic leak, bladder neck contracture, wound infection, organ injury, ileus, deep-vein thrombosis and pulmonary embolism are presented in *Tables 10–17*. Abstracted data concerning other specific adverse events not included in the meta-analysis are detailed in *Appendix 10*. All adverse events were additionally categorised according to the Clavien–Dindo system and the data meta-analysed according to Clavien–Dindo score (see *Tables 59–70*).

Blood transfusion

Meta-analysis of data from the 30 studies[90–92,94–96,100,101,104–108,112,113,116,119–123,125,127–129,132–134,137,140] that reported blood transfusion rates (*Table 10*) showed a relative reduced need for blood transfusion with robotic prostatectomy compared with laparoscopic prostatectomy (OR 0.71; 95% CrI 0.31 to 1.62) but this was not statistically significant (probability outcome favours robotic prostatectomy = 0.780). The predicted rate of blood transfusion in the mixed-treatment comparison model was 3.5% for robotic prostatectomy and 5% for laparoscopic prostatectomy. Restriction of the meta-analysis to the studies at low risk of bias changed the direction of effect to favour the laparoscopic procedure but precision was reduced (OR 1.45; 95% CrI 0.38 to 6.21; probability that outcome favours laparoscopic prostatectomy = 0.257).

Bladder neck contracture

Meta-analysis of data from the 13 studies[92,104,106,108,112,113,124–126,128,133,139,146] reporting bladder neck contracture (*Table 11*) showed a reduced rate for men undergoing robotic prostatectomy but this was not statistically significant (probability outcome favours robotic prostatectomy = 0.805). The predicted event probability in the mixed-treatment comparison model was 1% for robotic and 2.2% for laparoscopic prostatectomy. Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were categorised as high risk.

Anastomotic leak

Meta-analysis of data from 14 studies[90,94,96,97,101,104,112,113,125,126,128,134,139,140] that reported anastomotic leak (*Table 12*) showed a statistically significant reduced rate of anastomotic leaks in men following robotic prostatectomy (OR 0.21; 95% CrI 0.05 to 0.76; probability outcome favours

TABLE 10 Blood transfusion

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Al-Shaiji 2010[121]		3/70 (4.3)	42/70 (60.0)
[a]Anastasiadis 2003[122]		6/230 (2.6)	6/70 (8.6)
Artibani 2003[123]		45/71 (63.4)	17/50 (34.0)
[a]Bolenz 2010[100]	12/262 (4.6)	4/211 (1.9)	32/156 (20.5)
Brown 2004[125]		1/60 (1.7)	31/60 (51.7)
Carlsson 2010[104]	58/1253 (4.6)		112/485 (23.1)
Chan 2008[119]	5/660 (0.8)		11/340 (3.2)
Doumerc 2010[105]	2/212 (0.9)		10/502 (2.0)
Drouin 2009[101]	4/71 (5.6)	5/85 (5.9)	8/83 (9.6)
Ficarra 2009[106]	2/103 (1.9)		15/105 (14.3)
Fornara 2004[127]		2/32 (6.3)	6/32 (18.8)
Fracalanza 2008[107]	7/35 (20.0)		12/26 (46.2)
[a]Ghavamian 2006[128]		5/70 (7.1)	22/70 (31.4)
Gosseine 2009[91]	4/122 (3.3)	8/125 (6.4)	
[a]Greco 2010[129]		3/150 (2.0)	9/150 (6.0)
[a]Guazzoni 2006[90]		8/60 (13.3)	32/60 (53.3)
Hu 2006[92]	5/322 (1.6)	8/358 (2.2)	
Joseph 2007[94]	10/754 (1.3)	35/800 (4.4)	
Kim 2007[132]		7/30 (23.3)	10/45 (22.2)
Kordan 2010[120]	7/830 (0.8)		14/414 (3.4)
Krambeck 2009[108]	15/294 (5.1)		77/588 (13.1)
Lama 2009[133]		7/56 (12.5)	23/59 (39.0)
Martorana 2004[134]		1/50 (2.0)	5/50 (10.0)
Menon 2002[95]	0/40	1/40 (2.5)	
Nadler 2010[112]	10/50 (20.0)		45/50 (90.0)
Ou 2009[113]	4/30 (13.3)		18/30 (60.0)
[a]Poulakis 2007[137]		2/72 (2.8)	13/70 (18.6)
Rozet 2007[96]	13/133 (9.8)	4/133 (3.0)	
Salomon 2002[140]		3/155 (1.9)	31/151 (20.5)
Tewari 2003[116]	0/200		67/100 (67.0)
Predicted probability of event	0.035	0.050	0.227
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.71 (0.31 to 1.62); 0.780	
	Low-risk studies only	1.45 (0.38 to 6.21); 0.257	

a Study included in the low risk of bias meta-analysis.

robotic prostatectomy = 0.990). Predicted probability of this event in the model was 1.0% following robotic and 4.4% following laparoscopic prostatectomy. Restriction of the meta-analysis to only studies at low risk of bias was not possible because the zero event rate in the robotic studies produced unstable model convergence.

Wound or urinary infection

Meta-analysis of data from 12 studies[92,96,101,104,108,116,123,125–128,140] that reported infection rates (*Table 13*) showed a reduction in the rate of this event after robotic prostatectomy compared with laparoscopic prostatectomy but this was not statistically significant (probability outcome favours robotic prostatectomy = 0.662). The probability of an infection predicted by the model was 0.8% following robotic prostatectomy and 1.1% for laparoscopic prostatectomy. Restriction of the meta-analysis to only the studies at low risk of bias changed the direction of effect but precision was reduced.

TABLE 11 Bladder neck contracture

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Bhayani 2003[124]		0/33	6/24 (25.0)
Brown 2004[125]		0/60	2/60 (3.3)
Carlsson 2010[104]	3/1253 (0.2)		22/485 (4.5)
Dahl 2009[126]		2/104 (2.0)	0/102
Ficarra 2009[106]	3/103 (3.0)		6/105 (5.7)
Ghavamian 2006[128]		1/70 (1.4)	3/70 (4.3)
Hu 2006[92]	2/322 (0.6)	8/358 (2.2)	
Krambeck 2009[108]	3/248 (1.2)		23/492 (4.7)
Lama 2009[133]		5/56 (8.9)	1/59 (1.7)
Nadler 2010[112]	2/50 (4.0)		7/50 (14.0)
Ou 2009[113]	1/30 (3.3)		0/30
Remzi 2005[139]		3/80 (3.8)	4/41 (9.8)
Wagner 2007[146]		2/75 (2.7)	12/75 (16.0)
Predicted probability of event	0.010	0.021	0.049
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.48 (0.09 to 2.93); 0.805	
	Low-risk studies only	Not estimable	

TABLE 12 Anastomotic leak

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Brown 2004[125]		9/60 (15.0)	2/60 (3.3)
Carlsson 2010[104]	13/1253 (1.0)		8/485 (1.6)
Dahl 2009[126]		2/104 (1.9)	0/102
[a]Drouin 2009[101]	0/71	2/85 (2.4)	1/83 (1.2)
[a]Ghavamian 2006[128]		2/70 (2.9)	3/70 (4.3)
[a]Guazzoni 2006[90]		8/60 (13.3)	20/60 (33.3)
Joseph 2007[94]	12/754 (1.6)	112/800 (14.0)	
Martorana 2004[134]		1/50 (2.0)	2/50 (4.0)
Nadler 2010[112]	2/50 (4.0)		2/50 (4.0)
Ou 2009[113]	0/30		2/30 (6.7)
Remzi 2005[139]		8/80 (10.0)	6/41 (14.6)
Rozet 2007[96]	1/133 (0.8)	1/133 (0.8)	
Salomon 2002[140]		4/155 (2.6)	2/151 (1.3)
Sundaram 2004[97]	0/10	1/10 (10.0)	
Predicted probability of event	0.010	0.044	0.033
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.21 (0.05 to 0.76); 0.990	
	Low-risk studies only	Not estimable	

a Study included in the low risk of bias meta-analysis.

Organ injury

In descending order of frequency the reported injuries affected the rectum, ureter and bowel. Meta-analysis of data from the 17 studies[93,101,104–106,113,116,123–125,127–129,133,134,139,140] that reported organ injuries (*Table 14*) showed a reduction in the event rate following the robotic procedure that was statistically significant (OR 0.16; 95% CrI 0.03 to 0.76; probability outcome favours robotic prostatectomy = 0.987). The event probability predicted by the model was 0.4% for robotic prostatectomy and 2.9% for laparoscopic prostatectomy. Restriction of the meta-analysis to only the studies at low risk of bias maintained the direction and magnitude of effect.

TABLE 13 Infection

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		16/71 (22.5)	8/50 (16.0)
Brown 2004[125]		0/60	2/60 (3.3)
Carlsson 2010[104]	25/1253 (2.0)		8/50 (16.0)
Dahl 2009[126]		1/104 (1.0)	0/102
[a]Drouin 2009[101]	1/71 (1.4)	0/85	6/83 (7.2)
Fornara 2004[127]		0/32	2/32 (6.3)
[a]Ghavamian 2006[128]		1/70 (1.4)	1/70 (1.4)
Hu 2006[92]	7/322 (2.2)	16/358 (4.5)	
Krambeck 2009[108]	3/248 (1.2)		9/249 (3.6)
Rozet 2007[96]	12/133 (9.0)	5/133 (3.8)	
Salomon 2002[140]		2/155 (1.3)	14/151 (9.3)
Tewari 2003[116]	0/200		4/100 (4.0)
Predicted probability of event	0.008	0.011	0.048
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.75 (0.18 to 3.35); 0.662	
	Low-risk studies only	2.26 (0.02 to 295); 0.349	

a Study included in the low risk of bias meta-analysis.

TABLE 14 Organ injury

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		4/71 (5.6)	0/50
Bhayani 2003[124]		1/33 (3.0)	0/24
Brown 2004[125]		2/60 (3.3)	0/60
Carlsson 2010[104]	6/1253 (0.5)		10/485 (2.0)
Doumerc 2010[105]	1/212 (0.5)		0/502
[a]Drouin 2009[101]	0/71	1/85 (1.2)	1/83 (1.2)
Ficarra 2009[106]	2/103 (2.0)		0/105
Fornara 2004[127]		1/32 (3.1)	0/32
[a]Ghavamian 2006[128]		2/70 (2.9)	0/70
[a]Greco 2010[129]		2/150 (1.3)	1/150 (0.7)
Hu 2006[93]	3/322 (0.9)	23/358 (6.4)	
Lama 2009[133]		0/56	1/59 (1.7)
Martorana 2004[134]		2/50 (4.0)	0/50
Ou 2009[113]	2/30 (6.7)		1/30 (3.3)
Remzi 2005[139]		1/80 (1.3)	1/41 (2.4)
Salomon 2002[140]		4/155 (2.6)	3/151 (2.0)
Tewari 2003[116]	0/200		1/100 (1.0)
Predicted probability of event	0.004	0.029	0.008
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.16 (0.03 to 0.76); 0.987	
	Low-risk studies only	0.00 (0.00 to 0.20); 0.992	

a Study included in the low risk of bias meta-analysis.

Ileus

Meta-analysis of data from 12 studies[92,95,106,108,112,116,123,125,128,134,139,140] that reported ileus (slowness of recovery of bowel function) rates (*Table 15*) showed a reduction in the event rate following the robotic procedure that was not statistically significant (OR 0.46; 95% CrI 0.12 to1.51; probability

outcome favours robotic prostatectomy = 0.920). The predicted probability of ileus was 1.1% with the robotic procedure and 2.4% with the laparoscopic procedure. This difference should be treated with caution given that one study[92] contributed one-third of all data. Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were categorised as high risk.

Deep-vein thrombosis

Meta-analysis of data from eight studies that reported deep-vein thrombosis rates (*Table 16*) showed an increased risk following the robotic procedure that was not statistically significant (OR 2.67; 95% CrI 0.26 to 50.3; probability outcome favours robotic prostatectomy = 0.193). The predicted probability of a deep-vein thrombosis was 0.6% with the robotic procedure and 0.2% with the laparoscopic procedure. Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were categorised as high risk.

Pulmonary embolism

Because of the low event rate and the small number of studies reporting this outcome (*Table 17*) meta-analysis was not possible. Using crude combining of events across all studies, the

TABLE 15 Ileus

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		1/71 (1.4)	0/50
Brown 2004[125]		2/60 (3.3)	3/60 (5.0)
Ficarra 2009[106]	1/103 (1.0)		1/105 (1.0)
Ghavamian 2006[128]		2/70 (2.9)	1/70 (1.4)
Hu 2006[92]	9/322 (2.8)	19/358 (5.3)	
Krambeck 2009[108]	5/286 (1.7)		10/564 (1.8)
Martorana 2004[134]		1/50 (2.0)	0/50
Menon 2002[95]	1/40 (2.5)	1/40 (2.5)	
Nadler 2010[112]	2/50 (4.0)		0/50
Remzi 2005[139]		1/80 (1.3)	0/41
Salomon 2002[140]		4/155 (2.6)	0/151
Tewari 2003[116]	3/200 (1.5)		3/100 (3.0)
Predicted probability of event	0.011	0.024	0.009
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.46 (0.12 to 1.51); 0.920	
	Low-risk studies only	Not estimable	

TABLE 16 Deep-vein thrombosis

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Brown 2004[125]		0/60	2/60 (3.3)
Ghavamian 2006[128]		1/70 (1.4)	1/70 (1.4)
Hu 2006[92]	2/322 (0.6)	0/358	
Krambeck 2009[108]	1/248 (0.4)		6/492 (1.2)
Lama 2009[133]		0/56	1/59 (1.7)
Nadler 2010[112]	0/50		1/50 (2.0)
Salomon 2002[140]		1/155 (0.6)	2/151 (1.3)
Tewari 2003[116]	1/200 (0.5)		1/100 (1.0)
Predicted probability of event	0.006	0.002	0.014
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	2.67 (0.26 to 50.3); 0.193	
	Low-risk studies only	Not estimable	

percentage of men suffering pulmonary emboli was 2/1634 (0.1%) for robotic prostatectomy and 2/392 (0.5%) for laparoscopic prostatectomy.

Clavien–Dindo scores

The predicted event rates based on the meta-analysis statistical models for each Clavien–Dindo category are shown in *Table 18*. The individual study data contributing to each meta-analysis are given in *Appendix 9*. The OR for each Clavien–Dindo score was in favour of the robotic procedure but only that for Clavien IIIb, adverse event requiring intervention under general anaesthesia, was statistically significant (*Figure 11*).

TABLE 17 Pulmonary embolism

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Carlsson 2010[104]	2/1253 (0.2)		5/485 (1.0)
Dahl 2006[147]		1/104 (1.0)	0/102
Krambeck 2009[108]	0/248		5/492 (1.0)
Rozet 2007[96]	0/133	1/133 (0.8)	
Salomon 2002[140]		1/155 (0.6)	1/151 (0.7)

TABLE 18 Predicted rates of event for each Clavien–Dindo score

Clavien–Dindo category (see *Table 3*)	Robotic (%)	Laparoscopic (%)	Open (%)
Clavien I	2.1	4.1	4.2
Clavien II	3.9	7.2	17.5
Clavien IIIa	0.5	2.3	1.8
Clavien IIIb	0.9	3.6	2.5
Clavien IVa	0.6	0.8	2.1
Clavien V	<0.1	0.2	0.2

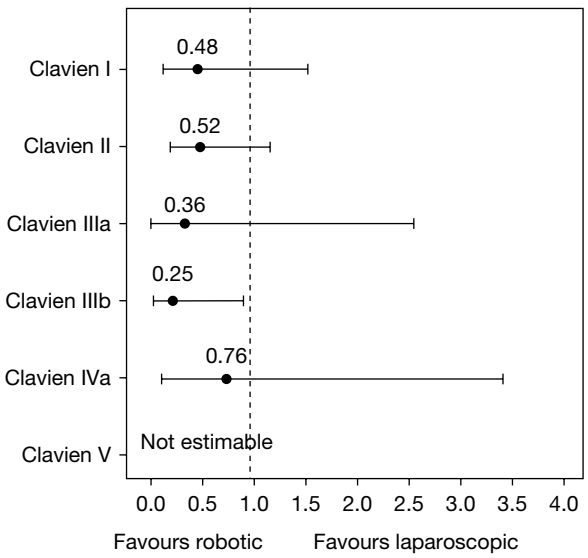

FIGURE 11 Odds ratio and 95% CrI by Clavien–Dindo score.

Descriptors of care

Equipment failure

Two studies reported equipment failure affecting the performance of the prostatectomy equipment. Menon and colleagues[95] reported eight initial problems with the voice recognition system of the voice-controlled AESOP camera holder (Computer Motion, Goleta, CA, USA) during laparoscopic prostatectomy while Hu and colleagues[92] reported two cases of equipment malfunction during robotic prostatectomy.

Conversion to open surgery

Meta-analysis of data from the 17 studies that reported rates of conversion from robotic or laparoscopic to open prostatectomy surgery (*Table 19*) showed lower rates for robotic prostatectomy but the difference was not statistically significant (OR 0.28; 95% CrI 0.03 to 2.00; probability outcome favours robotic prostatectomy = 0.893). The rate of conversion to open surgery predicted by the model was 0.3% with the robotic procedure and 0.9% with the laparoscopic procedure. Restriction of the meta-analysis to only the studies at low risk of bias was not possible because all studies were categorised as high risk.

Operation time

The criteria used to define and measure operation time varied considerably between studies and are detailed in *Appendix 9*. To attempt to minimise the effect of substantive variation between studies, meta-analysis was restricted to eight studies that directly compared robotic and laparoscopic operation times (*Table 20*). The pooled estimate demonstrated a statistically significant reduction in operation time of –12.4 minutes (95% CrI –16.5 minutes to –8.1 minutes) in favour of robotic prostatectomy. This difference should be treated with caution given uncertainty in whether robot docking time before commencing the surgery was included in the measured operation time in all studies.

TABLE 19 Conversion to open surgery

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)
Bhayani 2003[124]		3/36 (8.3)
Chan 2008[119]	6/660 (0.9)	
Drouin 2009[101]	0/71	1/85 (1.2)
Ghavamian 2006[128]		0/70
Greco 2010[129]		0/150
Hu 2006[92]	0/322	3/358 (0.8)
Jurczok 2007[131]		0/163
Martorana 2004[134]		0/50
Menon 2002[95]	0/40	1/40 (2.5)
Namiki 2005[135]		0/45
Ou 2009[113]	2/30 (6.7)	
Remzi 2005[139]		1/80 (1.3)
Rozet 2007[96]	4/133 (3.0)	0/133
Soric 2004[143]		3/26 (11.5)
Tewari 2003[116]	0/200	
Trabulsi 2008[98]	0/50	7/197 (3.6)
White 2009[118]	0/50	
Predicted probability of event	0.003	0.009
OR (95% CrI); probability outcome favours robotic prostatectomy	All studies	0.28 (0.03 to 2.00); 0.893
	Low-risk studies only	Not estimable

TABLE 20 Operation time in minutes – directly comparative studies only

Study	Robotic, *n*, mean (SD)	Laparoscopic, *n*, mean (SD)
Bolenz 2009[102]	264, 198[a] (58.7)	220, 235[a] (66.9)
Drouin 2009[101]	71, 199.6 (36.6)[b]	85, 257.3 (94.3)[b]
Gosseine 2009[91]	122, 237 (67.4)	125, 241 (68.3)
Hu 2006[92]	322, 186[a] (55.9)	358, 246[a] (69.3)
Joseph 2007[94]	754, 194 (57.8)	800, 179 (54.3)
Menon 2002[95]	40, 274 (94.3)[b]	40, 258 (80.3)[b]
Rozet 2007[96]	133, 166 (51.2)	133, 160 (49.8)
Sundaram 2004[97]	10, 290 (78.7)	10, 394 (99.7)
Predicted mean time (minutes)	225.1	237.5
Mean difference (95% CrI)	All studies	–12.4 (–16.5 to –8.1)
	Low-risk studies only	Not estimable

a Median values assumed to be same as mean.
b The SD was *not* imputed.

Duration of catheterisation

Postoperative catheterisation policies varied considerably across the 23 studies[90,91,94,96,101,105,106,113,114,116,122–124,127,129,131–134,137,139,140,143] that included relevant details and no meta-analysis was possible given the diversity of type of summary outcome measures reported. Of the four directly comparative studies of robotic and laparoscopic procedures, two[94,96] reported a shorter duration of catheterisation in men undergoing laparoscopic prostatectomy and two[91,101] reported a shorter duration of catheterisation for robotic prostatectomy. Only the report by Gosseine and colleagues[92] showed that the difference in duration of catheterisation was statistically significant, being 1.5 days shorter for robotic prostatectomy ($p = 0.01$).

Length of hospital stay

Length of hospital stay varied considerably across the 28 studies[91,96,97,102,105–108,112–114,116,119,121,123–128,131–134,137–140,143] that gave this information and no meta-analysis was possible given the diversity of type of summary outcome measures reported. Of the four studies directly comparing robotic and laparoscopic prostatectomy,[91,96,97,102] two reported a 1-day shorter length of stay for laparoscopic prostatectomy and two reported a 1-day shorter length of stay for robotic prostatectomy; none demonstrated any statistical significance.

Assessment of the learning curve

The variables of numbers of surgeons acting as lead operator, the number of procedures conducted by each surgeon prior to study commencement, the number of procedures carried out by each surgeon during the study and reported outcomes used to assess learning were abstracted from each included study (see *Appendix 9*). In general, the extent of reporting of relevant data on these variables was limited and data were often not given in a clear form suited to meta-analysis. The number of surgeons performing the surgery on men included in each study for both procedures was reported in 43/58 (74%) studies (see *Appendix 9*). Of these, nine[90,91,97,105,109,112,113,128,134] were single-surgeon studies. Studies that provided information on surgeons' previous experience did so in a number of different ways including using categories such as 'experienced', 'fellowship trained' or 'performed radical retropubic prostatectomies for 15 years prior to study'.

We focused on the rate of positive surgical margins as the key outcome to assess the effect of increasing surgeon experience to maintain consistency with the findings of the systematic review and the importance of this outcome to the economic modelling (see *Chapter 5*). The proportion of positive surgical margins for robotic and laparoscopic radical prostatectomy was plotted against the number of procedures carried out by the participating surgeons in each included study (*Figure 12*). Regression modelling illustrated that there was no evidence of trends across increasing experience (the dashed line is the predicted linear relationship for laparoscopic studies and the solid line is the predicted linear relationship for robotic studies), with $R^2 < 0.02\%$, demonstrating no statistical significance.

No data on parameters of the 'shape' of the learning curve, such as rates of positive margins for set number of cases performed, were identified in the included comparative studies. The inclusion criteria were therefore extended to include case series of laparoscopic and robotic radical prostatectomy that included more than 200 men. This specific extended search identified six robotic case series and four laparoscopic case series (*Table 21*). Two studies[155,156] reported only a mathematical shape to the learning curve, thereby precluding any formal modelling of the learning curve parameters (starting point, rate of learning and asymptote). All studies reported a decrease in positive surgical margin rate with increasing surgeon experience except for that by Eden and colleagues[157] who reported a consistently low rate throughout the series of men undergoing laparoscopic prostatectomy. The positive margin rate data plotted against the first and last reported level of experience for each case series are shown in *Figure 13*. There was some

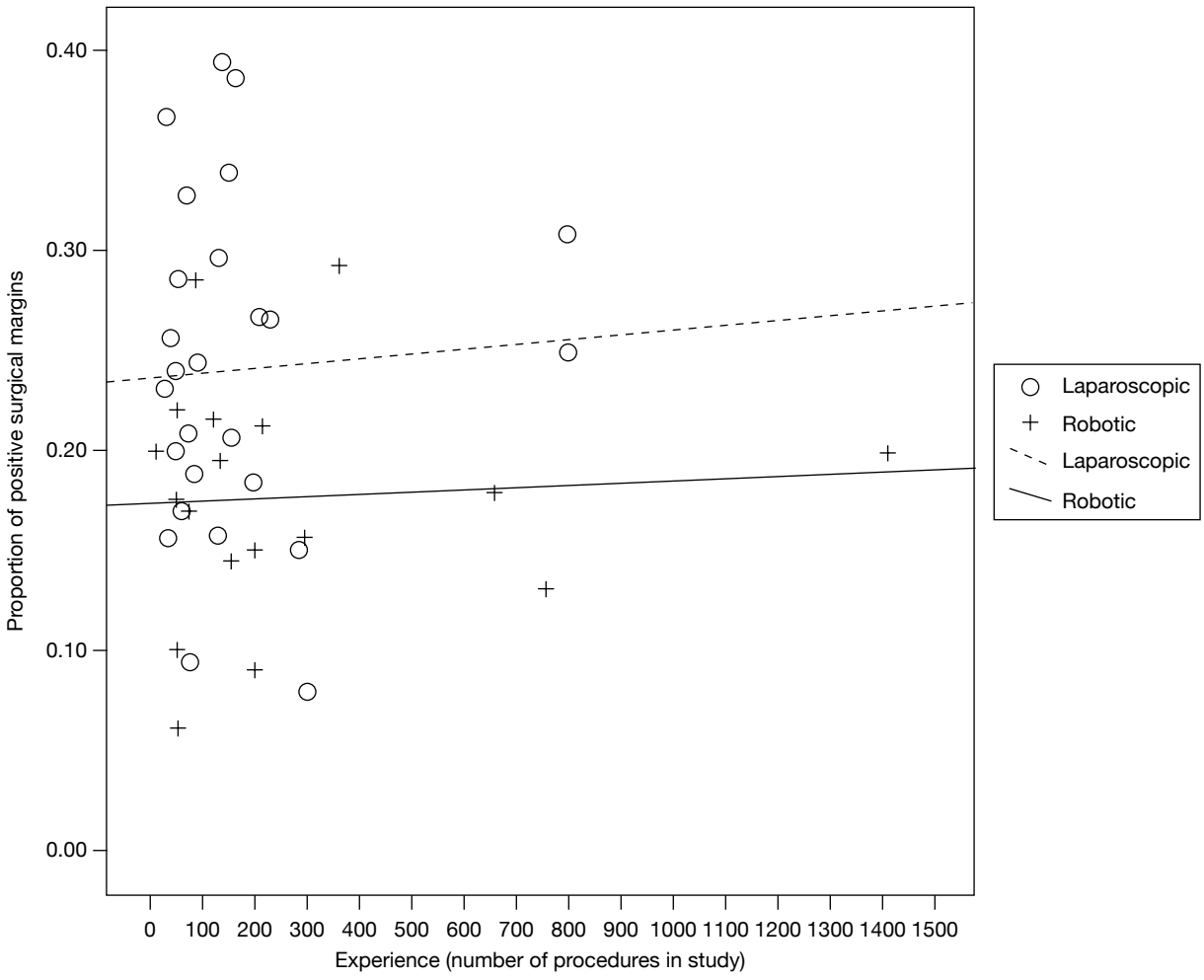

FIGURE 12 Proportion of positive surgical margins with increasing experience in included studies.

TABLE 21 Summary of learning curve measures in case series

Study	Reported outcomes/ measures	Number of cases	Robotic	Laparoscopic	Other information reported in study
Secin 2010[158]	Margin rate	6274		Case 1: 24% Case 250: 9%	
Hong 2010[155]	Margin rate	469	Case 1: 27% Case 200: 25% Case 400: 21%		Linear trend
Tewari 2010[154]	Margin rate	1340	Case 1: 9% Case 100: 7%		
McNeill 2010[156]	Margin rate	300		Case 1–50: 27% Case 251–300: 14.7%	Log-linear trend
	Operation time			Case 1: 200 minutes Case 200: 140 minutes	
	Complications			Case 1: 29% Case 250: < 1%	
Samadi 2010[159]	Margin rate	1181	Case 1: 8.5% Case 590: 4.3%		
Rodriguez 2010[160]	Margin rate	400		Case 1: 32% Case 400: 13.3%	
Jaffe 2009[161]	Margin rate	278	Case 1–12: 58% Case 12–189: 23% Case 278: 9%		
	Operation time		Case 1–12: 250 minutes Case 12–189: 165 minutes Case 278: 134 minutes		
Eden 2009[157]	Margin rate	1000		Series average: 13.3%	No trend noted
	Complications				No trend noted
	Blood loss			Series average: 200 ml	Stabilised after 200 cases
	Potency			Case 1: 23% Case 1000: 86%	Stabilised after 700 cases
	Operation time			Series average: 177 minutes	Stabilised after 200 cases
Vickers 2009[162]	Biochemical recurrence	4702		Case 10: 16% Case 250: 15.5% Case 750: 8.2%	
Martinez-Pineiro 2006[163]	Margin rate	604			Decreased significantly by 101 cases
	Blood transfusion			Case 1: 25% Case 600: 7%	Stabilised by 200 cases
	Operation time			Series average: 201 minutes	

evidence that a non-linear (logarithmic) relationship with increasing experience fitted the data better than a linear relationship; however, this was not statistically significant (log-experience –0.02; 95% CI –0.043 to 0.003; $p = 0.08$). This equated to an average surgical margin rate of 25.6% at case one, reducing to 14.5% by 250 cases and 11.7% by 1000 cases. The data provided

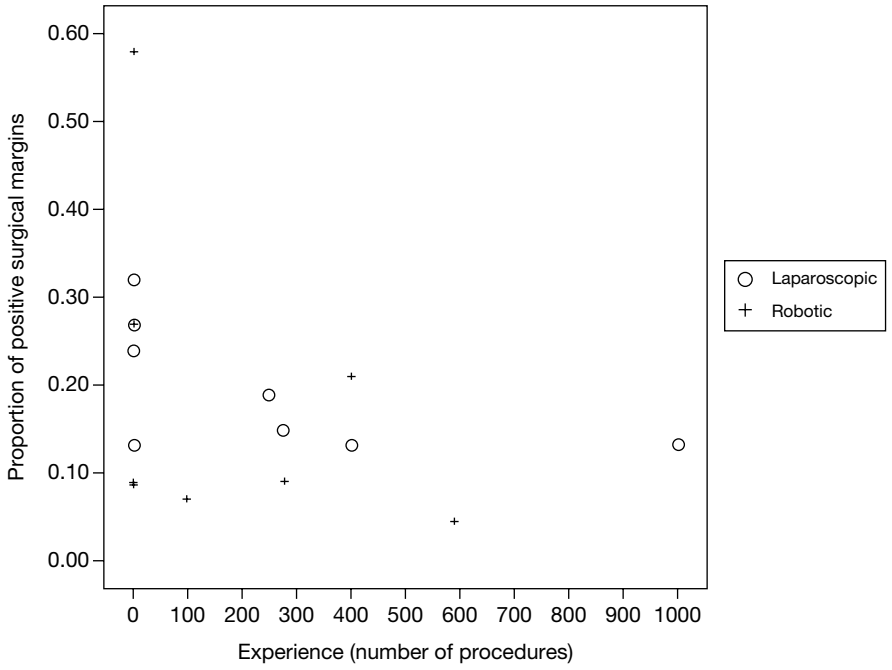

FIGURE 13 Proportion of positive surgical margins with increasing experience in case series.

no evidence that learning contributed differently to positive margin rates between the two procedures (mean difference in level –0.02; 95% CI –0.16 to 0.12; $p = 0.755$).

To summarise the results, the two approaches to assessing whether or not surgeon learning affected the rate of positive margins gave conflicting findings. Across the studies included in the meta-analyses of positive margin rates, there was no evidence that experience contributed as a significant confounder to the results, whereas the larger case series suggested a reduction over time in positive margin rates. There was no empirical evidence, however, that the rate of learning differed between the two surgical procedures. Caution is therefore required in the interpretation of these findings.

Summary and conclusions of the evidence of comparative effectiveness

This review considered data from 19,064 patients across one RCT and 53 non-randomised comparative studies with very few studies considered at low risk of bias. Results should be interpreted cautiously to reflect the poor quality of the evidence base and the variation in definitions of outcomes. It was noteworthy that, when meta-analyses were restricted to studies assessed to be at low risk of bias, the effect sizes tended to move from favouring robotic prostatectomy towards no difference. There were limited published data on long-term efficacy of robotic and laparoscopic radical prostatectomy in reducing morbidity and no data comparing mortality from prostate cancer. We found no evidence for any difference in patient-reported outcomes. There was strong statistical evidence that positive surgical margin rates, a proxy measure for cancer control, may be reduced by the use of robotic radical prostatectomy; however, it was unclear in the literature how these differences impact on cancer recurrence and long-term efficacy outcomes and restricting the analysis to low risk of bias studies showed no statistical evidence of a difference. This finding should therefore be interpreted with caution. In addition, the studies showed variation in the pathology protocols employed, which may have biased the

determination of positive margin status and prevented accurate comparison between studies. Improvement in reporting pathology findings is necessary if evidence syntheses across studies are to be undertaken. The recent ISUP Consensus Conference[72] aims to promote consistency in the handling and reporting of radical prostatectomy specimens and provide detailed guidelines that are feasible for most practising pathologists to implement and may be a major advance towards providing more comparable data in the published literature.

There was a general trend for robotic surgery to have fewer perioperative adverse events, apart from rarely reported deep-vein thrombosis, and the differences reached statistical significance for anastomotic leak and organ injury in particular, and those classified as Clavien IIIb in general. There were limited data on the important longer-term functional adverse effects of urinary incontinence and erectile dysfunction. The available data suggested no evidence of a difference in the proportion of men suffering urinary incontinence at 12 months. There were insufficient data to draw any conclusions on the likely size of any differential effect on rates of erectile dysfunction.

There was conflicting evidence on the impact of the learning curve for both procedures. There was no evidence that experience contributed as a significant confounder to the meta-analysis results, but case series data suggested a reduction over time in positive margin rates. There was, however, no empirical evidence that the rate of learning as expressed by changes in positive margin rates differed between the two surgical procedures and therefore little support for including the learning curve relationship in the base-case economic model.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Figure 14*. This should be interpreted in light of the comments made earlier in the chapter.

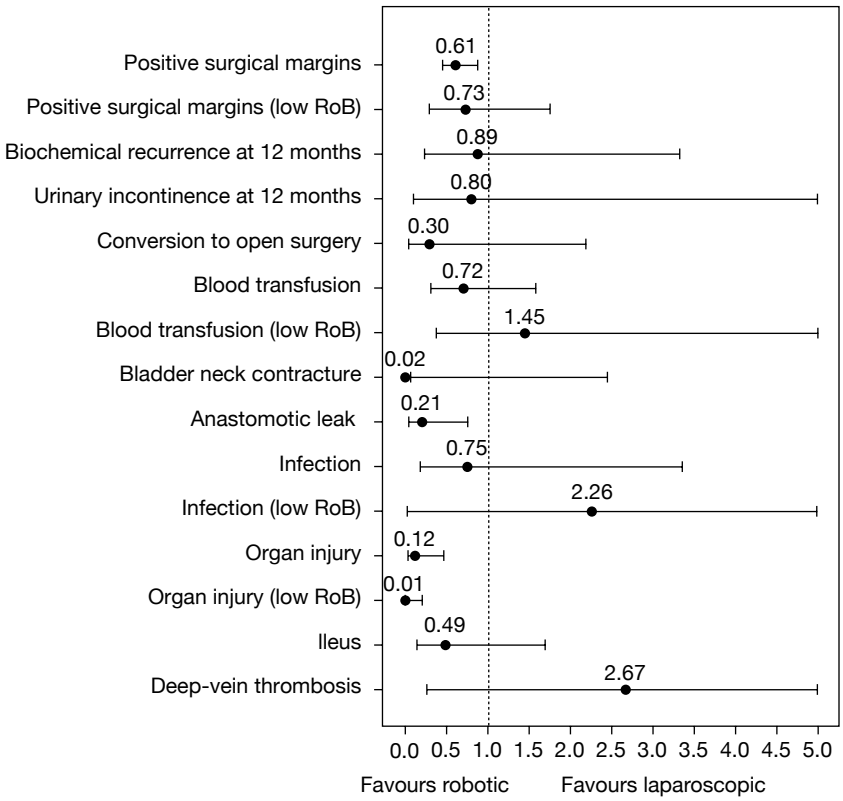

FIGURE 14 Summary of the clinical effect sizes (ORs and 95% CrIs) from meta-analyses. To improve visual display the upper CrI has been truncated to 5.0. Low RoB denotes estimate from low risk of bias studies only.

Chapter 5

Methods for health economic evaluation

Introduction

In this chapter we report the methodology and parameter value selection for a health economic evaluation comparing robotic radical prostatectomy with laparoscopic radical prostatectomy. This economic evaluation was conducted using a discrete-event simulation model described in detail in subsequent sections. This represents a change to the modelling specified in the original protocol. This change was required to account for the degree of complexity encountered while defining the treatment care pathways.

The original study protocol (see *Appendix 1*) specified the use of a Markov state transition model in order to explore aspects of heterogeneity within cohorts undergoing treatment for localised prostate cancer. Once the treatment care pathways were defined, however, it became clear that the use of a state transition model would be impracticable for several reasons:

1. The number of potential health states and their transitions was large.
2. The discrete-event model explicitly included multiple adverse events that may occur during progression along the care pathway trajectory while also accounting for potential feedback to one or more previous states within the care pathway. Inclusion of multiple event states would necessitate very large transition matrices.
3. The study required a modelling approach that would provide a high degree of flexibility in modelling interconnected care processes while also accounting for heterogeneity in the populations modelled. In addition, the discrete-event simulation adopted allows the incorporation of interdependent and simultaneously occurring health events and internal feedback loops, a characteristic found within the treatment care pathways. These would be difficult to achieve using a Markov-type approach; this is an important limitation of decision tree-based approaches. The approach adopted also provided more detailed reporting of each individual's journey through the disease trajectory.

Before conducting the economic evaluation we attempted to identify and summarise any existing economic evaluations on this topic systematically (see the following section). The economic evaluation itself involved several stages, described later in this chapter.

Systematic review of previous economic evaluations

We searched for economic evaluations comparing both costs and outcomes of the two surgical procedures systematically. To be included studies had to include costs and effects, regardless of the way that each were estimated. We found no economic evaluations that fully met the inclusion criteria (see *Appendix 11*). Three publications were identified that reported cost comparisons between robotic and open radical prostatectomy,[164–166] five publications reported cost comparisons between laparoscopic and open radical prostatectomy[121,167–170] and three publications reported cost comparisons between robotic and laparoscopic surgery.[171–173] The publications by Bolenz and colleagues[171] and Lotan and colleagues[172] estimated the procedure costs of robotic and laparoscopic prostatectomy for a USA setting based on a retrospective patient cohort and a

hypothetical costing exercise respectively. In both cases, excluding the capital cost of the robotic system, robotic prostatectomy was $500–700 more expensive per case than laparoscopic surgery. Bolenz and colleagues[171] reported that the additional purchase and maintenance costs of a single robotic da Vinci system were $340,000 per year, while Lotan and colleagues[172] reported that, assuming 300 cases per year, the cost of purchase plus maintenance costs were an additional $857 per case. Following a financial appraisal, again conducted in a USA setting, Steinberg and colleagues[173] concluded that robotic prostatectomy was not financially viable in low-volume centres performing fewer than approximately 80 procedures per year under current tariffs. Although the method used to establish procedure costs in these three papers was clear, none considered costs beyond the hospital period and none attempted to compare procedures in terms of both costs and outcomes. Although the paucity of the evidence base was anticipated at the outset of the study, the results of this systematic attempt to identify relevant economic evaluations have highlighted the need for the economic evaluation that is reported in this monograph.

Methods

Model specification: purpose and design

The purpose of this model was to simulate the outcomes and costs during and following a radical prostatectomy procedure using either a robotic or laparoscopic technique performed in an appropriate UK NHS hospital on a man with clinically apparent localised prostate cancer.[43] The model was specified to follow the predefined care pathway for individual men for 10 years from the time of surgery, this being the anticipated duration of use of the current robotic technology under study (Intuitive Surgical, June 2010, personal communication). We also included as a sensitivity analysis the ability to specify the model over the lifetime of the individual, consistent with the epidemiological characteristics of localised prostate cancer, which typically has a long natural history with survival benefits for radical treatment needing at least 10–15 years to accrue.[44]

We selected an individual-based event model in which surgical procedure, steps in the care pathway, the occurrence of longer-term adverse events and ultimately death are modelled as discrete events for individuals within the model.[174] The transition of individual men between events was driven by the previous health states, processes involved in their clinical treatment and subsequent care that arose as a consequence of the surgery, the underlying disease and natural lifespan. These included adverse events associated with the prostatectomy, events during clinical management of individuals who were cured of prostate cancer by the surgery and events driven by disease persistence or recurrence following prostatectomy. The clinical characteristics of individuals entering the simulation could be varied to represent the complete spectrum of patient and disease characteristics among the overall population of men with localised prostate cancer requiring radical prostatectomy. Each event and each subsequent patient management decision at all decision points in the pathway was modelled probabilistically based on available data relevant to patient care in the UK NHS. The hierarchy of data sources used was in the order of the associated systematic review, available relevant literature including web-based sources and consultation with relevant experts. The model was parameterised using data obtained from these sources describing disease progression, survival and the prevalence of adverse events. Data on costs to the UK NHS of laparoscopic and robotic prostatectomy were predominantly obtained directly from the manufacturer of the robotic system, Intuitive Surgical,[30] and from national and local NHS sources (see *Costs*). To enable analysis of cost-effectiveness, utility values for the various health states within the care pathway were obtained from the literature (see *Utilities*). The model was constructed using the scripting language available for the R statistical package for computing.[175]

State variables and timescales

State variables

Postoperatively each individual was assigned a combination of eight state variables. The first was age at the time of surgery. This was simulated by drawing a random deviate from a triangular distribution with minimum, peak and maximum shape parameters derived respectively from the 25th percentile, median and 75th percentile of the age distribution of men undergoing radical prostatectomy. The age range for each intervention was identical.

Four variables specified individual disease characteristics following pathological examination of the removed prostate:

- surgical margin: negative or positive
- tumour stage: pT0–T2 or pT3–pT4
- Gleason sum score: ≤ 7 or 8–10
- lymph node status: unknown, negative or positive.

Three variables indicated adverse events arising from prostatectomy that would not be resolved in the 3-month treatment phase:

- bladder neck contracture (stenosis): absent or present
- urinary incontinence (moderate or severe): absent or present
- erectile dysfunction (bothersome to individual): absent or present.

Time step

The modelled time step (cycle length) was a quarter (3 months). For variables for which only annual data could be obtained the probabilities were converted to a standard time base of a quarter using *Equation 1*:

$$P' = 1 - \left((1 - P)^{1/4} \right) \qquad \text{[Equation 1]}$$

where P is the yearly probability of an event occurring and P' is the probability of an event occurring in a 3-month period.

Time horizons

The base-case time horizon for the model was 10 years, this being consistent with the anticipated duration of use of the current technology under test – the da Vinci surgical robotic system. A longer time horizon (40 years) that would cover the expected lifetime of the men included in the model was also used, consistent with the epidemiology of localised prostate cancer.[176]

Assumptions within the model

Modelled events at each decision point within the pathway were discrete and independent. For example, surveillance for biochemical recurrence was simulated in the same way irrespective of events previously experienced by the individual. In the absence of suitable data the probability of further biochemical recurrence was independent of previous biochemical recurrences that had been successfully treated. In practice, care options inevitably are affected by previous disease characteristics and other related events, but the multitude of possibilities of care for particular individuals during the course of their cancer care subsequent to radical prostatectomy could not be fully parameterised in the model in the absence of sufficiently detailed individual-level data sets. Proportions of individuals undergoing different procedures within the care pathway were defined by the probability of being assigned to those procedures. This simplification was necessary because of the lack of data on the underlying causal factors leading to events; they were therefore modelled as random processes (see *Modelling of discrete events*).

The imprecision/uncertainty surrounding parameter estimates used within the model was characterised by assigning statistical distributions to parameters. For parameter estimates provided by the systematic review, the log-normal distribution was used to define the degree of surrounding uncertainty. Other parameters derived from the literature or other sources were considered for accuracy, credibility and plausibility at meetings of the expert panel. Identifying a suitable distribution for estimates and describing the uncertainty around these values was problematic. In such circumstances, uncertainty was calculated as a potential range of plausible values of ±25% of the estimate.

For parameters not defined by the systematic review we assumed that the point estimate was the most likely 'real' value and therefore did not consider that a uniform rectangular distribution was appropriate. Furthermore, by defining the extreme limits of the distribution using the triangular method (as described above) we ensured that the upper and lower bounds of variability did not exceed clinical plausibility. And finally, the way in which variability was calculated ensured that the degree of uncertainty applied to each intervention equally.

Modelling the care pathway

Following robotic or laparoscopic prostatectomy each individual was entered into the specific pathway dictated by his clinical and disease state after the operation (*Figure 15*). This state was characterised in terms of, first, cancer status and, second, the presence of one or more of the three adverse events that were deemed to persist beyond the treatment period: bladder neck contracture, urinary incontinence and erectile dysfunction. The individuals then proceeded through a series of events dependent on where they were in the care pathway and which would result in changes to, or resolutions of, differing health states. This would particularly include remission or relapse following additional treatment for recurrent prostate cancer or resolution of a longer-term adverse event by treatment.

Events were modelled probabilistically using data derived from the hierarchy of sources defined previously in *Model specification: purpose and design*. Where possible the data used were relevant to both the clinical context of radical prostatectomy and current practice in the UK NHS.[43] Parameters, their values, their distributions and their sources are listed in abbreviated form in the relevant sections. Events experienced by individuals were scheduled in interacting 'streams'. Surveillance, cancer treatment and mortality were first simulated either until the end of the time horizon if the individual survived or until a process within the care pathway led to death either from prostate cancer or from any other cause (see *Figure 15*). This provided the framework for each individual's trajectory through the cancer care pathway. The second set of events simulated the management of the three postoperative dysfunctions: bladder neck contracture, urinary incontinence and erectile dysfunction. If a process led to an intervention event, such as surgery for urinary incontinence, this was scheduled only after at least 12 months of surveillance without a cancer-related event.

Modelling of discrete events

All events were assumed to be binomial in the sense that an event either occurred, 1, or did not occur, 0. Simulation of the occurrence of an event for an individual was undertaken by drawing random uniform deviates and comparing the observed deviate with the known probability of that event occurring given the relevant conditions. Thus, if x represents the proportion of men who experienced bothersome erectile dysfunction after laparoscopic prostatectomy, any random deviate drawn for an individual that was less than x would lead to that individual suffering the dysfunction and progressing down the appropriate pathway of care, whereas any deviate greater than x corresponded to no dysfunction. The proportion of men experiencing each event in each pathway was derived where possible from the systematic review reported in detail in *Chapter 4*. Other relevant literature or expert opinion were used where necessary.

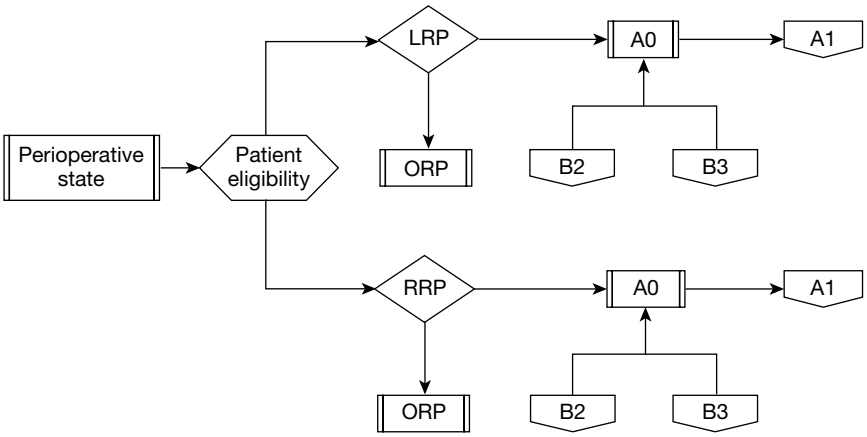

FIGURE 15 Schematic showing care pathway for the perioperative state during and immediately after radical prostatectomy. A0, perioperative health state; A1, postoperative health state; B2, surgeon learning effect; B3, perioperative complication classified using the Clavien–Dindo system; LRP, laparoscopic radical prostatectomy; ORP, open radical prostatectomy; RRP, robotic radical prostatectomy.

Model health states and associated parameter values

Perioperative state

In line with the objective of this HTA all patients were assumed to have undergone radical prostatectomy by either laparoscopic or robotic means (see *Figure 15*). In addition, those individuals deemed to be at intermediate or high risk of early biochemical recurrence according to preoperative disease characteristics (*Table 22*) were allocated to undergo a concurrent pelvic lymph node dissection; the probability of this was defined from an appropriate additional literature source[177] as the information was not available from the systematic review. Adverse events during surgery could initiate two further model events. First, the probability of suffering perioperative adverse events, categorised using systematic review data according to the Clavien–Dindo system into one of six levels, was defined as the proportion of patients who suffered that event[68,69] (*Figure 16*). Second, and independently of adverse events categorised by the Clavien–Dindo system, a proportion of men undergoing laparoscopic or robotic prostatectomy were deemed to require conversion to an open procedure because of intraoperative difficulties. The rate for each of the procedures was determined from the systematic review and the consequence in terms of costs was defined as an extra 3-day hospital stay, decided by expert opinion (see *Table 22*).

For each specific Clavien–Dindo level or adverse event the associated financial cost was modelled solely through the extra duration of hospitalisation measured in days that a patient would require according to expert opinion (*Table 23*). These events were assumed to have resolved during the 3-month perioperative state.

Postoperative state

Immediate further cancer treatment

A proportion of men were assigned to require and undergo immediate further cancer treatment; the probability of this occurring was defined according to the findings of the systematic review, other literature sources and consensus of expert opinion (*Table 24*). First, men who had undergone pelvic lymphadenectomy as part of their radical prostatectomy and were found to have lymph node metastases on pathological examination of the removed lymph nodes were automatically selected for immediate further treatment.[178] The proportion of men who underwent lymphadenectomy and the proportion of those who were positive were assigned independently from other variables according to the observed rates following either type of surgery from

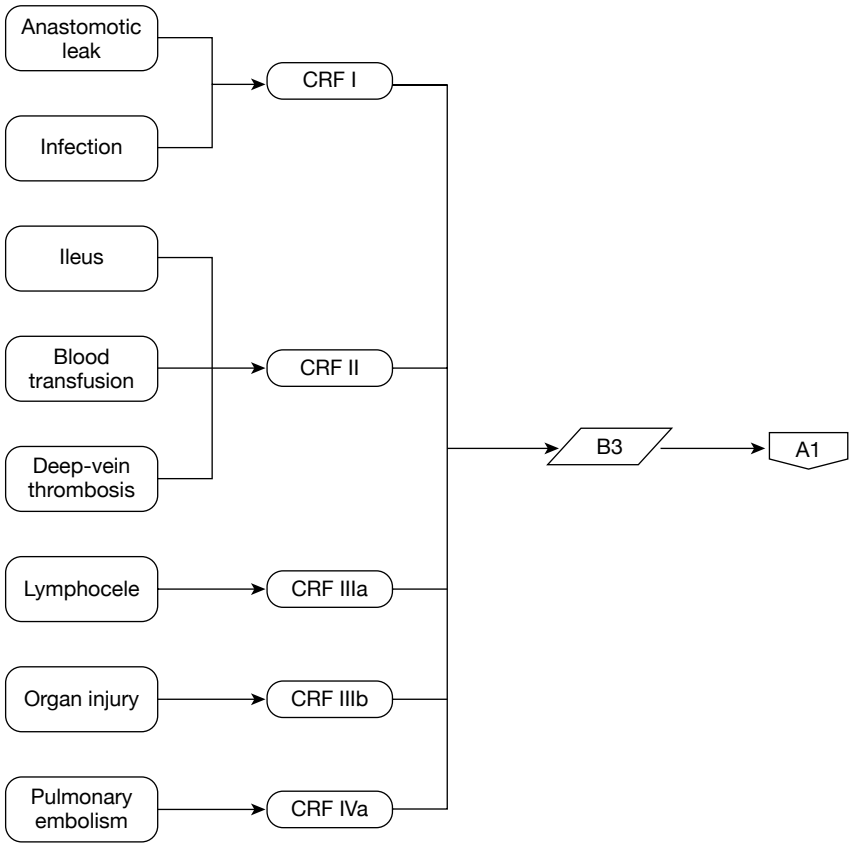

FIGURE 16 Flow chart illustrating the classification of various intraoperative adverse events using the Clavien–Dindo system for the grading of operative complications and their input into the perioperative care pathway. A0, perioperative health state; CRF, Clavien–Dindo risk factor; B3, perioperative complication categorised by the Clavien–Dindo system.

literature sources validated by our expert panel.[177,179] Expert opinion deemed that all men with positive lymph nodes were assigned to further cancer treatment without the opportunity for a period of surveillance.

Second, men who had *two or more* of the following features found on pathological examination of the removed prostate were considered for immediate further treatment:

- positive surgical margin
- Gleason score 8–10
- tumour stage pT3–pT4.

If *only one* of these pathological disease characteristics was present the individual entered the surveillance pathway (*Figure 17*).

Parameterisation of this decision-based approach required linked data for individuals concerning the three features and this was not available from the systematic review. We therefore decided on the following approach. Linked values of postoperative Gleason sum score and postoperative tumour stage for 4669 individuals were kindly provided from a large single institutional database of men undergoing radical prostatectomy maintained at the Vanderbilt-Ingram Cancer Center, TN, USA (D Barocas, February 2011, personal communication). The numbers of men from this data set with each combination of Gleason sum score and tumour stage were then multiplied by the probability of men having a negative or positive surgical margin following robotic or laparoscopic prostatectomy defined by the systematic review and meta-analysis (see *Table 24*).

TABLE 22 Parameter values with distributions and sources for the perioperative state for individuals undergoing robotic or laparoscopic prostatectomy

Perioperative state	Value	Probability	Interquartile range	Assigned distribution	Source
Robotic surgery					
Age (years)	61.5		39–74	Triangular	Systematic review
Rate of pelvic lymphectomy (%)	58.20		43.65–72.75	Triangular	Sharma 2011[177]
Conversion to alternative surgical technique (%)	0.3		0.03–2.16	Triangular	Ollendorf 2010[2]
Operative time (minutes)	225			NA	Systematic review
Clavien risk factor I	1	0.021	0.006–0.064	Log-normal	Systematic review
Clavien risk factor II	2	0.039	0.016–0.064	Log-normal	Systematic review
Clavien risk factor IIIa	3	0.005	0.000–0.033	Log-normal	Systematic review
Clavien risk factor IIIb	3	0.009	0.002–0.033	Log-normal	Systematic review
Clavien risk factor IVa	4	0.006	0.001–0.027	Log-normal	Systematic review
Clavien risk factor V (death)	5	1.39×10^{-19}	1.22×10^{-61}–1.60×10^{-20}	Log-normal	Systematic review
Laparoscopic surgery					
Age (years)	63		43–76	Triangular	Systematic review
Rate of pelvic lymphectomy	58.94%			43.7–72.8% (triangular)	Sharma 2011[177]
Conversion to alternative surgical technique	0.009%			0.000–0.018 (triangular)	Ollendorf 2010[2]
Operative time (minutes)	237.5			N/A	Systematic review
Clavien risk factor I	1	0.041		0.000–0.167 (log-normal)	Systematic review
Clavien risk factor II	2	0.072		0.019–0.143 (log-normal)	Systematic review
Clavien risk factor IIIa	3	0.013		0.000–0.077 (log-normal)	Systematic review
Clavien risk factor IIIb	3	0.036		0.010–0.160 (log-normal)	Systematic review
Clavien risk factor IVa	4	0.008		0.000–0.039 (log-normal)	Systematic review
Clavien risk factor V (death)	5	0.002		0.0004–0.0023 (log-normal)	Systematic review

NA, not applicable.

TABLE 23 Care consequences in terms of increased length of stay according to level of perioperative complication

Clavien–Dindo category	Number of additional bed-days
I	1
II	2
IIIa	3
IIIb	3
IVa	4
V	NA (results in death)
Conversion to open procedure	3

NA, not applicable.

The calculated patient numbers were then converted to percentages of the sample population, which defined the probability of each combination of the three variables (margin, Gleason sum score and tumour stage) for each procedure. These probabilities were then mapped to the decision matrix. The decision matrix, which directed the subsequent care pathway for individual men in the model, was formulated by rounds of consensus building with relevant members of the expert panel. The decision to be made was whether men would enter the surveillance

TABLE 24 Parameter values (base case) with distributions and sources for lymph node metastases (for men undergoing pelvic lymphadenectomy) and positive margin status (all men)

Perioperative state	Probability	Lower limit[a]	Upper limit[a]	Assigned distribution	Source
Robotic surgery					
Positive margin	0.163	0.119	0.225	Log-normal	Systematic review
Lymph node metastases	0.026	0.0195	0.0325	Triangular	Kawakami 2006[179]
Laparoscopic surgery					
Positive margin	0.236	0.080	0.394	Log-normal	Systematic review
Lymph node metastases	0.026	0.0195	0.0325	NA	Kawakami 2006[179]

NA, not applicable.
a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate. Upper and lower limits of log-normal distribution set at 95% CI.

TABLE 25 Immediate further cancer treatment matrix for individuals following robotic prostatectomy according to findings on pathological examination of the removed prostate

Margin status	Tumour stage	Gleason score	Number (%) of men in category	Probability of event in model	Management decision
Negative	Negative	Negative	2900 (62.1)	0.621	Surveillance
Negative	Negative	Positive	132 (2.8)	0.028	Surveillance
Negative	Positive	Negative	612 (13.1)	0.131	Surveillance
Negative	Positive	Positive	264 (5.6)	0.056	Treatment
Positive	Negative	Negative	565 (12.1)	0.121	Surveillance
Positive	Negative	Positive	26 (0.6)	0.005	Treatment
Positive	Positive	Negative	119 (2.6)	0.026	Treatment
Positive	Positive	Positive	51 (1.1)	0.011	Treatment

Margin status: negative/positive; tumour stage: negative pT1–pT2, positive pT3–pT4; Gleason score: negative ≤ 7, positive 8–10.

TABLE 26 Immediate further cancer treatment matrix for individuals following laparoscopic prostatectomy according to findings on pathological examination of removed prostate

Margin status	Tumour stage	Gleason score	Number (%) of men in category	Probability of event in model	Management decision
Negative	Negative	Negative	2647 (56.7)	0.567	Surveillance
Negative	Negative	Positive	121 (2.6)	0.026	Surveillance
Negative	Positive	Negative	558 (12.0)	0.120	Surveillance
Negative	Positive	Positive	241 (5.2)	0.052	Treatment
Positive	Negative	Negative	818 (17.5)	0.175	Surveillance
Positive	Negative	Positive	37 (0.8)	0.008	Treatment
Positive	Positive	Negative	173 (3.7)	0.037	Treatment
Positive	Positive	Positive	74 (1.6)	0.016	Treatment

Margin status: negative/positive; tumour stage: negative pT1–pT2, positive pT3–pT4; Gleason score: negative ≤ 7, positive 8–10.

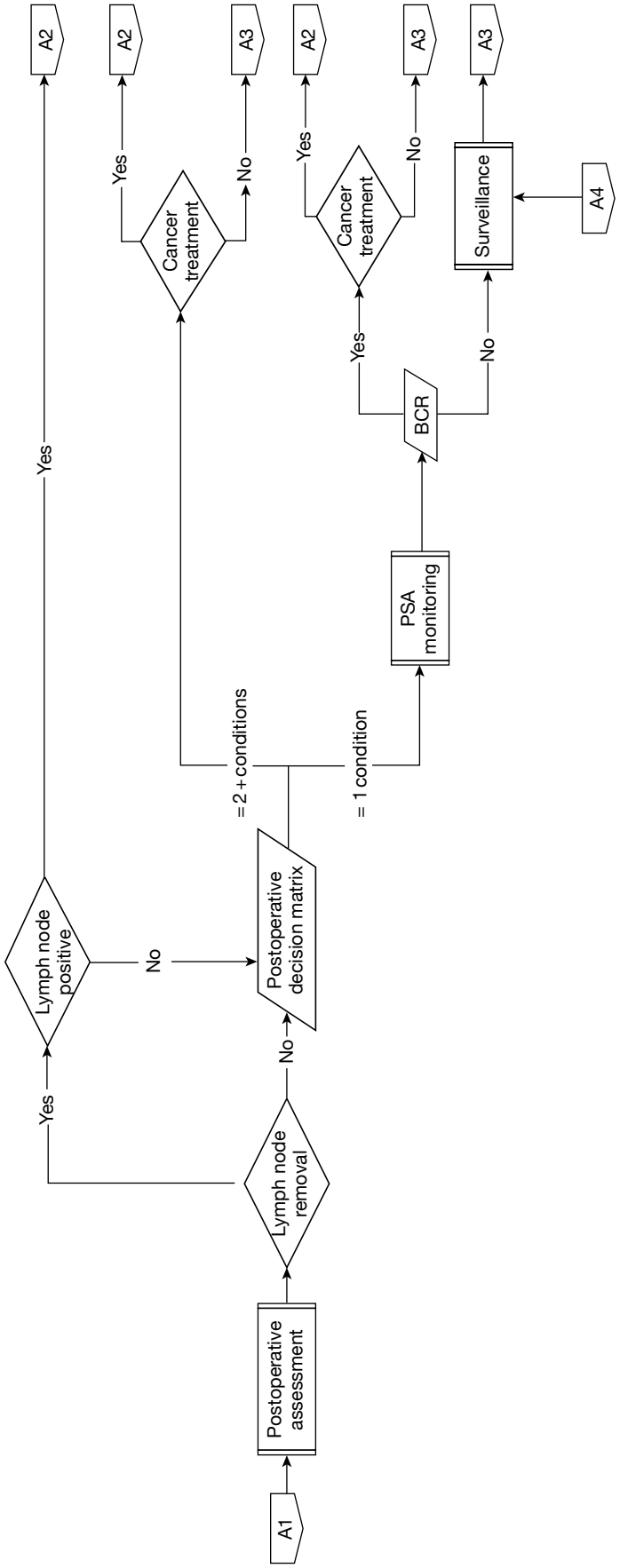

FIGURE 17 Schematic representation of postoperative care pathway for men being considered for immediate further cancer treatment. A1, postoperative health state; A2, further cancer treatment state; A3, long-term adverse event dysfunction state; A4, surveillance state; BCR, biochemical recurrence.

state or proceed to further cancer treatment (*Tables 25* and *26*). The decision matrix gave total probabilities of 0.098 following robotic prostatectomy and 0.113 following laparoscopic prostatectomy for individual men requiring consideration for immediate further treatment.

Death due to causes other than prostate cancer

The age-related quarterly probability of non-prostate cancer-related mortality was obtained from actuarial tables published by the UK Office for National Statistics[180] and was treated as a separate event from prostate cancer-related mortality.

Biochemical recurrence

The probability of biochemical recurrence was calculated for each 3-month time step according to the time since either prostatectomy or the most recent localised cancer event for men successfully treated for recurrent localised cancer by radical radiotherapy. The 12-month probability of biochemical recurrence was derived from the systematic review and then was assumed to decline exponentially according to published longer-term data (*Table 27*).[181] As described later, the use of selected alternative values for biochemical recurrence was explored in a sensitivity analysis.

At each decision point the individual would continue surveillance without recurrence or experience a biochemical recurrence leading to further treatment or die from causes other than prostate cancer. In base-case simulations with a 10-year time horizon an individual could remain in the surveillance state or else be in a recurrence state at the end of the simulation and would be recorded as surviving without or with recurrent cancer respectively. If biochemical recurrence occurred, this was recorded before initiating the further cancer treatment process. Each time step that an individual spent under surveillance incurred a utility and a cost (described in *Costs* and *Utilities*).

TABLE 27 Parameter values with distributions and sources for the further cancer treatment state for all individuals in the model

Variable	Value	Probability (quarterly)	Lower limit[a]	Upper limit[a]	Assigned distribution	Source
Biochemical recurrence rate						
Biochemical recurrence event rate 1 year	4.9%	0.0125	0.0094	0.0156	Triangular	Menon 2010[181]
Biochemical recurrence event rate 3 years	9.4%	0.0109	0.0082	0.0136	Triangular	Menon 2010[181]
Biochemical recurrence event rate 5 years	13.4%	0.0095	0.0072	0.0119	Triangular	Menon 2010[181]
Biochemical recurrence event rate 7 years	18.9%	0.0099	0.0074	0.0124	Triangular	Menon 2010[181]
Further cancer treatment						
Radiotherapy	20.0%	NA	0.150	0.250	Triangular	Moreira 2010[182]
Androgen deprivation therapy	21.0%	NA	0.158	0.263	Triangular	Moreira 2010[182]
Combined treatment	10.0%	NA	0.075	0.125	Triangular	Moreira 2010[182]
Surveillance	49.0%	NA	0.368	0.613	Triangular	Moreira 2010[182]
Prostate cancer mortality						
Cancer-specific survival	NA	0.76	0.69	0.83	Triangular	Bria 2009[183]
Overall survival	NA	0.86	0.80	0.93	Triangular	Bria 2009[183]

NA, not applicable.
a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate.

Cancer treatment allocation

Men with pathologically involved lymph nodes or with two or more adverse pathological characteristics listed earlier were immediately assigned to the cancer treatment process following prostatectomy (*Figure 18*). The extent of the likely residual disease was defined as localised or systemic (metastatic) and this was randomly determined according to known probabilities using the same method described in *Modelling of discrete events*; this was independent of the precise cancer state variables (see *Table 27*). A similar process was used for men who underwent an initial period of surveillance and then suffered biochemical recurrence.

Localised cancer treatment

Diagnosis of persistent or recurrent cancer localised to the prostatic bed was an event with three outcomes. First, further cancer treatment in the form of radical radiotherapy with or without a 6-month course of androgen deprivation therapy could be successful, resulting in the remission event; these men then returned to the surveillance process. Second, further cancer treatment could be unsuccessful, leading to metastases, further treatment for systemic cancer by lifelong androgen deprivation therapy and cancer-related death. The probability of either of these two events was determined by survival rates from the literature concerning radical radiotherapy used to treat localised recurrence after prostatectomy (see *Table 27*). Finally, the individual could suffer non-prostate cancer-related mortality before completing treatment. For the base-case simulation individuals could be in the further cancer treatment state at the end of the 10-year period and were considered to be survivors with prostate cancer recurrence. The time from further cancer treatment and remission or cancer-related death was randomly determined according to rates of survival obtained from the literature.

Systemic (metastatic) cancer treatment

Diagnosis of systemic cancer was an event occurring because of unfavourable disease characteristics such as positive lymph nodes in the immediate postoperative period or because of failure of radical radiotherapy for localised recurrence or following the process of biochemical recurrence. Such men were treated with androgen deprivation therapy (medical castration) until cancer-related death, the only outcome possible. In the base-case simulation with a 10-year time horizon it was possible for men to survive if they remained in the systemic cancer treatment state at the end of the 10 years; the duration of survival while on treatment for systematic cancer was randomly determined according to known metastatic prostate cancer mortality rates (see *Table 27*).

Persistent adverse event states

Introduction

The incidence of the considered postoperative adverse events or dysfunctions – bladder neck contracture, urinary incontinence and erectile dysfunction – was defined according to the

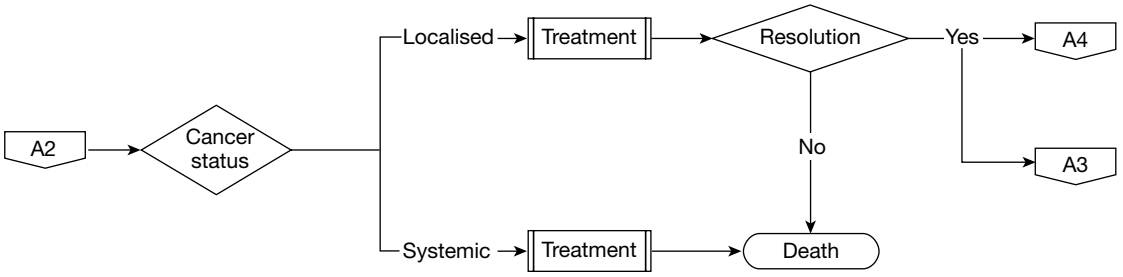

FIGURE 18 Schematic diagram for the further cancer treatment care pathway. A2, cancer treatment health state; A3, long-term adverse event dysfunction health state; A4, surveillance health state.

standard parameterisation hierarchy described above. Management of these postoperative dysfunctions was modelled by treating them as independent processes. If dysfunctions were found to be present, self-management and/or treatment began immediately according to current clinical practice (*Figures 19* and *20*). Each of the three dysfunction-related state variables was recorded as a categorical variable encoding the presence or absence of the pathological condition. These three variables were randomly determined to be present according to the observed rates following either type of surgery defined by the systematic review, other literature source or expert opinion (*Table 28*). We assumed that there was no systematic co-occurrence of dysfunctions, so they were assigned independently. In this way it was possible for an individual to experience each dysfunction simultaneously.

Bladder neck contracture

All men who suffered bladder neck contracture (stenosis) were assumed to require treatment during the first quarter time step following radical prostatectomy. The intervention required was taken to be endoscopic bladder neck incision. This event incurred a one-off cost that was included in the first-year costs for that individual, and an appropriate utility value was assigned to the quarter during which the individual suffered the condition (see *Costs* and *Utilities*). Discussion within our expert group suggested that recovery was likely to occur in most cases following a single treatment and this was supported by the available literature.[70] For the purposes of the model we therefore chose to assume that recovery occurred after a single incision in all cases with no continuing costs and utility returned to that of the surveillance state. We acknowledge, however, that this is likely to be a simplification of day-to-day patient care.

Urinary incontinence

In the second quarter immediately following their prostatectomy, men with moderate or severe urinary incontinence commenced self-management using containment pads, which incurred a cost and was associated with a specific utility value every quarter. There were three outcomes allowed for this self-management: spontaneous recovery, further surgery consisting of insertion of an AUS, or a persistent state that remained until the end of the studied time horizon or the man's death and continued to accrue costs and associated disutility. The probability of the first two outcomes was assessed at each time step; if neither event occurred then the patient remained in a state of persistent incontinence. Men who recovered ceased to incur a cost and their utility was returned to that of the surveillance state. Men with persistent incontinence were eligible for insertion of an artificial sphincter as long as they had spent at least 12 months in the surveillance state since prostatectomy without biochemical recurrence, were not currently undergoing cancer treatment and had not previously undergone unsuccessful sphincter insertion. Surgical insertion of an artificial sphincter resulted in either recovery (success) or persistence (failure) of urinary incontinence according to published success rates of this surgery. The surgery incurred a one-off cost that was assigned to that year's total cost for the individual. We chose to assume that implantation of an artificial sphincter would continue to successfully resolve symptoms throughout the studied time horizon without the need for any further treatment of incontinence. The proportion of men suffering recurrent incontinence after initial successful implantation is approximately 25% at 5 years but given the low overall probability of need for this device and the

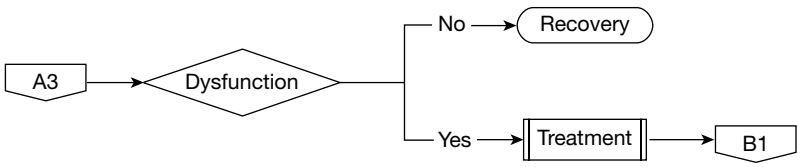

FIGURE 19 Schematic showing care pathway for individuals in long-term adverse event state with bladder neck contracture, urinary incontinence and erectile dysfunction. A3, adverse event state; B1, treatment of adverse event.

lack of difference in incontinence rates between the procedures under study we elected not to build this failure rate into our model.[184]

Erectile dysfunction

Immediately following prostatectomy men who suffered bothersome erectile dysfunction were assigned to either self-management or drug therapy, incurring extra costs if relevant and associated with a defined utility value every quarter. Costs for drug treatments were obtained from the *British National Formulary*[185] whereas cost information relating to surgical intervention was obtained from the Department of Health's reference costs 2008–9.[186] Self-management was defined as no active treatment. Men undergoing drug therapy were assumed to be taking either oral medication, with sildenafil (Viagra®, Pfizer Inc., USA) being the index drug, or intrapenile medication, with intracavernosal injection of alprostadil (Caverject®, Pfizer Inc., USA) being the index treatment. The rates of use of these options were obtained from relevant literature. There were three outcomes of both self-management and drug therapy: the man could recover, undergo surgical implantation of a penile prosthesis to cure erectile dysfunction or enter a persistent state of continued self-management or drug use that remained until the end of the time horizon or the man's death. The probability of the first two outcomes was assessed at each time step; if neither event occurred then the patient remained in a state of persistent erectile dysfunction. Men who recovered ceased to incur a cost and their utility returned to that of the cancer surveillance state. Individuals were eligible for penile prosthesis implantation if after at least 12 months of surveillance they did not have a biochemical recurrence, were not currently undergoing cancer treatment and had not already had a penile prosthesis implanted. Implantation of a penile prosthesis resulted in either recovery of erectile function or a persistent state, which was determined according to the success rates of this surgery published in the literature. The surgery incurred a one-off cost assigned to that year's total cost for the specific individual.

Costs

Perioperative costs

General

A general cost for the standard length of hospital stay was derived from the relevant excess NHS bed-day cost tariff for the procedure (LB22Z) of £255[186] multiplied by the average hospital stay for robotic/laparoscopic prostatectomy within the NHS of 3.48 days obtained from hospital episode statistics for 2008–9.[48] Hospital stay estimates from the systematic review were not used because they derived from a number of different heath-care systems. A cost per hour of NHS operating theatre time was derived from the baseline information calculated from General Hospital (Acute) obtained from ISD (Information Services Division) Scotland Theatre Services R140[193] (*Table 29*). This was then multiplied by the duration of laparoscopic and robotic prostatectomy derived from the systematic review (see *Table 22*). The cost of pathological examination of the removed prostate and lymph nodes of £329.82 was obtained from the Newcastle upon Tyne Hospitals NHS Foundation Trust (D Evans, May 2010, personal communication).

Equipment costs

The cost of undertaking one procedure using either intervention was obtained by adding together the basic unit cost of each surgical system, the cost of any specialised surgical equipment and the cost of any consumables. These costs were then adjusted for the lifetime of the equipment and by the number of cases performed per year to obtain a cost for each procedure. This cost did vary with the number of procedures performed in each centre per year, principally because the contribution of capital equipment costs was different.

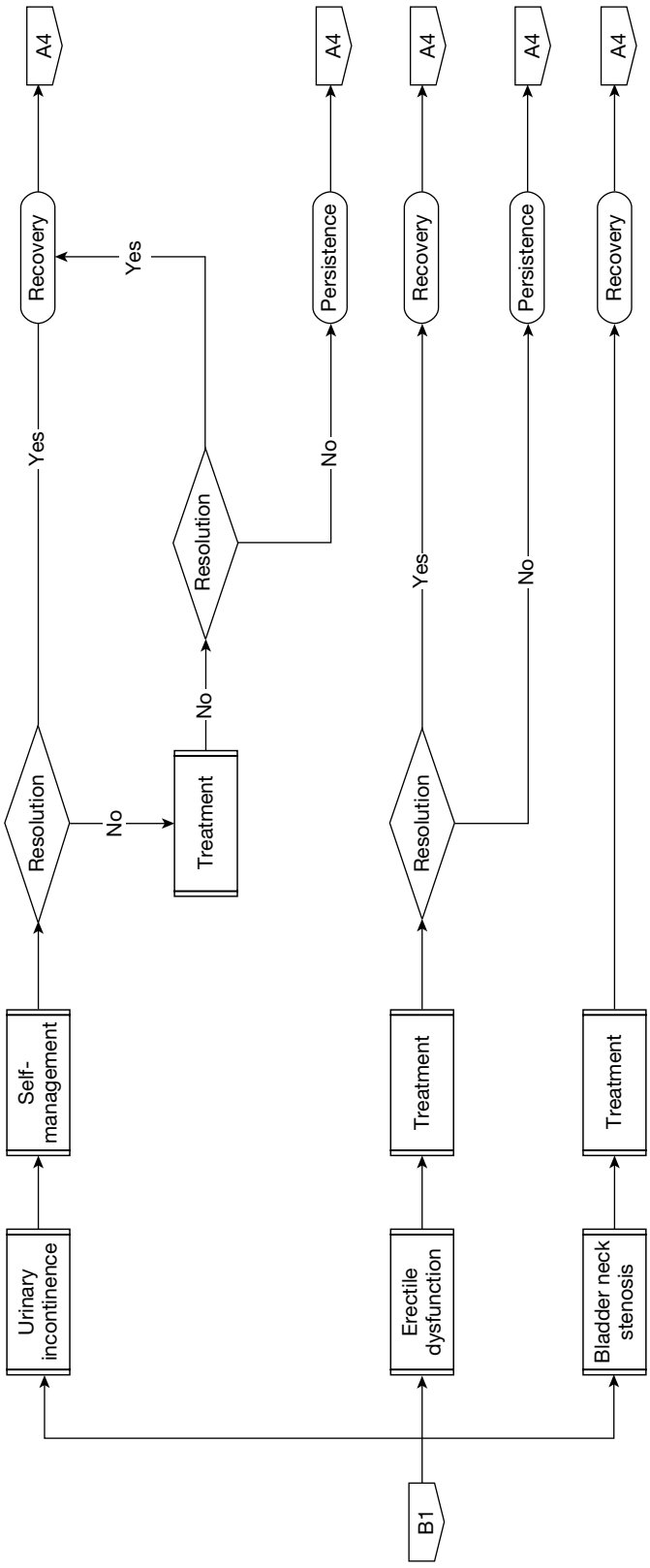

FIGURE 20 Expanded care pathway for the management and treatment of individuals incurring long-term postoperative adverse events. A4, surveillance health state; B1, treatment of long-term adverse events.

TABLE 28 Parameter values with distributions and sources for longer-term adverse events for individuals undergoing robotic or laparoscopic prostatectomy

Longer-term adverse event	Value	Probability	Lower limit[a]	Upper limit[a]	Assigned distribution	Source
Bladder neck contracture						
Procedure rate robotic		0.008	0.002	0.052	Log-normal	Systematic review
Procedure rate laparoscopic		0.021	0.008	0.150	Log-normal	Systematic review
Urinary dysfunction management						
Self-management < 1 year robotic		0.043	0.007	0.224	Log-normal	Systematic review
Self-management success at 1 year		0.957	0.720	1.000	Log-normal	MAPS cohort[77]
Self-management < 1 year laparoscopic		0.079	0.000	0.357	Log-normal	Systematic review
Surgical implantation of AUS	5.20%		3.90%	6.50%	Triangular	Clinical expert panel
AUS success rate	90.00%		67.50%	100.00%	Triangular	Clinical expert panel
Erectile dysfunction						
Erectile dysfunction at 6 months	80.20%		60.00%	100.00%	Triangular	Stanford 2000[187]
Erectile dysfunction at 1 year	71.80%		54.00%	90.00%	Triangular	Stanford 2000[187]
Erectile dysfunction at 2 years	59.90%		45.00%	75.00%	Triangular	Stanford 2000[187]
Erectile dysfunction management						
Treatment for erectile dysfunction	57.00%		42.80%	71.30%	Triangular	MAPS cohort (table 7.9)[77]
Reduction in erectile dysfunction treatment rate at 1 year	50.00%		37.50%	62.50%	Triangular	Matthew 2005[188]
Sildenafil: 100 mg once weekly	82.20%		61.70%	100.00%	Triangular	Schover 2002[189]
Sildenafil success rate overall	31.00%	0.690	23.30%	38.80%	Triangular	Blander 2000[190]
Alprostadil: 20 µg once weekly	15.40%		11.60%	19.30%	Triangular	Schover 2002[189]
Alprostadil success rate overall	57.10%	0.429	42.80%	71.40%	Triangular	Costabile 1998[191]
Penile prosthesis implantation	0.24%		0.20%	0.30%	Triangular	Schover 2002[189]
Penile prosthesis success rate	92.00%		69.00%	100.00%	Triangular	Meuleman 2003[192]

MAPS, men after prostate surgery trial.

a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate. Upper and lower limits of log-normal distribution set at 95% CI.

TABLE 29 Standard operating theatre costs per hour derived from ISD Scotland cost data

Variable	Mean (£)	Median (£)	Minimum (£)	Maximum (£)
Operating theatre cost per hour	1155.79	1051.11	376.7	2574.06

The specific costs to the NHS in terms of specialised equipment were obtained from individual NHS units carrying out the procedures, including hospitals in Aberdeen, Cambridge and Newcastle upon Tyne, UK. The list of reusable equipment and consumables used during a laparoscopic radical prostatectomy came from the Newcastle upon Tyne Hospitals NHS Foundation Trust (Maggie Birkbeck, Urology Theatre Manager, personal communication, June 2010). UK costs for the robotic system and ancillary devices or instruments were obtained from the manufacturer of the da Vinci system, Intuitive Surgical.[30] For the robotic system we chose to use for the base-case analysis the capital and maintenance costs of the most expensive system available (a four-arm manipulator and two consoles) but also performed sensitivity analyses using the least costly system available. For both procedures the process of calculating costs

involved summing the following costs per procedure: unit cost + service contract cost (for robotic procedure only) + specialised equipment cost + consumables cost.

For the robotic system, as an alternative to outright purchase, various permutations of payment and leasing plans were considered, such as payments spread over differing number of years, paid either in advance or in arrears. The cost per procedure varied markedly between these payment options; it also varied by the anticipated throughput of patients per annum. The cost per procedure according to number of procedures performed per year using the equipment purchase plan defined for the base-case analysis is shown in *Table 30*. These costs are based on the use of the most expensive system option consisting of a four-arm manipulator and two consoles and are calculated on the basis of different throughputs, with 200 cases per year representing a maximum number and 50 cases per year representing the throughput of one of the smaller UK centres. These costs represent the higher range of expected costs of equipment and in sensitivity analysis we explore the impact of using less expensive system options. The costs of laparoscopic equipment were similarly estimated. For laparoscopic equipment we have assumed that reusable equipment was reused 200 times per year. The cost per procedure of laparoscopic equipment was £94.48. *Appendices 12* and *13* describe the equipment costs in detail for both robotic and laparoscopic surgery.

Costs associated with perioperative adverse events

As described in *Model health states and associated parameter values, Perioperative state*, perioperative adverse events were categorised using the Clavien–Dindo classification. For each Clavien level a judgement was made by the project team and expert panel about the implications for further care of a particular adverse event occurring (*Table 31*). This extra care was categorised in terms of the extra length of stay that an individual would undergo, which was combined with information on the cost of an additional day in hospital[186] to obtain a cost of each adverse event. A similar process was followed for the cost of conversion to open surgery.

TABLE 30 Cost per procedure of equipment used for robotic prostatectomy: procurement cost based on purchase plan 1 (base case)

Total system cost (£)	Number of procedures	Service life	Cost per procedure (£)	Cost of surgical equipment (£)	Cost of consumables (£)	Total cost (£)
3,090,000	200	7	2207.14	66.10	1194.11	3467.35
3,090,000	150	7	2942.86	88.14	1194.11	4225.11
3,090,000	100	7	4414.29	132.21	1194.11	5740.61
3,090,000	50	7	8828.57	264.42	1194.11	10,287.10

TABLE 31 Additional costs for individuals who suffered perioperative adverse events, including conversion to open surgery

Perioperative adverse event:	Unit cost (£)[a]	Equivalent cost of Clavien–Dindo risk factor/conversion (£)	Number of extra bed-days
Clavien level I	255.00	255.00	1
Clavien level II	255.00	510.00	2
Clavien level IIIa	255.00	765.00	3
Clavien level IIIb	255.00	765.00	3
Clavien level IVa	255.00	1020.00	4
Conversion to open surgery	255.00	765.00	3

a Calculated from the proportion of men incurring an extra day of hospital stay from Department of Health reference costs 2008–9.[186]

Costs associated with postoperative care

Surveillance

The cost of a single PSA test at £5.91 was obtained from the Newcastle upon Tyne Hospitals NHS Foundation Trust laboratory services directorate and applied throughout the period of surveillance according to the defined follow-up schedule (*Table 32*).

The costs of further cancer treatment were derived from the tariff applied to the relevant HRG code[186] in the case of radiotherapy and from the *British National Formulary*[185] in the case of drug treatments. The one-off cost used for radiotherapy was calculated on the basis of 33 treatments at £135 = £4455. The cost of androgen deprivation therapy was based on an initial 14-day course of cyproterone acetate at £63.08 followed by a monthly cost for the LHRH agonist goserelin acetate (Zoladex®, Astra Zeneca) of £403.80, which was continued for the specified duration of treatment (6 months for localised recurrent cancer and lifelong for systemic recurrent cancer) (*Table 33*).

The costs of treatment of adverse events beyond the perioperative period were again derived from the relevant NHS tariff through the HRG code[186] or from the *British National Formulary*[185] or from a recent HTA-funded trial of conservative treatment for urinary incontinence after prostatectomy (men after prostate surgery trial, MAPS; C Glazener, Aberdeen University 2011, personal communication; *Table 34*).[77] We did not apply costs related to outpatient visits for follow-up or GP visits for associated care. Patient costs and societal costs were also not included.

Utilities

A utility value was assigned to each individual in each 3-month time step over the 10-year or lifetime horizon. The utility value encompassed the cancer management state (surveillance, biochemical recurrence, localised cancer, systemic cancer) and the longer-term adverse event state (bladder neck contracture, urinary incontinence and erectile dysfunction) (*Table 35*). Individuals present in more than one state during any 3-month step – localised recurrence and urinary incontinence, for example – were assigned a utility value equal to the product of the utility values applying to each of the states.

TABLE 32 Cost of PSA testing during surveillance schedule for individuals in the model

PSA testing	Number of units per year	Unit cost (£)[a]	Cost per year (£)
During first year	4	5.91	23.64
Beyond year 1	1	5.91	5.91

a Newcastle upon Tyne Hospitals NHS Foundation Trust.

TABLE 33 Cost of cancer treatment

Cancer treatment	Unit cost (£)
33 sessions of radiotherapy	4455.00[a]
Monthly cost of goserelin acetate	403.80[185]
14-day course of cyproterone acetate	63.08[185]

a Derived from the average tariff in pounds sterling applied to HRG SC24Z from the Department of Health reference costs 2008–9.[186]

TABLE 34 Costs associated with longer-term postoperative adverse events following laparoscopic and robotic prostatectomy

Long-term adverse event	Unit cost (£)
Bladder neck contracture	
Bladder neck incision (HRG LB27Z)	1269.00[a]
Urinary incontinence	
Self-management per year	263.59[77]
Implantation of AUS (HRG LB50Z)	3928.00[a]
AUS device	4918.00[a]
Erectile dysfunction	
Sildenafil 100 mg once weekly	5.88[185]
Alprostadil 20 µg once weekly	11.94[185]
Penile prosthesis implantation (HRG LB47Z)	2262.00[a]
Penile prosthesis device	5023.00[a]

a Derived from average tariff in pounds sterling applied to HRG codes LB27Z, LB50Z and LB47Z from the Department of Health reference costs 2008–9.[186]

TABLE 35 Utility values and their distributions used in the model

Variable	Value	Lower limit[a]	Upper limit[a]	Assigned distribution	Source
General states – surveillance					
Postoperative state 1 year	0.900	0.750	1.000	Triangular	Korfage 2005[194]
Death	0			Triangular	
Further cancer treatment					
Biochemical recurrence	0.730	0.548	0.913	Triangular	Cowen 1998[195]
Localised recurrence	0.820	0.660	0.984	Triangular	Korfage 2005[194]
Systemic recurrence	0.420	0.311	0.529	Triangular	Cowen 1998[195]
Longer-term adverse event					
Bladder neck contracture	0.720	0.560	0.930	Triangular	Volk 2004[196]
Urinary incontinence	0.830	0.750	1.000	Triangular	Volk 2004[196]
Erectile dysfunction	0.840	0.770	1.000	Triangular	Volk 2004[196]

a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate.

Data analysis

The model compared effectiveness and cost-effectiveness [defined as incremental cost per quality-adjusted life-year (QALY)] for robotic compared with laparoscopic radical prostatectomy. The timing and nature of each event was recorded, allowing the construction of individual trajectories through the care pathways. When processes incurred costs, these were added to the total costs accrued for that patient in that year. When processes led to a change in utility then the value of that new utility was multiplied by the current QALYs for that patient in that year. Estimates of the mean costs, QALYs and incremental cost per QALY were obtained by simulating the outcomes for a group of 5000 men for each treatment. In the base-case analysis the time horizon has been taken to be 10 years. Both costs and QALYs are discounted at 3.5%.[197]

Variations around the estimates of mean costs and QALYs were obtained by producing 1000 bootstrap estimates for mean costs and QALYs for each treatment. These data were then used to produce cost-effectiveness acceptability curves (CEACs). In the base-case analysis CEACs have been used to illustrate the imprecision surrounding the results caused by the variation in care and events experienced by the men modelled. These curves illustrate the likelihood that a strategy is cost-effective at various threshold values for society's willingness to pay for an additional QALY. The CEACs are the product of a probabilistic analysis. In this analysis we have assumed that each of the parameters is associated with a degree of imprecision, as described in each of the data input tables, characterised by a triangular distribution. This distribution was chosen as the data available to inform an alternative distributional form were sparse.

Sensitivity analyses

Extension of the time horizon to 40 years

In this sensitivity analysis we explored the impact of extending the time horizon. Conceptually this should allow more time for any benefits of robotic surgery to offset the increased procedure costs.

Changes in the costs of robotic equipment

Robotic equipment comes in several different variants and can be obtained from the manufacturers using several different payment plans. The precise cost of each of these variants may vary between provider and *Appendix 12* provides illustrative examples of the cost variants. These costs have been converted into an annual cost, assuming the manufacturers' recommended lifespan of the equipment of 7 years, and a cost per procedure estimated. In this analysis we explore what the impact on the incremental cost per QALY is of using a lower cost for the robotic system. This analysis has been repeated for the different numbers of annual cases performed (from 50 per year to 200 per year). From these results it was possible to determine the effect on estimates of cost-effectiveness of varying the cost per procedure of robotic prostatectomy consequent to any particular payment plan or throughput.

Changes in the risk of having a positive margin

The estimates of positive margin rates following robotic and laparoscopic surgery were based on the point estimates derived from the systematic review. In this sensitivity analysis we explored the impact of using both the lower and the upper 95% CrI limits of the OR of the difference in positive margin rates between robotic and laparoscopic surgery (base-case OR 0.69; 95% CrI 0.506 to 0.955). The further cancer treatment matrices defined by using the lower and higher risks of having a positive margin following robotic surgery are shown in *Tables 36* and *37*, respectively. The probabilities for laparoscopic surgery remained the same as in the base case.

Combining change in costs per procedure and positive margin rates

In this analysis we explored the impact on the incremental cost per QALY of changes in both the cost per procedure and the risk of a positive margin. These data have been presented as plots of the incremental cost per QALY against the positive margin rate, defined in terms of an OR, for different numbers of procedures performed per year.

Changes in the risk of biochemical recurrence

In the base-case analysis it was assumed that the risk of biochemical recurrence was the same regardless of which procedure a man received. The rationale behind this assumption was that the meta-analysis reported in *Chapter 4* provided no evidence of any difference; the CI surrounding the OR was wide and included 1. In the first sensitivity analysis concerning biochemical recurrence rates we assumed that on average robotic surgery was associated with a lower rate of

TABLE 36 Immediate further cancer treatment matrix for individuals following robotic prostatectomy according to findings on pathological examination of the removed prostate: lower limit of CrI for positive margin (OR = 0.506)

Margin status	Tumour stage	Gleason score	Number (%) of men in category	Probability of event in model	Management decision
Negative	Negative	Negative	3053 (65.4)	0.654	Surveillance
Negative	Negative	Positive	139 (3.0)	0.030	Surveillance
Negative	Positive	Negative	664 (13.8)	0.138	Surveillance
Negative	Positive	Positive	278 (5.9)	0.059	Treatment
Positive	Negative	Negative	412 (8.8)	0.088	Surveillance
Positive	Negative	Positive	19 (0.4)	0.004	Treatment
Positive	Positive	Negative	87 (1.9)	0.019	Treatment
Positive	Positive	Positive	37 (0.8)	0.008	Treatment

Margin status: negative/positive; tumour stage: negative pT1–pT2, positive pT3–pT4; Gleason score: negative ≤ 7, positive 8–10.

TABLE 37 Immediate further cancer treatment matrix for individuals following robotic prostatectomy according to findings on pathological examination of the removed prostate: higher limit of CrI for positive margin (OR = 0.955)

Margin status	Tumour stage	Gleason score	Number (%) of men in category	Probability of event in model	Management decision
Negative	Negative	Negative	2685 (59.59)	0.575	Surveillance
Negative	Negative	Positive	122 (2.72)	0.026	Surveillance
Negative	Positive	Negative	567 (12.57)	0.121	Surveillance
Negative	Positive	Positive	244 (5.42)	0.052	Treatment
Positive	Negative	Negative	780 (14.62)	0.167	Surveillance
Positive	Negative	Positive	36 (0.67)	0.008	Treatment
Positive	Positive	Negative	164 (3.08)	0.035	Treatment
Positive	Positive	Positive	71 (1.33)	0.015	Treatment

Margin status: negative/positive; tumour stage: negative pT1–pT2, positive pT3–pT4; Gleason score: negative ≤ 7, positive 8–10.

biochemical recurrence. This lower rate was estimated by combining the long-term rates from Menon and colleagues[181] with the point estimate of the OR for risk of biochemical recurrence at 12 months obtained from the systematic review (0.89). The CIs around the OR were not clinically plausible and therefore we assumed a triangular distribution with upper and lower limits for the 12-month risk of biochemical recurrence for robotic surgery set at ±2% (based on the finding of Menon and colleagues[181]; *Table 38*).

In a second sensitivity analysis around the risk of biochemical recurrence we explored the impact of there being a higher rate of biochemical recurrence. The rationale behind this analysis was that the rates reported by Menon and colleagues[181] were approximately 50% of those predicted in the meta-analysis. Therefore, in this sensitivity analysis we have simply doubled the rates observed by Menon and colleagues[181] (*Table 39*).

TABLE 38 Biochemical recurrence estimated using the OR from the systematic review multiplied by the rates found by Menon and colleagues[181] to obtain a plausible difference between therapies

Variable	Probability	Lower limit[a]	Upper limit[a]
Robotic surgery			
Biochemical recurrence event rate 1 year	0.0112	0.0084	0.0140
Biochemical recurrence event rate 3 years	0.0097	0.0073	0.0121
Biochemical recurrence event rate 5 years	0.0085	0.0064	0.0106
Biochemical recurrence event rate 7 years	0.0088	0.0066	0.0110
Laparoscopic surgery[b]			
Biochemical recurrence event rate 1 year	0.0125	0.0094	0.0156
Biochemical recurrence event rate 3 years	0.0109	0.0082	0.0136
Biochemical recurrence event rate 5 years	0.0095	0.0072	0.0119
Biochemical recurrence event rate 7 years	0.0099	0.0074	0.0124

a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate. Upper and lower limit of log-normal distribution set at 95% CI.
b Values are the same as in the base-case analysis.

TABLE 39 Biochemical recurrence estimated by doubling the rates from Menon and colleagues[181] and using an OR = 0.89 favouring robotic prostatectomy

Variable	Probability	Lower limit[a]	Upper limit[a]
Robotic surgery			
Biochemical recurrence event rate 1 year	0.0222	0.0167	0.0278
Biochemical recurrence event rate 3 years	0.0164	0.0123	0.0205
Biochemical recurrence event rate 5 years	0.0170	0.0127	0.0212
Biochemical recurrence event rate 7 years	0.0177	0.0133	0.0221
Laparoscopic surgery			
Biochemical recurrence event rate 1 year	0.0250	0.0187	0.0312
Biochemical recurrence event rate 3 years	0.0218	0.0164	0.0273
Biochemical recurrence event rate 5 years	0.0191	0.0143	0.0239
Biochemical recurrence event rate 7 years	0.0199	0.0149	0.0248

a Upper and lower limits of triangular distribution calculated at ±25% of the point estimate.

Chapter 6

Results of the health economic evaluation

Base-case analysis

In the base-case analysis robotic surgery was compared with laparoscopic surgery over a 10-year time horizon under the scenario that a centre with a single robot would perform 200 procedures per year and was using a da Vinci Si HD Dual Console that was purchased outright. Under this scenario, robotic surgery is more costly (primarily because of the cost of the equipment) but more effective (primarily because of the lower risk of having a positive margin). As a consequence, the incremental cost per QALY gained from robotic compared with laparoscopic surgery is £18,329, well below the threshold typically adopted by the National Institute for Health and Clinical Excellence (NICE) (*Table 40*).[197] These data do not suitably illustrate the uncertainty surrounding the costs and QALYs and the incremental cost per QALY. This is illustrated in the plot of cost and QALY pairs for each individual in the cohort for each treatment (*Figure 21*). Further details of the distribution of costs and QALYs are shown in *Figure 22*; here, density plots compare the distribution of costs and QALYs for each sample of 5000 men who received each intervention.

Figure 23 shows the plot of bootstrapped estimated mean costs and QALYs for each treatment; as this figure shows, it appears likely that the robotic surgery is both more costly and more effective than laparoscopic surgery. Thus, as *Figure 24* illustrates, the robotic surgery has an approximately 95% chance of being considered cost-effective compared with laparoscopic surgery when society's maximum willingness to pay for a QALY is £30,000.

The results of the base-case analysis are sensitive to the costs of the robotic equipment. This is illustrated by exploring the impact of changing the number of surgeries performed per year (from 200 down to 50). As the number of procedures per year falls, the cost of the robotic equipment per procedure increases. As *Table 40* illustrates, as the number of procedures per year

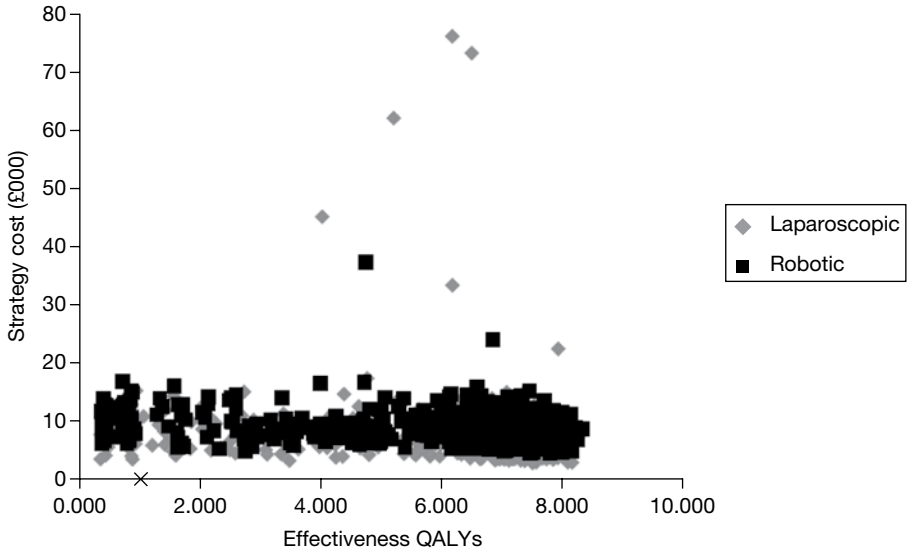

FIGURE 21 Plot of costs and QALYs for each sample of 5000 men who received each intervention.

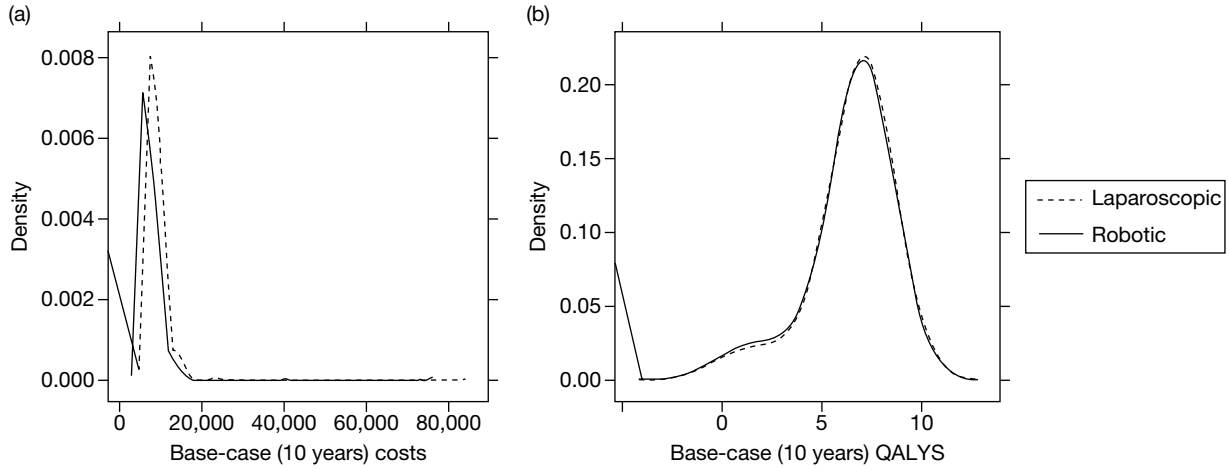

FIGURE 22 Density charts describing the distribution of total costs (a) and QALYs (b) for the cohorts of modelled men.

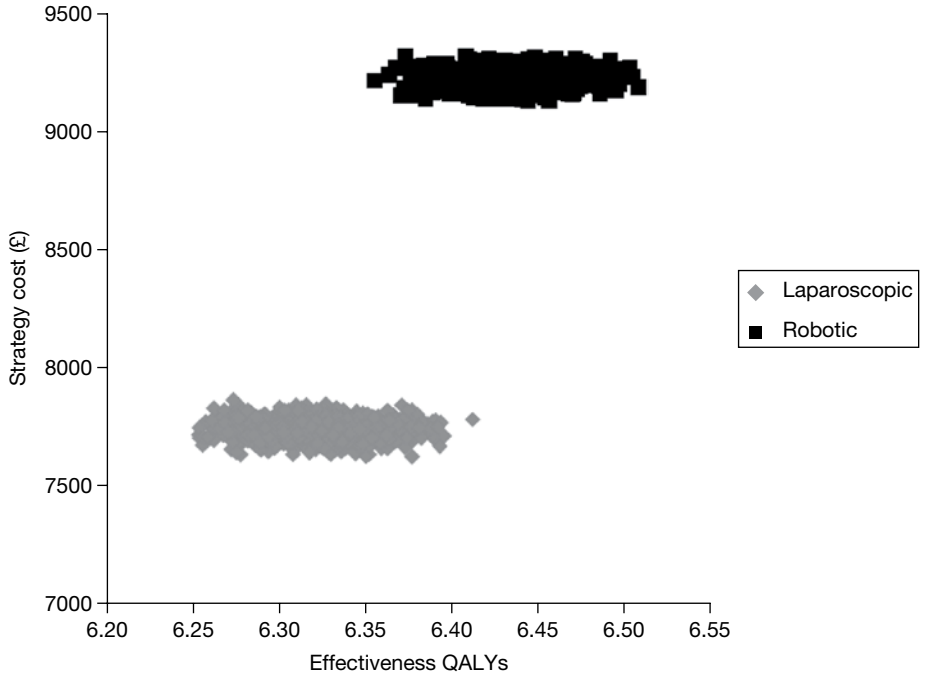

FIGURE 23 Plot of bootstrapped estimated mean costs and QALYs for each treatment for the base-case analysis.

falls from 200 to 50 and hence the cost of robotic equipment per procedure increases from £3467 to £10,287 (see *Appendix 12* for details of how these costs were estimated), the mean incremental cost per QALY increases from £18,329 to £106,839. Consequently, the probability that robotic surgery would be considered cost-effective at a cost per QALY threshold typically used by NICE (£20,000) falls from 56% in the base-case analysis to virtually zero when the number of procedures per year is 50.

These data are based on the use of more expensive robotic equipment (da Vinci Si HD Dual Console). Should a less costly set-up be used instead, such as the da Vinci S EZ (three-arm) system, the equipment costs for the robotic procedure would be **£2596** and in this situation the incremental cost per QALY gained for robotic compared with laparoscopic surgery would be **£7009**.

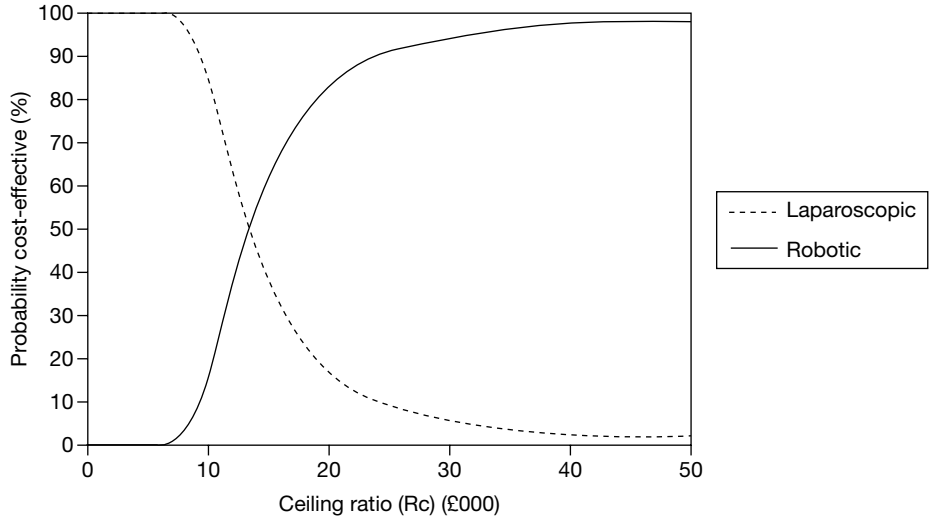

FIGURE 24 Cost-effectiveness acceptability curves for the base-case analysis.

TABLE 40 Results of the base-case analysis according to throughput and two different robotic systems [the highest (base-case) and lowest cost scenarios]

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9040	6.517	18,329	0.00	0.03	0.56	0.79	0.92
	Laparoscopic	7628	6.440		1.00	0.97	0.44	0.21	0.08
150	Robotic	9799	6.517	28,172	0.00	0.00	0.20	0.53	0.82
	Laparoscopic	7628	6.440		1.00	1.00	0.80	0.47	0.18
100	Robotic	11,312	6.517	47,822	0.00	0.00	0.00	0.11	0.52
	Laparoscopic	7628	6.440		1.00	1.00	1.00	0.89	0.48
50	Robotic	15,859	6.517	106,839	0.00	0.00	0.00	0.00	0.00
	Laparoscopic	7628	6.440		1.00	1.00	1.00	1.00	1.00
200[a]	Robotic	8168	6.517	7009	0.00	0.72	0.93	0.96	0.97
	Laparoscopic	7628	6.440		1.00	0.28	0.07	0.04	0.03

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

Sensitivity analysis

For each of the sensitivity analyses, mean costs and QALYs are shown for each treatment along with the incremental cost per QALY. Also shown is the likelihood that an intervention would be cost-effective at different threshold values for society's willingness to pay for a QALY. *Appendix 15* shows the plots of mean costs and QALYs and CEACs for each sensitivity analysis. *Appendix 14* shows estimates of survival for each sensitivity analysis.

Increasing the time horizon

When the time horizon increases, the costs and QALYs for both types of surgery increase; however, for all of the scenarios that were modelled (*Table 41*), costs increase only slightly whereas there is a much larger proportionate increase in QALYs. As a consequence, the incremental cost per QALY for all scenarios modelled is lower than in the base case and the probability of robotic surgery being cost-effective at threshold values for a QALY that society might be willing to pay[197] increases towards 1.

Changes to the positive margin rate

In the base-case analysis we assumed that the OR for the difference in the positive margin rate between robotic and laparoscopic surgery was 0.69. In the first sensitivity analysis we took the difference in positive margin rates to be equal to the lower end of the CrI of the OR calculated in the meta-analysis reported in Chapter 4 (OR = 0.506). This resulted in robotic surgery having a lower rate of positive margins than in the base case and consequently a lower incremental cost per QALY (*Table 42*). Conversely, when the upper CrI limit of the OR for positive margins was used (OR = 0.955) the difference in positive margin rate between robotic and laparoscopic surgery was smaller than in the base case. As would be expected, the incremental cost per QALY increased as the number of procedures performed per year decreased. Indeed, only for the most optimistic scenario for robotic surgery modelled (the procurement cost of robotic equipment being equivalent to £2596) was the incremental cost per QALY < £30,000, and even in this

TABLE 41 Sensitivity analysis using a lifetime time horizon

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					£0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9179	12.12	1436	0.00	1.00	1.00	1.00	1.00
	Laparoscopic	8075	11.36		1.00	0.00	0.00	0.00	0.00
150	Robotic	9937	12.12	2422	0.00	1.00	1.00	1.00	1.00
	Laparoscopic	8075	11.36		1.00	0.00	0.00	0.00	0.00
100	Robotic	11,184	12.12	4045	0.00	1.00	1.00	1.00	1.00
	Laparoscopic	8075	11.36		1.00	0.00	0.00	0.00	0.00
50	Robotic	15,998	12.12	10,306	0.00	0.41	1.00	1.00	1.00
	Laparoscopic	8075	11.36		1.00	0.59	0.00	0.00	0.00
200[a]	Robotic	8309	12.12	304	0.00	1.00	1.00	1.00	1.00
	Laparoscopic	8075	11.36		1.00	0.00	0.00	0.00	0.00

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

TABLE 42 Sensitivity analysis changing positive margin rate: OR for positive margins for robotic vs laparoscopic surgery was set at the lower CrI limit (OR = 0.506)

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					£0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9095	6.57	11,731	0.00	0.27	0.92	0.99	0.99
	Laparoscopic	7628	6.44		1.00	0.73	0.08	0.01	0.01
150	Robotic	9853	6.57	17,798	0.00	0.00	0.65	0.92	0.99
	Laparoscopic	7628	6.44		1.00	1.00	0.35	0.08	0.01
100	Robotic	11,097	6.57	27,743	0.00	0.00	0.09	0.60	0.94
	Laparoscopic	7628	6.44		1.00	1.00	0.91	0.40	0.06
50	Robotic	15,914	6.57	66,259	0.00	0.00	0.00	0.00	0.12
	Laparoscopic	7628	6.44		1.000	1.00	1.00	1.00	0.88
200[a]	Robotic	8223	6.57	4760	0.00	0.97	0.99	0.99	1.00
	Laparoscopic	7628	6.44		1.00	0.03	0.01	0.01	0.00

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

scenario the likelihood that robotic surgery would be considered cost-effective was still only 60% at typical threshold values for society's willingness to pay for a QALY (*Table 43*).[197] Overall, this sensitivity analysis illustrates the sensitivity of the results to changes in the effectiveness of robotic surgery because at the lower levels of throughput the mean incremental cost per QALY approaches or exceeds typical threshold values for society's willingness to pay for a QALY (see *Table 43*).[197]

Changes in the costs and positive margin rates

To explore the relationship between positive margin rates, incremental cost per QALY and cost per procedure, we have plotted the incremental cost per QALY for the different ORs for positive margin against the changing cost of the procedure determined by varying the number of procedures performed per year and the purchase cost of the robotic system (*Figure 25*). The data have been presented in this way as the cost per procedure is likely to vary markedly between centres according to throughput. The costs per procedure for different throughputs and for five alternative scenarios of robotic system cost are summarised in *Table 44* (see *Appendix 12* for details of how these costs were estimated).

As *Figure 25* illustrates, as the cost per procedure increases with lower throughput and the OR for positive margin rate approaches 1 (no difference between procedures), the incremental cost per QALY increases beyond threshold values that society might be willing to pay.[197]

TABLE 43 Sensitivity analysis changing positive margin rate: OR for positive margins for robotic vs laparoscopic surgery was set at the upper CrI limit (OR = 0.955)

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					£0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9099	6.47	50,502	0.00	0.00	0.13	0.30	0.49
	Laparoscopic	7628	6.44		1.00	1.00	0.87	0.70	0.51
150	Robotic	9859	6.47	76,564	0.00	0.00	0.02	0.12	0.34
	Laparoscopic	7628	6.44		1.00	1.00	0.98	0.88	0.66
100	Robotic	11,105	6.47	119,342	0.00	0.00	0.00	0.01	0.15
	Laparoscopic	7628	6.44		1.00	1.00	1.00	0.98	0.85
50	Robotic	15,923	6.47	284,694	0.00	0.00	0.00	0.00	0.00
	Laparoscopic	7628	6.44		1.00	1.00	1.00	1.00	1.00
200[a]	Robotic	8230	6.47	20,675	0.000	0.214	0.48	0.60	0.67
	Laparoscopic	7628	6.44		1.000	0.786	0.52	0.40	0.33

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

TABLE 44 Effect of varying throughput on cost per procedure

Procedures per year	Type of equipment	Cost per procedure
200	da Vinci S EZ (three arm)	£2595.92
200	da Vinci Si HD Dual Console	£3467.35
150	da Vinci Si HD Dual Console	£4225.10
100	da Vinci Si HD Dual Console	£5740.60
50	da Vinci Si HD Dual Console	£10,287.09

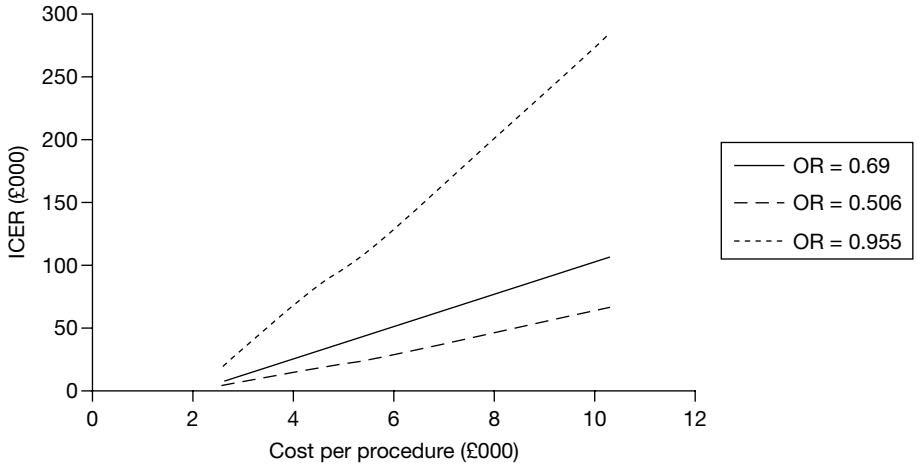

FIGURE 25 Incremental cost per QALY for different costs per procedure and relative differences in positive margin rates for robotic versus laparoscopic surgery. OR, OR for positive margin rate for robotic versus laparoscopic surgery.

For illustrative purposes these data have also been presented to show how the incremental cost per QALY changes as the relative difference in positive margin rate changes for different annual throughputs (*Figure 26*). As this figure illustrates, the incremental cost per QALY increases as the OR approaches 1.

Changes to the risk of biochemical recurrence

In the base-case analysis it was assumed that the risk of biochemical recurrence was the same for both robotic and laparoscopic surgery. In the sensitivity analysis it has been assumed that on average robotic surgery is associated with a lower risk of biochemical recurrence (although the distribution attached to the value includes the possibility that there is no difference). A priori it would be expected that this would improve the relative efficiency of robotic surgery compared with laparoscopic surgery and, as *Table 45* illustrates, on average this is what happened; however, the probability that robotic surgery would be considered cost-effective compared with the base case does not greatly alter over all threshold values considered.

In a second sensitivity analysis on biochemical recurrence rate we explored the impact of a higher risk of biochemical recurrence for both robotic and laparoscopic surgery (*Table 46*). The impact of this was to increase the costs of and reduce the QALYs from robotic surgery. As a consequence the incremental costs per QALY increased and for situations in which the annual number of procedures was ≤ 100 the incremental cost per QALY would be above thresholds currently adopted by NICE.[197] Consequently, the probability that robotic surgery would be considered cost-effective increases compared with the base case although at the lowest throughputs considered robotic surgery is still highly unlikely to be considered cost-effective (see *Table 40*).

Summary of results of modelling cost-effectiveness of procedures

In the base-case analysis we have taken the best available evidence to inform the model, which in turn has been structured to reflect the current process of care. This analysis was based on the use of the most costly variant of the robotic equipment and explored the impact of variations in the number of procedures performed per year. As the number of procedures per year was reduced to < 150, the incremental cost per QALY became greater than threshold values that society might typically be willing to pay.[197]

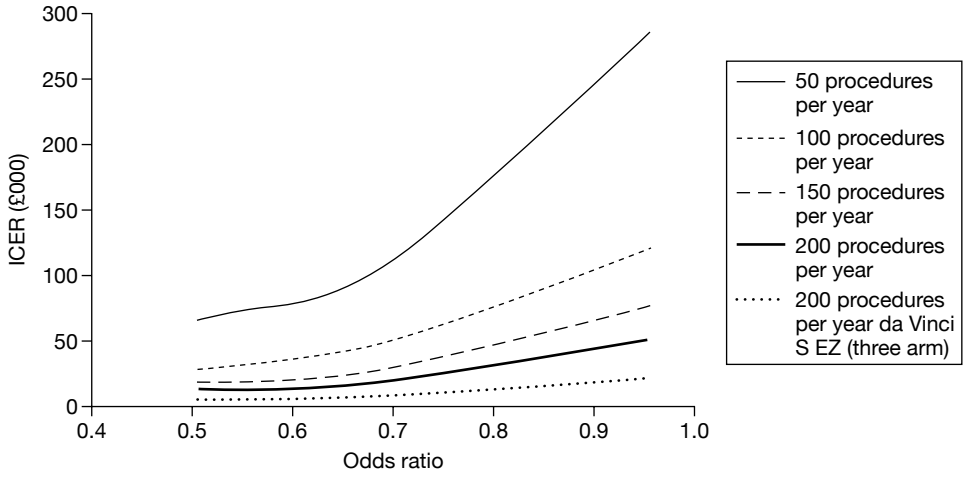

FIGURE 26 Incremental cost per QALY plotted against the OR for the relative difference in positive margin rate between robotic and laparoscopic surgery and for different numbers of procedures performed per year.

TABLE 45 Sensitivity analysis: biochemical recurrence estimated using OR from the systematic review to obtain difference between therapies

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					£0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9056	6.52	16,859	0.00	0.06	0.63	0.85	0.95
	Laparoscopic	7628	6.44		1.00	0.94	0.37	0.15	0.05
150	Robotic	9813	6.52	25,795	0.00	0.00	0.25	0.61	0.88
	Laparoscopic	7628	6.44		1.00	1.00	0.75	0.39	0.12
100	Robotic	11,059	6.52	40,506	0.00	0.00	0.01	0.21	0.65
	Laparoscopic	7628	6.44		1.00	1.00	0.99	0.79	0.35
50	Robotic	15,877	6.52	97,393	0.00	0.00	0.00	0.00	0.02
	Laparoscopic	7628	6.44		1.00	1.00	1.00	1.00	0.98
200[a]	Robotic	8183	6.52	6546	0.00	0.789	0.949	0.97	0.98
	Laparoscopic	7628	6.44		1.00	0.211	0.051	0.03	0.02

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

Given the available data, the main determinants of relative cost-effectiveness are the cost that centres would need to pay per procedure for the robotic equipment and the positive margin rate. The costs per procedure are influenced by the capital cost of the robotic system and the rate of use of each robotic system. The capital cost is determined by a number of different factors including the purchase plan taken for the robotic equipment, the type of equipment used and, not considered in this evaluation, the cost of any alterations to existing facilities. The rate of use of each system will also determine the cost per procedure, with higher throughput centres gaining significant economies of scale. The second key determinant of cost-effectiveness is the positive margin rate because of the effect of this parameter on determining subsequent cancer outcomes. The positive margin rate, along with other model parameters, is associated with considerable imprecision, but because of its role in determining management (see *Tables 25* and *26*) it was not possible to incorporate this uncertainty into the probabilistic sensitivity analysis. Nevertheless, when the uncertainty surrounding the OR for positive margins for robotic compared with

TABLE 46 Sensitivity analysis: absolute biochemical recurrence rates twice those estimated in the base case (and closer to those predicted by the meta-analysis reported in *Chapter 4*)

Surgical capacity	Intervention	Mean cost (£)	Mean QALYs	ICER (£)	Probability cost-effective at different threshold values for WTP per QALY				
					£0	£10,000	£20,000	£30,000	£50,000
200	Robotic	9190	6.47	11,890	0.00	0.29	0.90	0.97	0.99
	Laparoscopic	7842	6.35		1.00	0.71	0.10	0.03	0.01
150	Robotic	9949	6.47	18,582	0.00	0.00	0.58	0.89	0.97
	Laparoscopic	7842	6.35		1.00	1.00	0.42	0.12	0.03
100	Robotic	11,194	6.47	29,567	0.00	0.00	0.07	0.52	0.90
	Laparoscopic	7842	6.35		1.00	1.00	0.93	0.48	0.10
50	Robotic	16,008	6.47	72,029	0.00	0.00	0.00	0.00	0.09
	Laparoscopic	7842	6.35		1.00	1.00	1.00	1.00	0.91
200[a]	Robotic	8317	6.47	4191	0.00	0.96	0.99	1.00	1.00
	Laparoscopic	7842	6.35		1.00	0.04	0.01	0.00	0.00

ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.
a Based on an equipment cost per procedure of £2595.92, derived from the use of a da Vinci S EZ (three-arm) system.

laparoscopic surgery was incorporated into a deterministic sensitivity analysis the incremental cost per QALY was shown to increase as the OR approached 1. Indeed, when the OR was 0.955, higher than the point estimate based on data from studies at a low risk of bias, the incremental cost per QALY typically increased well beyond usual thresholds, especially when the number of procedures per year was low.

Overall, the results of the economic evaluation are suggestive that robotic radical prostatectomy could potentially be cost-effective but that this will depend on the long-term performance of robotic surgery in terms of cancer control and the number of procedures that can be performed per year in a centre where a robotic system is installed. This suggests that robotic surgery is more likely to be considered worthwhile in larger centres that manage ≥ 200 cases per year.

Chapter 7

Discussion

This review sought to answer the following question posed by the UK National Institute for Health Research HTA programme: 'What is the clinical effectiveness of robotic surgery compared with laparoscopic surgery in the management of localised prostate cancer?'

Summary of findings

This HTA review, using the best available evidence and an appropriately complex health economic model, found that robotic prostatectomy was more effective but more costly than laparoscopic prostatectomy, and predicted that in the UK NHS it may be cost-effective provided that a minimum throughput is achieved for each robotic system and the cost of the system can be minimised. The implications of this review in terms of planning the best care in the NHS for men who require radical prostatectomy for treatment of their localised prostate cancer are therefore substantial, but the uncertainty surrounding our findings, associated with the inadequate evidence base, encourages a cautious approach. At present, of the 5000 men undergoing radical prostatectomy each year in the UK, approximately 50% are operated on using the open technique, 25% using the laparoscopic technique and 25% using the robotic technique.[52] With a further five robots being installed in UK NHS hospitals during 2011 to join the 16 already in service, it is likely that the proportion of men undergoing robotic surgery will increase. This review will help inform the setting of criteria, particularly related to monitoring of positive margin rate and minimum throughput, by which these robotic systems should be used to provide most benefit for men with localised prostate cancer and to the NHS. For the future there is an urgent need to standardise recording and reporting of relevant outcomes of treatments for localised prostate cancer within the NHS to allow better analysis of relative effectiveness and modelling of health economic benefits.

Clinical effectiveness

The methodology used in this report makes best use of the current evidence comparing the safety and outcome of radical prostatectomy performed for men with localised prostate cancer by open, laparoscopic or robotic techniques. In the mixed-treatment meta-analysis, only studies that involved a comparator arm were included when estimating differences between treatments. It is noteworthy that none of the studies eligible for inclusion in the meta-analysis comes from a UK centre. The prevalence of radical prostatectomy for localised prostate cancer within a particular community or health-care system is predominantly governed by the prevalence of PSA testing, which continues to be low in the UK relative to other countries with similarly developed health-care systems.[35] Although we used uncontrolled data derived from studies performed in many different countries, we did not find any large discrepancies in demographic and disease variables that may have resulted in differences in outcome between UK men undergoing radical prostatectomy and those from other countries. In terms of the surgical teams, most will have undergone mentored training in established laparoscopic and robotic centres elsewhere in Europe or in the USA, with updates from conference and 'master class' attendance. Generalisation of our results to the UK context does seem appropriate given this face validity, but a degree of caution needs to be exercised.

As is commonly the case with attempts to summarise outcomes from treatments for prostate cancer, we were unable to identify comparative estimates of cancer survival. Instead, we had to use proxy measures of disease outcome including positive surgical margins and rates of biochemical recurrence at 1 year.[74] Although both are considered to be predictive of cancer-specific survival, proof of this relationship is lacking.[199,200] Despite these caveats, the findings from the systematic review on differences in the process of care, safety and cancer outcome between robotic and laparoscopic prostatectomy appear to have face validity. The systematic review involved > 19,000 men with an average age of 61 years with preoperative cancer characteristics that were balanced between the groups and consistent with current recommendations for the use of this treatment.[43] Overall, 96% of men had cT1–cT2 disease and 94% a Gleason sum score on preoperative biopsy of ≤ 7. Latest data from the British Association of Urological Surgeons (BAUS)[201] on 2225 men undergoing radical prostatectomy, submitted by participating institutions in the UK during 2010, suggest that disease characteristics are similar in the UK, with a median age of 60 years, 92% having cT1 or cT2 disease and 93% a preoperative Gleason sum score of ≤ 7. Following surgery, the meta-analysis showed an overall upstaging, with 21% of men in both the laparoscopic and robotic groups being pT3, but no overall worsening of Gleason sum score. The proportion of men having pT3 disease is a key variable because it is predictive of both positive surgical margin rates and ultimate survival. Data from the 60 UK centres contributing to the BAUS 2010 dataset showed that 36% of men undergoing radical prostatectomy had pT3 disease. Additional recent case series from UK centres performing purely laparoscopic or robotic prostatectomy reported pT3 rates of 26% and 46% respectively.[156,177] In summary, men included in our study were broadly typical of the population requiring this intervention in the UK NHS, but with a possible lower rate of pT3 disease, reflecting higher use of on-demand PSA testing in the USA and other Western European countries.

Patient-driven outcomes

Safety

Both laparoscopic and robotic radical prostatectomy had a good safety profile, with low rates of major morbidity and only one treatment-related death across all included studies. For most perioperative adverse events the direction of effect was in favour of robotic prostatectomy, suggesting potentially lower rates using the robotic system. The likelihood of this being a real difference was high only for the Clavien IIIb category concerning adverse events that required an additional operative intervention, particularly inadvertent rectal injury. The better vision and instrument dexterity afforded by the robotic system may have contributed to this although it should be noted that the absolute rates were low, increasing the chance that this was a random rather than a systematic difference between the procedures. There was no evidence of any difference in the rate of conversion to an open procedure, even though conversion could occur as an additional risk of machine failure in the case of robotic radical prostatectomy. Although we were unable to assess other relevant patient outcomes such as analgesic requirement, return to full activities or return to employment, given the similarity between these two minimally invasive approaches it is unlikely that there would be any differences.[33,202] Overall, our results do suggest that the improved vision and instrument manipulation afforded by the robotic system translates to improved operative patient safety.

Cancer control

All men with localised prostate cancer who embark on radical prostatectomy do so with the expectation that the operation will be curative and save them from the morbidity and early death associated with metastatic disease.[203,204] Information that our economic model of longer-term effectiveness could provide on this issue was dependent on estimates of positive margin rates (17.6% for robotic prostatectomy vs 23.6% for laparoscopic prostatectomy) and biochemical recurrence at 1 year (no evidence of a difference), which were the only relevant outcomes obtained from the meta-analysis. Although the evidence was that positive surgical margin rates,

a proxy measure for cancer control, may be reduced by the use of robotic radical prostatectomy, the relevance of this in terms of cancer recurrence and long-term efficacy outcomes was unclear. This finding differed from that reported in a previous systematic review,[205] which provided no evidence of a statistically significant difference in pooled estimates of surgical margin positivity. Restricting our analysis to low risk of bias studies continued to provide evidence of a lower rate of positive margin rates following robotic prostatectomy but with greater uncertainty and a lower probability that the difference was real. Our conclusion that robotic radical prostatectomy resulted in a lower rate of positive margins should therefore be interpreted with caution given this increased uncertainty around the estimates. In addition, a thorough review by our pathologist expert of the pathology protocols used in included studies showed that they provided limited detail and illustrated technical variation, which may have biased the categorisation of positive margin status and prevented accurate comparison between studies.

We used the best evidence from other literature and help from our expert panel to project, using a mathematical model, these short-term cancer outcome data from our systematic review to estimate long-term cancer-free survival over the subsequent 10 years or the individual's lifetime. The findings suggest that overall survival was higher at 10 years for men undergoing robotic radical prostatectomy than for men undergoing laparoscopic radical prostatectomy, even if the upper CrI limit of the difference in positive margin rates (worse case) was used. In the base case the use of robotic prostatectomy resulted in an average gain of 0.045 life-years. Sensitivity analyses using lower differences in positive margin rates reduced the differences in 10-year overall survival as did increasing the overall biochemical recurrence rate. In all cases the estimates for 10-year survival rates were in the range of 70–80%, in line with those found in previous systematic reviews.[41]

Long-term adverse events

Although the point estimate for the rate of bladder neck contracture was lower for robotic prostatectomy the degree of uncertainty meant that this was unlikely to represent a true difference. The lack of difference in rates of persistent urinary incontinence (~6% after either procedure) or persistent erectile dysfunction (~40% after either procedure) suggests that both techniques provide similar preservation of the key structures of urinary sphincter and neurovascular bundles. It is likely that erectile dysfunction in particular is highly dependent on preoperative sexual activity status and ability to preserve one or both neurovascular bundles at operation rather than on the type of surgery.[192,206] The reduced risks of rectal injury and anastomotic leak seen with robotic prostatectomy suggest that a greater accuracy of surgical dissection may be achieved. We do not, however, have sufficient comparative data at present on longer-term continence and sexual function rates to determine whether this translates to improved functional outcomes over the standard laparoscopic technique.

Surgeon outcomes

Uptake of robotic technology among surgeons who undertake radical prostatectomy has generally been enthusiastic, particularly in well-funded health-care systems where detection rates for localised prostate cancer are high. The experience from the USA, where 80,000 men underwent radical prostatectomy in 2007, suggests that if urologists have a choice between practising laparoscopic or robotic procedures most will concentrate on the robotic technique.[54] It is unclear how this experience will relate to surgeon preference in countries with lower rates of both use of radical prostatectomy and health-care expenditure. One suggested advantage of the robotic technique is that surgeons may need fewer cases to become fully competent in the procedure as mentoring and learning are facilitated by the console-based surgery.[207] Case series with > 200 men were reviewed together with the previously included comparative studies to ascertain possible learning effects and we found some evidence of improved positive margin rates with increasing experience; however, in contrast to previous studies we found no evidence

of a differential learning effect for surgeons using laparoscopic or robotic techniques – the same learning curve was identified for both procedures. Part of the reason for this may have been our use of a patient-relevant outcome – positive margin rate – rather than operating time or blood transfusion rates, which are more often used for such comparisons. These data are consistent with the suggestion that it is the individual surgeon's rate of learning that is the dominant factor rather than the technology used.[208] The volume of cases was not a confounding factor for the estimation of positive margin rates in the meta-analysis although, as stated above, there was a decrease in positive margin rates with increasing experience when the large case series were included.

Another stated advantage from the surgeon's perspective is the ergonomic advantage of a seated position and scaling of hand movements available with the robotic system, causing less discomfort and a lower risk of chronic cervical pain.[209] To some extent this may relate to operating time. We did find that robotic prostatectomy was 15 minutes quicker on average to perform although the different ways of calculating this measure, in particular whether or not the docking time was included for the robotic procedure, give rise to some uncertainty. This saving of time is too small to allow increased productivity but may facilitate a greater rest period for the robotic surgical team.[210] Perhaps the most technically taxing part of the operation is achieving a watertight sutured join between the bladder neck and proximal urethral stump that remains patent in the longer term. We did find a significantly lower rate of urine leakage immediately postoperatively in the robotic prostatectomy group, suggesting a more reliable anastomosis, but this did not translate into higher rates of bladder neck contracture. Overall, the evidence that the robotic technology improved surgical operative performance for this particular step of the operation is weak.

Cost-effectiveness

No economic evaluations that compared the alternative forms of surgery from a UK perspective were identified and an economic evaluation based on a discrete-event simulation was planned. As described above, the findings of the systematic review were incorporated into the model and as a consequence the key determinants of cost-effectiveness were the time horizon, differences in positive margin rates and the relative costs of equipment. When a lifetime time horizon was adopted the costs and QALYs for both procedures increased but the increase in QALYs more than compensated for the increase in costs and hence the incremental cost per QALY was < £30,000 for all scenarios considered. This includes a scenario in which the number of procedures performed per year was 50 and in which the most costly robotic equipment was used. The principal reason for this is that adopting a longer time horizon allows more time for any benefits of robotic surgery to accrue and offset the initial higher equipment costs. Caution should, however, be exercised in interpreting the results as they rely on the extrapolation of relatively sparse short-term data within the model. There is uncertainty arising from both the quality of data and the mechanism for extrapolation.

The differences in positive margin rates translated into differences in QALYs and costs. For example, a higher positive margin rate resulted in lower QALYs, a greater need for further treatment and hence higher costs. With respect to costs, the cost per procedure was determined by the acquisition cost of the robotic system (which in turn depended on the specification of the equipment and the payment plan) and the number of procedures that might be performed annually using each robotic system. The costs of acquisition are to a certain degree under the control of a centre and depend on their own specific requirements and negotiations with the manufacturer. The number of procedures performed is a function of clinical need in the population that a centre serves and the population size. The results of the economic evaluation suggest that, when the difference in positive margins is equivalent to the point estimate estimated in the meta-analysis of all included studies, robotic radical prostatectomy was on average associated with an incremental cost per QALY that is less than threshold values typically adopted

by the NHS when the cost of acquisition was low or the number of procedures was at the upper end of what could plausibly be achieved under current UK NHS provision (approaching 150 procedures per year).[197] This result holds except when the costs of acquisition were at the upper end of those estimated (see *Appendix 12*). Because the point estimate for difference in positive margin rate was uncertain, sensitivity analysis that progressively changed the difference in rates between robotic and laparoscopic prostatectomy was performed. At more optimistic values (OR = 0.506) the incremental cost per QALY would be less on average than threshold values typically adopted by the NHS when the number of procedures per year approached 100 or the procurement costs were at the lower end of those considered. Not unexpectedly, increasing the OR (OR = 0.955) resulted in a reduction in the QALY gain associated with the use of robotic prostatectomy and an increased cost. With the scenario of an OR for positive margin difference of 0.955 the incremental cost per QALY was only below the threshold if the number of procedures performed using each robotic system was increased to 200 *and* the lowest procurement cost for robotic equipment was assumed.

The mean estimates of incremental cost per QALY presented, although suggestive that robotic radical prostatectomy could potentially be cost-effective at conventional thresholds compared with laparoscopic prostatectomy, do not fully illustrate the degree of imprecision that exists. In the base-case robotic radical prostatectomy had an approximately 80% chance of being cost-effective when the threshold value for a QALY was £30,000.[197] However, caution should be exercised as this result does not incorporate the statistical imprecision surrounding variation in positive margin rates, a key predictor of longer-term outcomes in the model. This indicates the need for further data on the comparative long-term performance of the two forms of surgery. In addition, the sensitivity of estimates from cost-effectiveness for robotic prostatectomy to volume of surgery carried out in each centre argues for careful planning of NHS provision. As an illustration of the current service provision of the 60 UK centres that contributed to the BAUS radical prostatectomy database in 2010, 13 performed > 50 cases per year, of which three performed > 150 cases per year.[201] It should be noted, however, that less invasive management options for localised prostate cancer are emerging, including active surveillance, that may slow the growth in use of radical prostatectomy.[211]

Strengths and weaknesses

Clinical effectiveness

The strength of the study is the systematic approach taken to review the literature. Exhaustive systematic searches were made of the major electronic databases. All potential studies were reviewed for eligibility, including non-English-language publications. The risk of bias for each included study was assessed using the best available tool. To prevent biases caused by selective data extraction all outcome parameters were predetermined by expert panel consensus and any data were extracted using standard forms. Despite these efforts it is possible that some relevant data remained hidden as a result of non-publication.

In total, 54 primary comparative studies were included. Although this haul of relevant studies is impressive, not every study contributed data to each outcome. Furthermore, differences in reporting between studies also limited the opportunities for comprehensive meta-analysis. As a consequence of the limited evidence base, the CIs around many estimates of differences were wide and included differences that would be clinically important but could favour either treatment. Another major limitation resulted from the fact that the majority of comparisons were made against open radical prostatectomy, with few head-to-head comparisons of robotic and laparoscopic technologies. Thus, the estimates generated by the meta-analysis make use of indirect comparisons. The mixed-treatment comparison models used to handle such data

are an effective method of handling evidence from many trials on several interventions in one analysis.[85] Like all analyses they require assumptions to be made that may or may not be reasonable and accordingly the results should be interpreted with a degree of caution. There were 80 non-randomised comparative studies in which the clinical stage of cancer at baseline was unclear, thereby excluding the studies from the review. Although every effort was made to contact the authors of those papers, only 19 replied. The subsequent finding that exclusion of 18 was appropriate provides some reassurance that these studies do not represent a source of missed useable data but there remains a possibility that some were excluded because of their inadequate reporting.

The review attempted to include only unique data from included studies but we experienced difficulty determining secondary publications because of a lack of clarity in reporting details of treatment centres. There were four study sets (Anastasiadis and colleagues[122] and Salomon and colleagues;[140] Ficarra and colleagues[106] and Fracalanza and colleagues;[107] Barocas and colleagues[103] and Chan and colleagues;[119] Greco and colleagues,[129] Jurczok and colleagues[131] and Fornara and colleagues[127]) in which details of the affiliated institute of the first author, type of treatment and treatment dates were similar but it was unclear from the reported text whether or not these studies included an overlap of the same men. It is therefore possible that five studies[107,119,127,131,140] have contributed to an overinclusion of men for some perioperative and efficacy outcomes.

The risk of bias assessment in the conduct of a systematic review is important. For this review a robust combined checklist, developed by the Cochrane Collaboration Non-Randomised Studies Methods Group [Barnaby C, Reeves, Jonathan J, Deeks, Julian PT, Higgins, *et al.* on behalf of the Cochrane Non-Randomised Studies Methods Group. Chapter 13: Including non-randomized studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011)], assessing different sources of bias was produced. A scoring scale approach based on design features was avoided as this has been reported to be inaccurate concerning the direction of bias and can include items that are unrelated to the internal validity of a study.[212] For example, the terms 'prospective study' and 'retrospective study' are particularly ambiguous. 'Prospective study' should imply that all design aspects were planned, including hypothesis generation, recruitment of participants, baseline data collection and outcome data collection. In practice, how prospective a study is can often be unclear as some aspects of a study can be prospective, such as hypothesis generation and determination of outcomes, whereas others are retrospective, such as length of stay data collection from hospital records. The potential for bias in designs with different attributes can therefore vary considerably. This systematic review identified few studies at low risk of bias. The moderate inter-rater agreement between the two independent reviewers that was found in our review illustrates that risk of bias can be interpreted in different ways by different people. This is particularly likely in the newly developing methodological area of summarising non-randomised studies in which the level of reporting is often poor.

Many studies failed to report point estimates and measures of variability, hindering their use in estimating weighted mean differences, which require mean estimates for each intervention and standard deviations. It is possible that if means and standard deviations were reported more consistently, effect sizes would be different. However, in the systematic review, when an appropriate measure of variability was not reported for continuous outcomes, consistency across studies reporting the outcome was investigated and this would serve to eliminate biases when determining the direction of effect, even though the magnitude of effect remains uncertain.

A more specific methodological limitation that frustrated pooled analysis was the use of differing definitions and measures of functional outcomes for both urinary and erectile dysfunction. The

variety of different ways of measuring dysfunction reduced the ability to compare data or to conduct a comprehensive meta-analysis. This was in part reflected by changing measurement methodologies for dysfunction across the time frame over which the studies were conducted, but it will remain a problem until consensus on important outcome measurements in this clinical area can be agreed. Initiatives such as the UK Medical Research Council-funded Core Outcome Measures in Effectiveness Trials (COMET) initiative[213] may be useful in this context. Such initiatives aim to help researchers and clinicians across all specialities to develop a standardised set of outcomes (or core outcomes) that should be measured and reported as a minimum in all clinical trials of a specific condition, in order to make it easier to compare, contrast and synthesise the results of trials, to reduce the risk of inappropriate outcomes being measured and to reduce outcome reporting bias.[214]

The examination of the influence of learning curves on the results was limited by poor reporting in the included studies. Given the general lack of data reported on the experiences of the centres included in the review, a proxy measure of 'experience' was used – namely the number of procedures performed. This measure may be inadequate to detect the differences between the interventions. In addition, when learning curve data were obtained from case series, the reported improvement with increasing experience may have limited applicability to current practice. This is partly because of the early reports of the effects of laparoscopic procedures focusing on refining the technique rather than on the acquisition of the technical skills required to perform the procedure in routine practice. If future studies conform to CONSORT reporting standards for non-pharmaceutical interventions[215] this may help to alleviate some of the problems.

In summary, we believe that we have used the best available techniques to identify, review and meta-analyse the data that were available to us. This approach has enabled us to make robust broad conclusions concerning the relative beneficial and adverse effects of robotic prostatectomy compared with laparoscopic prostatectomy but which are associated with a defined degree of uncertainty.

Discrete-event model and economic evaluation

The economic evaluation was based on a discrete-event model. The purpose of this model was not just to estimate relative cost-effectiveness but also to investigate potential differences in clinical outcome between laparoscopic and robotic radical prostatectomy. As the model is a further level of evidence synthesis that builds on the systematic review and meta-analysis, many of the limitations applicable to the clinical data also apply to the economic data.

The decision context, like many of those faced in the evaluation of health-care interventions, was complex. Within a clinical context there is considerable variation between individuals in terms of demographic status and disease progression. In addition, the range, frequency and management of postoperative adverse events following surgery and the variations required in the care pathways necessitated the use of a more complex model than originally envisaged. The model form adopted was able to incorporate the degree of heterogeneity needed to simulate the life trajectory of individuals following surgery. In developing this model, we did not compromise realism in defining how care was implemented in the model. Elements of care that could occur in a given clinical setting were included insofar as they were recognised by the expert panel of practitioners. This inclusive approach effectively led to a complex suite of pathways that could not be modelled using 'off-the shelf' modelling packages often used in economic evaluations.

The complexity of the model permitted the simulation of a multitude of possible patient trajectories through the model. This can be illustrated by taking the example of a man who presents with a tumour of stage cT1 and undergoes surgery for presumed localised cancer. On pathological examination of the removed prostate it might be found that the tumour margin is

positive but he is counselled to continue under surveillance with regular PSA checks. Happily there is no sign of biochemical recurrence and he remains in the surveillance state until the end of the 10-year time horizon of the study. In a more complex case, a man might remain under surveillance without cancer recurrence but require treatment for urinary dysfunction; he then subsequently requires further treatment for a localised recurrence, which is unfortunately unsuccessful, and he dies of prostate cancer following a period on androgen deprivation therapy. These complexities are required to model the costs and consequences of the differential outcomes of clinical effectiveness found in the systematic review but have the disadvantage of increasing the potential for error and misattribution. To guard against this the longer-term outputs of the model were checked for plausibility and credibility against existing literature sources and the opinions of our expert panel.

The major drivers of model design were heterogeneity in disease status and the requirement to describe realistic care pathways reflecting the range of postoperative adverse events and their treatment. Each health event and postoperative change in management was modelled probabilistically based on available data. As described in *Chapter 5* this involved first defining the risk of an event occurring and then, for each man in a simulated cohort, generating a random number between 0 and 1. If the random number was less than the defined risk then the event was assumed to have occurred for that man. This process inevitably led to a large data requirement and a trade-off between model accuracy and data availability.

The data used within the model came from a number of, often independent, sources, which ranged from quantitative data derived from the systematic review through to qualitative data provided by clinical expert members of our advisory panel. Furthermore, parameter estimates for each event were assumed to be unbiased and representative of the population of men requiring radical prostatectomy for localised prostate cancer in the UK NHS. The use of different data sources, although unavoidable, may have introduced biases into the model estimates as the data came from different samples of the worldwide population of men undergoing radical prostatectomy. Furthermore, it was not always possible to assess the likelihood of non-independence in the parameter estimates. To overcome these limitations the parameters estimates were validated by the expert panel and model output discussed within the project team for clinical plausibility.

To address the imprecision we incorporated estimates of uncertainty for some parameters from the results of the meta-analysis. For other parameters we assumed triangular distributions when we had some information on mid-point and upper and lower limits for parameters and then used sensitivity analysis to investigate the behaviour of the model when we varied parameters for which we had only a point estimate and which were crucial to the model output. The sensitivity of health-related and economic outcomes was explored by determining the impact of varying the two parameters perceived to be of crucial importance to overall outcome: rates of pathological positive margin status and incidence of biochemical recurrence. In the case of positive margin rates the parameter was only one of the inputs used for deciding the need for further cancer treatment postoperatively. This precluded the exploration of imprecision in the probabilistic analysis and therefore this parameter was the focus of extensive deterministic sensitivity analysis.

When considering the impacts of each intervention strategy on health states, further treatment for cancer following radical prostatectomy was estimated as a less frequent event following robotic surgery than following laparoscopic surgery. This resulted in fewer cancer-specific deaths following robotic radical prostatectomy than following laparoscopic radical prostatectomy. The consequence of this was greater QALYs following robotic surgery and it also partly compensated for the increased costs of the robotic equipment.

Despite considerable efforts to elicit relevant information it was not possible to precisely quantify the extra cost of the robotic surgery equipment per procedure. This was because there are a plethora of different procurement strategies provided by the manufacturer, Intuitive Surgical, which varied by both method of payment and specification of equipment. Furthermore, the number of procedures performed each period using a given piece of equipment is variable. In the base case we chose to use the highest procurement cost and the highest plausible throughput of 200 cases per year. Repeating the analysis using lower procurement costs and a reduced number of procedures resulted in variation in the proportion of the cost of the robotic system attributed to each procedure, from £3500 to £10,200 (see *Table 40*). In the base-case analysis, only when the cost was at the higher level determined by a throughput of approximately 150 cases per year was the incremental cost per QALY around £30,000. It should be noted that more favourable assumptions around the positive margin rate tended to reduce the incremental cost per QALY but the incremental cost per QALY would still be > £30,000 for annual throughputs of approximately 100 cases (or a cost of robotic equipment per procedure of approximately £6000). It should also be noted that less favourable but still plausible assumptions concerning the difference in positive margin rates also increased the incremental cost per QALY to > £30,000, particularly when combined with lower throughput of cases. These results indicate that further research is required to more accurately determine positive margin rates and also how they predict long-term cancer outcomes.

In addition to clinical data and costs the model also attempted to incorporate information on the value of different events to the men under treatment – health-state utilities – so that QALYs could be estimated. Searches were conducted to identify data of most relevance to a UK decision-making context but few data were found and not all data were available from a single source. It is possible that we may have misvalued some events, which, if these events occurred at different rates between the two procedures, would have introduced a bias into the analysis. Ideally, health-state utilities data applicable to a UK population should be elicited to overcome this shortcoming.

One aspect of cost not included in the model was the use of unscheduled GP and outpatient visits. There was a lack of data on the frequency of these events with which to model. Previous experience from trials that include men after treatment of prostate cancer would suggest that these costs are relatively modest compared with the cost of surgery. Furthermore, given the apparent lack of difference in effects we did not expect there to be a substantial differential use of these services between groups.

In summary, the discrete-event model attempted to synthesise current clinical practice with the best available estimates of economic and health data to evaluate the potential benefits of robotic prostatectomy in comparison with standard laparoscopic prostatectomy. The model was conservative in that we did not model processes for which we had no evidence of a difference between the two surgical approaches. Furthermore, it did not assume dependence between processes when there was no information available to support a modelled relationship. The model demonstrated that there are circumstances when robotic prostatectomy could be cost-effective as judged against conventional thresholds for willingness to pay for a QALY, especially if lower costs of equipment can be secured and when the surgical capacity is high.

Chapter 8

Conclusions

Implications for health care

There are currently approximately 5000 men who require radical prostatectomy in the UK each year. This number is most likely to increase over the next 5 years as increased detection of localised prostate cancer occurs, associated with more widespread use of PSA testing in the target population.[35] Emergence of less invasive treatments may, however, slow any growth in the use of radical prostatectomy.[211]

The results of this study, although associated with some uncertainty and lack of long-term direct measures of effectiveness, demonstrated that the outcomes were generally better for robotic than for laparoscopic surgery for major adverse events, and importantly for positive margin rates. This may lead to better cancer-related outcomes and fewer episodes of adjuvant radiotherapy for localised recurrence. At worst this review found no evidence to suggest that robotic prostatectomy is inferior to the standard laparoscopic technique.

Robotic prostatectomy will always be more costly to the NHS because of the fixed capital and maintenance charges for the robotic system. Our modelling does show, however, that this excess cost can be reduced by either or a combination of two mechanisms: minimisation of capital costs for purchase and maintenance of the robotic system by commercial negotiation, and maintenance of high usage by ensuring at least 100–150 procedures per year. Our study does provide some evidence that the cost-effectiveness of each procedure is dependent on the volume of cases but there was no evidence that this relationship differed between the procedures. It is self-evident that a higher throughput of cases facilitates training, mentoring and comparative auditing of surgeon performance in a sustainable team-based approach, which is required for effective use of complex equipment.[216]

At present our information suggests that eight centres in the UK NHS achieve these levels of throughput using a varying combination of open, laparoscopic and robotic techniques. It should be noted that surgeon interest in using the robotic system is expanding into renal surgery, gynaecology and complex head and neck surgery, potentially allowing required throughput to be shared between specialties. Offsetting capital costs in this way would have consequences for case volume and may reduce the reliance on high prostatectomy throughput to improve the cost-effectiveness of the robotic technique compared with alternatives.

Implications for research

The main gaps in the evidence base are the lack of direct comparative studies of robotic and laparoscopic prostatectomy with low risk of bias and the lack of longer-term data with more certain measures of cancer control, such as cancer-specific mortality and overall mortality. Given the current increasing adoption of the robotic technology into the NHS, it may be difficult to undertake a randomised comparison against open or laparoscopic prostatectomy in the UK. A feasibility study for such a comparison has been initiated with the support of Cancer Research UK through the LOPERA trial (http://public.ukcrn.org.uk/Search/StudyDetail.

aspx?StudyID=6766). It is at present uncertain whether recruitment trends will be sufficient to encourage a definitive trial.

A brief updated search of abstracts related to robotic prostatectomy only was conducted in November 2011. We identified a further 15 comparative studies of robotic compared with laparoscopic prostatectomy (including one possible RCT), four studies comparing robotic, laparoscopic and open prostatectomy and nine studies comparing robotic and open prostatectomy. Therefore, internationally, there continues to be a number of studies published, suggesting that the trajectory of the evidence base is still upwards. However, the quality of the studies is uncertain and there continues to be a lack of evidence from RCTs. If a formal RCT is not possible then the following are areas in which further research would be important:

- Well-designed prospective cohort studies directly comparing robotic and laparoscopic prostatectomies are required. Ideally such studies would be multicentre with long-term follow-up and would include predefined assessment of prostate cancer-specific survival as well as independent recording of learning curve, dysfunction and health-related quality-of-life measures.
- Further evidence as to how positive margin rates impact on long-term cancer control outcomes.
- Research to elicit the short- and long-term postoperative health-state valuations (e.g. utility values) associated with prostatectomy and the contribution of different dysfunctions as perceived by men.
- Agreed definitions of outcomes in urology and measures for recording them. This would require consensus work in partnership with governing bodies such as BAUS and national initiatives such as COMET.
- Research into strategies to improve planning of evaluation and potential dissemination of costly new technology in the UK NHS.

Acknowledgements

We thank Michael Trevor-Barnston (MBE JP DL), Peter Barton and Prostate UK for providing valuable consumer insight and advice through their participation as members of the study advisory group; Prokar Dasgupta (Professor of Robotic Surgery, Urological Surgeon and Urological Innovation/Consultant), Roger Kockelbergh (BAUS Chairman and Clinical Director of Urology) Alan McNeil (Consultant Urological Surgeon) and Anna O'Riordan (Consultant Urologist) for providing their clinical expertise as members of the project advisory group; Mr David Evans (Laboratory Manager) for providing pathological prostatectomy specimen sampling costing information; Surgical Intuitive Incorporated for providing procurement cost information for the da Vinci surgical robot system; Lara Kemp, Eleanor Lockhart and Winnie Yiu for providing secretarial support; and Graeme MacLennan for providing statistical advice and support.

This report was commissioned by the National Institute for Health Research (NIHR) HTA programme as project number 09/14/02. The Health Services Research Unit is core funded by the Chief Scientist Office of the Scottish Government Health Directorates. The views and opinions expressed are those of the authors and do not necessarily reflect those of the funders.

Contribution of authors

Craig Ramsay (co-principal investigator, Health Care Assessment Programme Director) oversaw and co-ordinated all aspects of the study and wrote the executive summary, the methods and results for the systematic review of clinical effectiveness and the discussion and conclusions chapters. Robert Pickard (co-principal investigator and Professor of Urology) jointly co-ordinated the study with Craig Ramsay, led and co-ordinated the economic evaluation and expert advisory group participation and wrote the background, the description of care pathways and the discussion and conclusions chapters. Clare Robertson (Research Fellow) led the day-to-day running of the study and reviewed the evidence for clinical effectiveness of the technologies with assistance from Tara Gurung (Research Fellow), Xueli Jia (Research Fellow), Graham Mowatt (Senior Research Fellow) and Pawana Sharma (Research Fellow). Andrew Close (Postdoctoral Research Associate) developed the care pathways with clinical advice from Robert Pickard and conducted the economic evaluation with supervision from Luke Vale (Professor of Health Economics), Mark Shirley (Research Associate) and Stephen Rushton (Professor of Biological Modelling). Andrew Close, Mark Shirley, Stephen Rushton, Luke Vale and Robert Pickard wrote the economic evaluation methods and results chapters. Nigel Armstrong (Health Economist) provided advice for conducting the economic evaluation at the start of the study. Daniel Barocas (MD Urologist) provided additional data for the economic evaluation. Cynthia Fraser (Information Specialist) developed and ran the search strategies and was responsible for obtaining full-text papers and for reference management. David Jenkinson (Research Fellow) provided statistical support. Thomas Lam (Senior Specialist Registrar and Honorary Clinical Lecturer) and Justine Royle (Consultant Urological Surgeon) classified reported adverse events into the Clavien–Dindo classification of surgical complications. Mary Robinson (Consultant Urological Pathologist) reviewed the quality of methods described for the handling, processing and pathologist reporting of radical prostatectomy specimens by papers included in the systematic review of clinical effectiveness. Christopher Eden (Consultant Urologist), David Neal (Professor of Surgical Oncology) and Naeem Soomro (Consultant Urologist) provided expert clinical advice on service and surgical aspects. All authors commented on drafts of the report.

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Appendix 1

Protocol

PROTOCOL FOR A SYSTEMATIC REVIEW AND ECONOMIC MODELLING OF THE RELATIVE CLINICAL BENEFIT AND COST-EFFECTIVENESS OF LAPAROSCOPIC SURGERY AND ROBOTIC SURGERY FOR REMOVAL OF THE PROSTATE IN MEN WITH LOCALISED PROSTATE CANCER

1. Background

Prostate cancer causes approximately 13% of cancer-related deaths and 4% of all deaths in the UK with an age-standardised mortality rate of 26/100,000, amounting to 10,000 men each year.[1] In the UK 35,000 new cases were reported in 2005.[1,2] In 1997 the annual cost to the NHS was estimated at £55 million[3] whereas in 2007 the drug cost alone was approximately £130 million[4] and with added costs for surgery, radiotherapy, and hospital and community care the current annual cost is likely to exceed £200 million.

The largest rise in incidence seen recently is among relatively younger men as a consequence of case-finding and screening for asymptomatic disease[5,6] using the serum marker, prostate specific antigen (PSA) and multiple trans-rectal ultrasound (TRUS) guided needle biopsies of the prostate.[5,6] The majority of these asymptomatic cancers appear confined to the prostate on clinical staging and are therefore amenable to cure through radical treatment.

Radical prostatectomy, whereby the prostate is completely removed surgically, remains the favoured curative treatment option for localised prostate cancer and has been demonstrated to improve disease-specific survival compared with watchful waiting, although this benefit takes 10 years to accrue.[7]

Open prostatectomy

Open radical prostatectomy involves the removal of the prostate gland together with the surrounding thin layers of connective tissue and is usually performed through a lower abdominal incision.[8] During the operation care is taken to minimise blood loss and to preserve the normal continence mechanism and, when tumour characteristics allow, the nerves and arteries supplying the penile erectile tissue. Despite this approximately 15% of men require blood transfusion, 7% have long-term urinary incontinence and 40% suffer erectile dysfunction after surgery although surgeons who perform larger numbers of cases tend to have better results.[9,10] These longer-term adverse effects reduce men's general level of well-being and surgeons have therefore sought ways to reduce the functional disturbance of the procedure but maintain its disease-curing potential.[11]

Laparascopic prostatectomy

Laparoscopic prostatectomy involves the insertion of five ports in the abdomen through which long, narrow instruments can be passed together with a camera. The ports are positioned ergonomically to enable the surgeon to dissect the prostate using the instruments with their

handles located outside the body. Increasing experience with the technique has demonstrated that it does result in reduced blood loss compared with open prostatectomy but hoped for reduction in rates of erectile dysfunction and incontinence remains uncertain and is likely to depend on surgeon experience.[12–15]

Robotic prostatectomy

The use of robotic technology allows the surgeon to control the surgical instruments from a console. Robotic prostatectomy involves the preliminary insertion of an umbilical camera port and three other ports for the instruments controlled by the four robotic arms. Additional ports are used for instruments operated by a human assistant and maintenance of pneumoperitoneum. The procedure is then carried out in an identical fashion to laparoscopic prostatectomy but with the surgeon remotely controlling the three or four slave manipulator arms whilst seated at a console which is usually, although not necessarily, sited adjacent to the patient in the operating room.[16] Over recent years there has been a rapid expansion in the availability of the 'da Vinci®' robot to the NHS for radical prostatectomy.[17–19]

Rationale

The main advantage claimed for robotic prostatectomy is a reduction in the learning curve due to increased degrees of freedom of the robotic arms that hold the instruments.[20] However, the impact of this has only been considered in one comparison,[21] in which the authors found that the direct costs associated with robotic procedures decreased substantially once their learning curve of 50 cases had been surpassed. Although the impact of more rapid gaining of competency on outcomes may be small, the impact on operating times, and hence on procedural costs might be significant and contribute to lower procedure costs in higher volume centres.[22,23] There is therefore a clear need to assess the relative clinical benefit and cost-effectiveness of laparoscopic and robotic prostatectomy in men with localised prostate cancer, including differential learning curve effects.

2. Aims and Objectives

The study aims to determine the clinical effectiveness and cost-effectiveness of robotic prostatectomy compared with laparoscopic prostatectomy in the treatment of patients with localised prostate cancer.

The specific objectives of the study are to:

- Describe clinical care pathways for laparoscopic and robotic prostatectomy in a UK context;
- Determine the clinical effectiveness and safety of each procedure;
- Determine the influence of the learning curve on estimates of effectiveness and safety;
- Perform a systematic review of existing economic evaluations of each procedure;
- Determine which procedure is most likely to be cost-effective for implementation into the UK NHS; and
- Identify future research needs.

3. Methods

3.1 Eligibility criteria

Types of study

We will consider evidence from randomised controlled trials (RCTs), non-randomised comparative studies and case series, the latter primarily for estimates of rare adverse events and longer-term effects. For estimating learning curve effects, information on the robotic or laparoscopic arms of comparative studies will be treated as case series. Systematic reviews of open prostatectomy will be considered in order to obtain evidence on the clinical effectiveness of open prostatectomy for the purposes of informing the economic model. We will include conference abstracts and non-English language reports of comparative studies only.

Types of participants

The types of participants considered will be men with localised prostate cancer, defined as cancer confined to the prostate gland and considered curable by radical removal of the prostate.

Types of interventions and comparators

The intervention considered will be robotic prostatectomy and the comparator laparoscopic prostatectomy. Open prostatectomy will also be considered as a comparator in studies comparing robotic prostatectomy with open prostatectomy, or laparoscopic prostatectomy with open prostatectomy, in order that such studies can be included in a mixed treatment comparison model assessing the relative effectiveness of robotic and laparoscopic prostatectomy.

Types of outcome measures

The following types of outcome measures will be considered:

- Cancer related
  - Rate of positive margin in resected specimen, according to consensus definition;[24]
  - Biochemical (PSA) recurrence, defined as two successive PSA levels ≥ 0.4 ng/ml;[25] and
  - Disease free survival, defined as absence of clinically detectable disease.
  - Death
- Functional
  - Recovery of sexual (penile erection) function, quantified by validated score (IIEF-5); and
  - Urinary continence, defined as use of ≤ 1 thin pad per day and/or validated symptom score.
- Adverse events
  - Peri-operative:
    - Blood loss – quantified as transfusion rate;
    - Conversion to open procedure;
    - Delayed discharge; and
    - Death.
  - Long term:
    - Anastomotic stricture.

Two surgeons will categorise each complication using the Clavien–Dindo Classification of Surgical Complications (as detailed in *Chapter 2*, *Table 3*)[26] with a third surgeon acting as arbitrar.

- Procedural
  - Learning curve;
  - Equipment failure;
  - Operative time;

  - Hospital stay; and
  - Duration of catheterisation.
- Patient-driven
  - Pain, quantified by validated pain score and analgesic requirements;
  - Productivity (time to return to full activity); and
  - Generic and disease-specific quality of life, measured through validated quality of life scores.

Exclusion criteria

The following types of report will be excluded:

- Studies of men with metastatic disease;
- Case series of open prostatectomy.

3.2 Search strategy

Comprehensive electronic searches will be conducted to identify reports of published studies. Highly sensitive search strategies will be designed, including appropriate subject headings and text word terms, interventions under consideration and included study designs. There will be no language restriction but searches will be restricted to years from 1995 onwards, reflecting the introduction of the techniques. Medline, Medline In Process, Embase, CINAHL, Biosis, Science Citation Index, Cochrane Controlled Trials Register (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Review of Effects (DARE) and the HTA databases will be searched. Reference lists of all included studies will be scanned in order to identify additional potentially relevant reports. We will also ask our expert panels to provide details of any additional potentially relevant reports.

Conference abstracts for the years 2006 onwards from meetings of the European, American and British Urological Associations will be searched. Ongoing studies will be identified through searching Current Controlled Trials, Clinical Trials, NIHR Portfolio and WHO International Clinical Trials Registry. Websites of manufacturers, professional organisations, regulatory bodies and the HTA will be checked to identify unpublished reports.

3.3 Quality assessment

We will use a modified version of the Cochrane risk of bias tool[27] which we have adapted to include potential topic-specific confounders, which were identified through discussions with members of our project advisory group and our knowledge of existing literature. The topic-specific confounders related to specific outcomes as shown in the modified risk of bias tool (see *Appendix 4*). Three sets of two reviewers will independently assess the risk of bias of included full text studies, with the exception of non-English publications and conference abstracts. Any differences in assessment or issues of uncertainty will be resolved by discussion and consensus. For the risk of bias tool individual outcomes will be scored as High risk of bias, Low risk of bias or Unclear. Any disagreements will be resolved by consensus or by a third party.

3.4 Data extraction

Three reviewers will independently screen titles and abstracts of all identified items. Full text copies of all potentially relevant reports will be obtained and independently assessed by two reviewers to determine whether they meet inclusion criteria. Three reviewers will independently extract details of study design, methods, participants, interventions and outcomes onto a data extraction form (see *Appendix 3*). Each reviewer's data extraction will be independently checked by a second reviewer for errors or inconsistencies. Any disagreements will be resolved through consensus or arbitration by a third party.

3.5 Data analysis

Data from each study will be tabulated and summarised for each procedure in a form appropriate for the mixed treatment comparison model. The lack of RCT evidence precludes undertaking a standard meta-analysis. Therefore we intend to adopt an indirect comparison (cross design) approach allowing inclusion of non-randomised comparative data and case series.[28] Reasons for heterogeneity of effects will be explored, including differences in populations, studies, outcome assessment and learning curve effects. We will examine heterogeneity between and within different study designs using a Bayesian hierarchical random effects model enabling use of all available evidence.[29]

We will use a previously successful approach developed by members of our project team to estimate the learning effects on key outcomes.[30] The expertise of the participating surgeons or centres in each included study will first be categorised by previous experience. Data on the three key features of learning, starting level, rate of learning and expert level, will then be extracted. A random effects meta-analysis will be performed to estimate the pooled effect of the key features together with an appropriate measure of uncertainty. These estimates will be used to determine the likely 'shape' of the learning curve and will be validated by our experienced and novice clinical experts. The pooled data will be used firstly to investigate heterogeneity of effects on the key outcomes in the systematic review of effectiveness and secondly to inform the economic modelling on the likely change over time on the key outcomes and patient mix. This approach will account for possible differences in an individual surgeon's learning curve for particular outcomes.

4. Cost-effectiveness

4.1 Systematic review of economic evaluations

Given that the results of any economic evaluation are particular to setting and time the main purpose of a review is to inform the modelling methodology and any parameter sources. This does not require a systematic review, but a review of *key sources*, i.e. those with a signal of high quality such as HTA reports. Therefore, there will be two reviews, a systematic one detailed below to identify the current status of the evidence on the technologies of interest and one of HTA reports, their citations and sources citing them looking at any technology for prostate cancer that uses modelling.

Search strategy

Highly sensitive search strategies will be designed to identify any economic evaluations where at least one of the technologies was laparoscopic or robotic surgery for prostate cancer. The following databases will be searched without language restriction for the years 1995 onwards: NHS EED, HTA Database, Medline, Medline In Process, Embase, Science Citation Index and Health Management Information Consortium (HMIC) database. Websites of HTA organisations will be consulted for additional reports. Reference lists of all included studies will be scanned and appropriate experts will be contacted for details of additional reports.

Quality assessment

Quality will be assessed according to the BMJ criteria, on which the NHS EED abstracts were largely based.[31]

Data extraction

Two reviewers will independently screen the titles and abstracts of all items identified by the search strategy. Full text copies of all potentially relevant reports will be obtained and assessed by two reviewers independently against the inclusion criteria. Any disagreements will be resolved

by consensus or arbitration by a third person. Two reviewers will independently extract details of study design such as economic perspective and type of analysis, methods such as model structure and costing, population, technologies, and outcomes such as QALYs onto specific data extraction forms in line with the NHS EED abstracts.

Reporting

Summaries of all studies will be tabulated. A brief critique according to model structure, paramaterisation and dealing with uncertainty will then be performed to identify methods that can be used together with limitations and recommendations for improvement that can be taken forward to the proposed model. Any sources of evidence of possible use in the proposed model will be recorded and reviewed by the research team.

4.2 Economic evaluation

Implications for the economic analysis

As no prior economic evaluation has been conducted from the perspective of the UK NHS we propose to construct a decision analytic model (DAM) comparing the cost-effectiveness of the two surgical techniques, which will make the best use of the evidence obtained from the systematic review[32] A novel aspect of this work will be the emphasis on the learning curves for surgical procedures and economies of scale from changes in centre volumes which are likely to drive differences in costs for the considered technologies, something that in a typical CEA as recommended by NICE[33] might be ignored. These particular facets are likely to be instrumental in driving differences in costs for the considered technologies and therefore need to be accorded greater weight in the analysis. In addition to this the impact of capital costs (approximately £1.5 million) and maintenance costs (approximately £150,000/year) for robotic prostatectomy are likely to be significant, particularly in lower volume centres. Changes from the recommended standard procedure would take time to implement, and require more intensive re-training involving use of mentors which, although associated with a briefer learning curve,[34] may have additional resource implications and therefore require consideration in the model.

Model structure

In order to incorporate the effect of disease progression and possible need for subsequent treatments for each patient undergoing laparoscopic or robotic prostatectomy, a state transition model will be used which estimates consequences for a cohort beginning treatment at the same time. However, in order to estimate effects due to the learning curves for laparoscopic and robotic techniques a multiple cohort analysis will be used.[35,36] Such an approach, by allowing for changing numbers of patients eligible for surgery over time, also permits estimation of capital outlay as a function of demand, which was the approach used in a previous model.[37] However, even if demand remains constant, it also allows availability of technology, which is a function of surgeon competence, to be expressed as a function of patient numbers. This also enables consideration of the most efficient number of treatment centres. A multiple cohort approach additionally allows for population heterogeneity in age; those who are eligible for treatment will vary by age[38] requiring the introduction of one cohort per age band per year. Although the technologies will be assumed to have a finite lifetime decided by manufacturer and clinical expert opinion and tested in a sensitivity analysis, each individual cohort will be followed up for various periods including the duration of patient lifetime in order to account for consequences for that cohort.[39]

The design for the state transition model* used for each cohort was informed by expert opinion and published models of the progression of prostate cancer.[40–42] Patient eligibility is defined according to:

1. Male.
2. Cancer localised to prostate

[*Please note that during consultation with the advisory group the modelling approach was changed to a discrete-event simulation model. Full details and rationale in *Chapter 5*, *Introduction*.]

These criteria, including age will thus define an initial pre-operative state. A patient will then undergo one of the procedures whereby a set of short-term complications can occur according to corresponding probabilities each of which are assumed to be resolved within a the cycle time of 3 months. Micro-simulation[43] will be used to analyse the model whereby an individual follows a random path over a lifetime using Monte Carlo Simulation (MCS). This reduces the need to define a separate health state of each of the set of criteria used to define a health state, e.g. presence or absence of each complication. Therefore, subsequent health states will be defined according to the following set of state variables:

1. Age
2. Margin (positive or negative)
3. Postoperative Gleason score (high or low)
4. Recurrence (none, local, systemic)
5. Erectile dysfunction (present or not)
6. Urinary incontinence (present or not)

Therefore transition probabilities (probability of moving to some health state in 3 months given current health state) will be defined according to the status of each of the state variables. For example, mortality rate increases with age and type of recurrence. Also, as can be seen in the care pathway, further treatments also depend on state variables so that, for example, the presence of urinary incontinence implies treatment for this condition. Postoperative evaluation of the surrounding tissue may lead to further treatment conditional on determining a positive or negative margin (*Fig. 2*). Where tissue margins are observed to be positive, then Gleason scores are used to identify an appropriate treatment within the pathway. Patients with high Gleason scores are immediately referred for further cancer treatment, whereas patients exhibiting low Gleason scores are monitored for Biochemical recurrence. Should biochemical recurrence be observed, patients may then devolve to additional treatment for cancer, otherwise surveillance will continue. Patients with a negative margin will be referred for surveillance with the possibility of further cancer treatment if necessary.

Pathways for treatments available to patients with prostate cancer are described in *Figure 3*. The treatment of localised cancers devolves into curative or palliative sub-pathways. Each sub-pathway may then lead to dysfunctions associated with the underlying condition and treatment. Ultimately, patients will reach a state of resolution or death. In the case of resolution of cancer, patients may then still be treated for the presence of one or more dysfunctions (*Fig. 4–5*). Patients may suffer from one or more dysfunctions simultaneously. In either case, interventions strategies may vary according to the severity of dysfunction. Ultimately, a patient may recover or reach a persistent state.

The economic perspective will be that of the United Kingdom National Health Service and discounting in the base case will be at 3.5%.[33] All modelling will pay attention to best practice[44] and guidance from the project expert advisory group. The model will be constructed in two software packages according to best practice[44] in C for speed and flexibility and TreeAge for presentation including any sensitivity analysis on demand.

[Please note that during consultation with the advisory group the modelling approach was changed to a discrete-event simulation model. Full details and rationale are given in *Chapter 5*, *Introduction*.]

Costing

Given the variation in costs due to learning and requirement for capital expenditure, it is essential to estimate the independent effect of staffing, equipment and overheads. As described above, some costs will be incurred as each patient progresses through the care pathway and thus would count as *variable* (with demand). However, a machine (and any additional building space) must be purchased regardless of numbers to be treated at least beyond the capacity of any existing machine. Therefore such a cost is fixed at least in the short term. The most appropriate sources will be used for each of these, such as expert opinion to determine appropriate staff mix, the systematic review to estimate operation times and length of stay as a function of technology, and purchase/maintenance costs from manufacturers and local users and their finance departments. Unit costs will be taken from appropriate routine sources for staffing,[45] *British National Formulary* for drugs, and from equipment manufacturers. Variability in parameters will be tested by one-way sensitivity analyses.

Utilities

A cost utility analysis (CUA) will be performed with outcomes estimated in quality-adjusted life years (QALYs).[46] Each health state of the state transition model will require a utility estimated using the best available data, ideally derived using EQ-5D.[47–50] If necessary, plausible assumptions will be made in order to use utility values derived from different patient population (e.g. using an additive model to combine the effects of disease progression and adverse events in one age group to estimate the effect in a different age group).

Epidemiology

Two main items of epidemiological data are required for the economic model: one at the individual level to estimate the transition probabilities of the state transition model and another at the population level for the incidence of eligible patients. The former will be based on data from the systematic review and include any effect of surgeon experience/learning. The latter will be informed by incidence data and any likely trends informed by expert opinion. Each parameter will correspond to transitions between states in the model, such as from first treatment to remission.

Uncertainty

Deterministic sensitivity analyses will be carried out to test for the effect of assumptions and variability.[51] Costs and QALYs will be estimated as the expectation over the joint distribution of the parameters, informed from the systematic review, other sampling distributions or expert opinion according to best practice. Any correlations, informed where possible by the systematic review, will be incorporated. A probabilistic sensitivity analysis will also be undertaken allowing presentation of results in a series of cost-effectiveness acceptability curves (CEAC) and the construction of the cost-effectiveness acceptability frontier (CEAF) for various threshold values of the willingness to pay (WTP) for a QALY.[52]

Identification of future research needs

A value of information analysis[53] will be conducted to identify the expected value of perfect information (EVPI) over the expected lifetime of the considered procedures and the value of further research to identify more precise and reliable estimates of parameters used in the model.

5. Timescale

Start of project: 1st March 2010

Develop protocol and data extraction form: March – April 2010

Run search strategies: April 2010

Assess studies for inclusion: April – June 2010

First expert panel meeting: May 2010

Data extraction and quality assessment: July – September 2010

First progress report: 10 October 2010

Data analysis: October – December 2010

Second expert panel meeting: February 2011

Economic modelling: May 2010 – March 2011

Second progress report: February 2011

Report writing: January – April 2011

Report submission: 16th May 2011

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Appendix 2

Search strategies

Clinical effectiveness of robotic compared with laparoscopic techniques

MEDLINE (1966–October week 3 2010), EMBASE (1980–2010 week 42) (MEDLINE In-Process & Other Non-Indexed Citations 25 October 2010)

Ovid Multifile Search URL: https://shibboleth.ovid.com/

1. exp prostatic neoplasms/su use mesz
2. exp prostate cancer/su use emez
3. prostatectomy/
4. (radical adj5 prostatectom$).tw.
5. or/1-4
6. prostatic neoplasms/ use mesz
7. exp prostate cancer/ use emez
8. (cancer adj3 (prostate or prostatic)).tw.
9. (carcinoma adj3 (prostate or prostatic)).tw.
10. (neoplas$ adj3 (prostate or prostatic)).tw.
11. (malignan$ adj3 (prostate or prostatic)).tw.
12. or/6-11
13. surgical procedures,operative/ use mesz
14. surgery/ use emez
15. su.fs.
16. (surgery or surgical or surgeon$).tw.
17. (resect$ or operation$ or operat$).tw.
18. or/13-17
19. 12 and 18
20. 5 or 19
21. laparoscopy/
22. laparoscopic surgery/ use emez
23. endoscopy/
24. video-assisted surgery/
25. surgical procedures, minimally invasive/ use mesz
26. minimally invasive surgery/ use emez
27. laparoscop$.tw.
28. endoscop$.tw.
29. (minimal$ adj3 (invasiv$ or access$)).tw.
30. (key hole or keyhole or robot$).tw.
31. video assist$.tw.
32. (trans peritoneal or transperitoneal or extra peritoneal).tw.
33. (montsouris or heilbronn).tw.
34. (da vinci or zeus).tw.
35. or/21-34
36. 20 and 35
37. meta-analysis.pt.

38. review.pt.
39. meta-analysis/
40. systematic review/
41. randomized controlled trials/
42. (controlled or design or evidence or extraction).ab.
43. (sources or studies).ab.
44. or/37-43
45. exp clinical trial/
46. randomized controlled trial.pt.
47. controlled clinical trial.pt.
48. randomization/ use emez
49. randomi?ed.ab.
50. placebo.ab.
51. drug therapy.fs.
52. randomly.ab.
53. trial.ab.
54. groups.ab.
55. or/45-54
56. comparative study/ use mesz
57. follow-up studies/ use mesz
58. time factors/ use mesz
59. Treatment outcome/ use emez
60. major clinical study/ use emez
61. controlled study/ use emez
62. clinical trial/ use emez
63. (preoperat$ or pre operat$).mp. use mesz
64. (chang$ or evaluat$ or reviewed or baseline).tw.
65. (prospective$ or retrospective$).tw. use mesz
66. (cohort$ or case series).tw. use mesz
67. (compare$ or compara$).tw. use emez
68. or/56-67
69. 36 and (44 or 55 or 68)
70. animals/ not (humans/ and animals/)
71. nonhuman/ not (human/ and nonhuman/)
72. 69 not (70 or 71)
73. limit 72 to yr="1995-2010"
74. remove duplicates from 73

Science Citation Index (1995–23 October 2010), BIOSIS (1995–19 October 2010)

ISI Web of Knowledge URL: http://wok.mimas.ac.uk/

#1 TS=prostatectomy

#2 TS= (cancer SAME (prostate or prostatic))

#3 TS= (carcinoma SAME (prostate or prostatic))

#4 TS= (neoplas* SAME (prostate or prostatic))

#5 TS= (malignan* SAME (prostate or prostatic))

#6 #2 or #3 or #4 or #5

#7 #6 and TS=surgery

#8 #6 and TS=surgical

#9 #6 and TS=resect*

#10 #6 and TS=operat*

#11 #1 OR #7 OR #8 OR #9 OR #10

#12 #11 and TS=laparoscop*

#13 #11 and TS=endoscop*

#14 #11 and TS=(key hole or keyhole or robot*)

#15 #11 and TS=(minimal* SAME (invasive* or access*))

#16 #11 and TS=video assist*

#17 #11 and TS=(trans peritoneal or transperitoneal or extra peritoneal)

#18 #11 and TS=(montsouris or heilbronn or da vinci or zeus)

#19 #12 or #13 or #14 or #15 or #16 or #17 or #18

#20 #19 and TS=trial*

#21 #19 and TS=random*

#22 #19 and TS=(compare or comparative or comparison)

#23 #19 and TS=evaluat*

#24 #19 and TS=cohort

#25 #19 and TS=case series

#26 #19 and TS=meta analysis

#27 #19 and TS=review*

#28 #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27

The Cochrane Library (CDSR Issue 10 2010, CENTRAL Issue 4 2010)

URL: http://www3.interscience.wiley.com/

#1 MeSH descriptor Prostatic Neoplasms explode all trees with qualifier: SU

#2 MeSH descriptor Prostatectomy, this term only

#3 (radical NEAR prostatectom*)

#4 (#1 OR #2 OR #3)

#5 MeSH descriptor Prostatic Neoplasms explode all trees

#6 (cancer NEAR/3 (prostate or prostatic))

#7 (carcinoma NEAR/3 (prostate or prostatic))

#8 (neoplas* NEAR/3 (prostate or prostatic))

#9 (malignan* NEAR/3 (prostate or prostatic))

#10 (#5 OR #6 OR #7 OR #8 OR #9)

#11 MeSH descriptor Surgical Procedures, Operative, this term only

#12 Any MeSH descriptor with qualifier: SU

#13 (surgery or surgical or surgeon*)

#14 (resect* or operation* or operat*)

#15 (#11 OR #12 OR #13 OR #14)

#16 (#10 AND #15)

#17 (#4 OR #16)

#18 MeSH descriptor Laparoscopy, this term only

#19 MeSH descriptor Endoscopy, this term only

#20 MeSH descriptor Video-Assisted Surgery, this term only

#21 MeSH descriptor Surgical Procedures, Minimally Invasive, this term only

#22 (laparoscop*) or (endoscop*) or (minimal* NEAR/3 (invasiv* OR access*)) or (key hole or keyhole) or (video assist*) or (robot*)

#23 (trans peritoneal OR transperitoneal) or (extra peritoneal) or (montsouris or heilbronn) or (da vinvi or zeus)

#24 (#18 OR #19 OR #20 OR #21 OR #22 OR #23)

#25 (#17 AND #24)

HTA/DARE (October 2010)

Centre for Reviews and Dissemination URL: http://nhscrd.york.ac.uk/welcome.htm

#1 MeSH prostatic neoplasms QUALIFIERS SU EXPLODE 1 2 3 4

#2 MeSH prostatectomy EXPLODE 1

#3 MeSH prostatic neoplasms EXPLODE

#4 surg* or laparoscop* or robot*

#5 (#2 or #3)

#6 #4 and #5

#7 #1 or #6

ClinicalTrials.gov (October 2010)

URL: http://clinicaltrials.gov/ct/gui/c/r

Condition=prostatic neoplasms AND (laparoscop* or robot*)

Current Controlled Trials (October 2010)

URL: www.controlled-trials.com/

Prostat% and (laparoscop% or robot%)

International Clinical Trials Registry Platform (ICTRP) (October 2010)

World Health Organization URL: www.who.int/ictrp/en/

Prostat* and (laparoscop* or robot*)

NIH RePORTER (October 2010)

URL: http://projectreporter.nih.gov/reporter.cfm

Prostat% and laparoscop%

Prostat% and robot%

Conference proceedings

American Society of Clinical Oncology (URL: www.asco.org)

Annual Meeting, Chicago, IL, 1–5 June 2007

Annual Meeting, Chicago, IL, 30 May–2 June 2008

Annual Meeting, Orlando, FL, 29 May–2 June 2009

Annual Meeting, Chicago, IL, 4–8 June 2010

American Urological Association (URL: www.auanet.org/)

Annual Meeting, Orlando, FL, 12–22 May 2008

Annual Meeting, Chicago, IL, 25–30 April 2009

Annual Meeting, San Francisco, CA, 29 May–3 June 2010

British Association of Urological Surgeons (URL: www.baus.org.uk/)

Annual Scientific Meeting, Manchester, UK, 23–27 June 2008.

Annual Scientific Meeting, Glasgow, UK, 22–25 June 2009

Annual Scientific Meeting, Manchester, UK, 21–24 June 2010

European Association of Urology (URL: www.uroweb.org/)

22nd Annual Congress, Berlin, Germany, 21–24 March 2007

23rd Annual Congress, Milan, Italy, 26–29 March 2008

24th Annual Congress, Stockholm, Sweden, 17–21 March 2009

25th Annual Congress, Barcelona, Spain, 16–20 April 2010

European Robotic Urology Symposium, Bordeaux, France, 29 September–1 October 2010

Websites consulted

American Society of Clinical Oncology (URL: www.asco.org)

American Urological Association (URL: www.auanet.org/)

British Association of Urological Surgeons (URL: www.baus.org.uk/)

Cancer Research UK (URL: http://info.cancerresearchuk.org/cancerstats/)

European Association of Urology (URL: www.uroweb.org/)

Intuitive Surgical – da Vinci prostatectomy (URL: www.davinciprostatectomy.com/)

Cost-effectiveness of robotic compared with laparoscopic techniques

MEDLINE (1966–October week 4 2010), EMBASE (1980–2010 week 43) (MEDLINE In-Process & Other Non-Indexed Citations 3 November 2010)

Ovid Multifile Search URL: https://shibboleth.ovid.com/

1. exp prostatic neoplasms/su use mesz
2. exp prostate cancer/su use emez
3. prostatectomy/
4. (radical adj5 prostatectom$).tw.
5. or/1-4
6. prostatic neoplasms/ use mesz

7. exp prostate cancer/ use emez
8. (cancer adj3 (prostate or prostatic)).tw.
9. (carcinoma adj3 (prostate or prostatic)).tw
10. (neoplas$ adj3 (prostate or prostatic)).tw.
11. (malignan$ adj3 (prostate or prostatic)).tw.
12. or/6-11
13. surgical procedures,operative/ use mesz
14. surgery/ use emez
15. su.fs.
16. (surgery or surgical or surgeon$).tw.
17. (resect $ or operation$ or operat$).tw.
18. or/13-17
19. 12 and 18
20. 5 or 19
21. laparoscopy/
22. laparoscopic surgery/ use emez
23. endoscopy/
24. video-assisted surgery/
25. surgical procedures, minimally invasive/ use mesz
26. minimally invasive surgery/ use emez
27. laparoscop$.tw.
28. endoscop$.tw.
29. (minimal adj3 (invasiv$ or access$)).tw.
30. (key hole or keyhole or robot$).tw.
31. video assist$.tw
32. (trans peritoneal or transperitoneal or extra peritoneal).tw.
33. (montsouris or heilbronn).tw.
34. (da vinci or zeus).tw.
35. or/21-34
36. 20 and 35
37. exp "costs and cost analysis"/
38. exp economic evaluation/ use emez
39. economics
40. exp economics,hospital/
41. exp economics,medical/
42. economics,pharmaceutical/
43. exp budgets/
44. exp models, economic/
45. exp decision theory/
46. ec.fs. use mesz
47. monte carlo method/
48. markov chains/
49. exp technology assessment, biomedical/
50. cost$.ti.
51. (cost$ adj2 (effective$ or utilit$ or benefit$ or minimis$)).ab.
52. economics model$.tw.
53. (economics$ or pharmacoeconomic$ or pharmo-economic$).ti.
54. (price$ or pricing$).tw.
55. (financial or finance or finances or financed).tw.
56. (value adj2 (money or monetary)).tw.
57. markov$.tw.

58. monte carlo.tw.
59. (decision$ adj2 (tree? or analy$ or model$)).tw.
60. or/37-59
61. 36 and 60
62. remove duplicates from 61

Science Citation Index (1995–30 October 2010)

ISI Web of Knowledge URL: http://wok.mimas.ac.uk/

#1 TS=prostatectomy

#2 TS=(cancer SAME (prostate or prostatic))

#3 TS=(cancinoma SAME (prostate or prostatic))

#4 TS=(neoplas* SAME (prostate or prostatic))

#5 TS=(malignan* SAME (prostate or prostatic))

#6 #2 or #3 or #4 or #5

#7 #6 and TS=(surgery or surgical)

#8 #6 and TS=(resect* or operat*)

#9 #1 or #7 or #8

#10 #9 AND TS=LAPAROSCOP*

#11 #9 AND TS=endoscop*

#12 #9 AND TS=(keyhole or key hole or robot*)

#13 #9 AND TS=(minimal* SAME (invasive* or access*))

#14 #9 AND TS=video assist*

#15 #9 AND TS=(montsouris or heilbronn or da vinci or zeus)

#16 #10 or #11 or #12 or #13 or #14 or #15

#17 TS=(cost* SAME effective*)

#18 TS=(cost* SAME benefit*)

#19 TS=(cost* SAME (utility or utilities))

#20 TS=(cost* SAME (minimis* or minimiz*))

#21 TS=economic*

#22 TS=(price OR pricing)

#23 TS=(financial OR finance OR finances OR financed)

#24 TS=(value SAME (money OR monetary))

#25 TS=(markov OR monte carlo)

#26 TS=(decision SAME (tree* OR analy* OR model*))

#27 #16 AND (#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #25 OR #26)

Health Management Information Consortium (1979–October 2010)

Ovid Multifile Search URL: http://gateway.ovid.com/athens

1. prostate cancer/
2. prostatectomy/
3. (radical adj5 prostatectom$).tw.
4. ((prostate or prostatic) adj3 (cancer or carcinoma or neoplas$ or malignan$ or tumo?r$)).tw.
5. or/1-4
6. minimally invasive therapy/
7. laparoscop$.tw.
8. (key hole or keyhole or robot$).tw.
9. (minimal$ adj3 (invasiv$ or access$)).tw.
10. video assist$.tw.
11. (da vinci or zeus).tw.
12. (montsouris or heilbronn).tw.
13. or/6-12
14. 5 and 13

NHS Economic Evaluation Database (October 2010)

Centre for Reviews and Dissemination URL: http://nhscrd.york.ac.uk/welcome.htm

#1 MeSH prostatic neoplasms QUALIFIERS SU EXPLODE

#2 MeSH prostatectomy EXPLODE

#3 MeSH prostatic neoplasms EXPLODE

#4 surg* or laparoscop* or robot*

#5 (#2 or #3)

#6 #4 and #5

#7 #1 or #6

Quality of life for robotic compared with laparoscopic techniques

MEDLINE (1966–October week 4 2010), EMBASE (1980–2010 week 43) (MEDLINE In-Process & Other Non-Indexed Citations 3 November 2010)

Ovid Multifile Search URL: https://shibboleth.ovid.com/

1. exp prostatic neoplasms/su use mesz
2. exp prostate cancer/su use emez
3. prostatectomy/
4. (radical adj5 prostatectom$).tw.
5. or/1-4
6. prostatic neoplasms/ use mesz
7. exp prostate cancer/ use emez
8. (cancer adj3 (prostate or prostatic)).tw.
9. (carcinoma adj3 (prostate or prostatic)).tw
10. (neoplas$ adj3 (prostate or prostatic)).tw.
11. (malignan$ adj3 (prostate or prostatic)).tw.
12. or/6-11
13. surgical procedures,operative/ use mesz
14. surgery/ use emez
15. su.fs.
16. (surgery or surgical or surgeon$).tw.
17. (resect $ or operation$ or operat$).tw.
18. or/13-17
19. 12 and 18
20. 5 or 19
21. laparoscopy/
22. laparoscopic surgery/ use emez
23. endoscopy/
24. video-assisted surgery/
25. surgical procedures, minimally invasive/ use mesz
26. minimally invasive surgery/ use emez
27. laparoscop$.tw.
28. endoscop$.tw.
29. (minimal adj3 (invasiv$ or access$)).tw.
30. (key hole or keyhole or robot$).tw.
31. video assist$.tw
32. (trans peritoneal or transperitoneal or extra peritoneal).tw.
33. (montsouris or heilbronn).tw.
34. (da vinci or zeus).tw.
35. or/21-34
36. 20 and 35
37. quality of life/
38. quality adjusted life year/
39. "Value of Life"/ use mesz
40. health status indicators/ use mesz
41. health status/ use emez
42. sickness impact profile/ use mesz
43. disability evaluation/ use mesz
44. disability/ use emez
45. activities of daily living/ use mesz

46. exp daily life activity/ use emez
47. cost utility analysis/ use emez
48. rating scale/
49. questionnaires/
50. (quality adj1 life).tw.
51. quality adjusted life.tw.
52. disability adjusted life.tw.
53. (qaly? or qald? or qale? or qtime? or daly?).tw.
54. (euroqol or euro qol or eq5d or eq 5d).tw.
55. (hql or hqol or h qol or hrqol or hr qol).tw.
56. (hye or hyes).tw.
57. health$ year$ equivalent$.tw.
58. (hui or hui1 or hui2 or hui3).tw.
59. (health adj3 (utilit$ or disutili$)).tw.
60. (health adj3 (state or status)).tw.
61. (sf36 or sf 36 or short form 36 or shortform 36).tw.
62. (sf6 or sf 6 or short form 6 or shortform 6).tw.
63. (sf12 or sf 12 or short form 12 or shortform 12).tw.
64. (sf16 or sf 16 or short form 16 or shortform 16).tw.
65. (sf20 or sf 20 or short form 20 or shortform 20).tw.
66. willingness to pay.tw.
67. standard gamble.tw.
68. trade off.tw.
69. conjoint analys?s.tw.
70. discrete choice.tw.
71. or/37-70
72. (case report or editorial or letter).pt.
73. case report/
74. 71 not (72 or 73))
75. 36 and 74
76. remove duplicates from 75

Science Citation Index (1995–30 October 2010)

ISI Web of Knowledge URL: http://wok.mimas.ac.uk/

#1 TS=prostatectomy

#2 TS=(cancer SAME (prostate or prostatic))

#3 TS=(cancinoma SAME (prostate or prostatic))

#4 TS=(neoplas* SAME (prostate or prostatic))

#5 TS=(malignan* SAME (prostate or prostatic))

#6 #2 or #3 or #4 or #5

#7 #6 and TS=(surgery or surgical)

#8 #6 and TS=(resect* or operat*)

#9 #1 or #7 or #8

#10 #9 AND TS=LAPAROSCOP*

#11 #9 AND TS=endoscop*

#12 #9 AND TS=(keyhole or key hole or robot*)

#13 #9 AND TS=(minimal* SAME (invasive* or access*))

#14 #9 AND TS=video assist*

#15 #9 AND TS=(montsouris or heilbronn or da vinci or zeus)

#16 #10 or #11 or #12 or #13 or #14 or #15

#17 TS=quality of life

#18 TS=quality adjusted life

#19 TS=disability adjusted life

#20 TS= (qaly* OR qald* OR qale* OR qtime* OR daly)

#21 TS=(euroqol* OR euro qol* OR eq5d OR eq 5d)

#22 TS=(hql OR hqol OR h qol OR hrqol OR hr qol)

#23 TS=health* year* equivalent*

#24 TS=(hye OR hyes OR hui OR hui1 OR hui2 OR hui3)

#25 TS=(health utilit* OR disutilit*)

#26 TS=willingness to pay

#27 TS=standard gamble

#28 TS=discrete choice.

#29 TS=trade off

#30 TS= conjoint analys*

#31 #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30

#32 #16 and #31

IDEAS (October 2010)

RePeC URL: http://ideas.repec.org/

(prostate | prostatic) + cancer

Appendix 3

Data extraction form

Data Extraction Form

Clinical effectiveness of robotic prostatectomy versus laparoscopic prostatectomy in the treatment of localised prostate cancer

Reviewer ID: Data extraction date:

Study ID (Author, year): Language if non-English:

Publication status: full-text papers / conference abstract / personal communication / other unpublished reports (specify)

Study IDs of any linked reports:

Study design

Aim of the study:

Study design:

☐ RCT ☐ Non-randomised comparative study ☐ Registry report

☐ Case Series ☐ Prospective ☐ Retrospective ☐ Unclear

☐ Systematic review (open prostatectomy)

For comparative studies, comparison:

☐ Robotic prostatectomy *versus* laparoscopic prostatectomy

☐ Robotic prostatectomy *versus* open prostatectomy

☐ Laparoscopic prostatectomy *versus* open prostatectomy

☐ Other comparison, specify:

For case series or registry, intervention:

☐ Robotic prostatectomy

☐ Laparoscopic prostatectomy

Number of study centres: Single centre / multicentre (specify number of centres) / not reported

Setting: hospital / other (specify) Country:

Study start – end dates: Duration of study:

For non-RCTs and case series, was patient recruitment consecutive: Yes /No / not reported

Length of follow-up:

Source of funding:

Additional information on study design:

Prospective/retrospective/not reported

For comparative studies, patients in the groups were recruited during the same period/different period/not reported

Patients				
Inclusion criteria:				
Exclusion criteria:				
Baseline Patient Characteristics				
	Intervention 1: **Robotic**	Intervention 2: **Laparoscopic**	Intervention 3: **Open**	Total
Number of patients enrolled				
Randomised (RCTs only)				
Withdrew/lost to follow-up, with reasons				
Number analysed				
Age (Mean/median, SD/range)				
BMI (Mean/median, SD/range)				
Co-morbidities, including previous abdominal or pelvic surgery, previous pelvic radiotherapy, n/N (%), specify				
Disease severity	--	--	--	--
PSA level, ng/ml, n, mean(SD) / median (range) /categorical				
Clinical stage, T1/T2/T3, specify staging method, e.g. digital rectal examination, MRI				
Biopsy Gleason Score ≤ 6, n 7, n 8-10, n				
Prostate size, ml, mean (SD) / median (range)				
Erectile dysfunction, n/N (%), specify measure and validated or not:				

Intervention
Intervention 1: **Robotic prostatectomy** Trade name and manufacturer of robot: ☐ da Vinci system by Intuitive Surgical Inc., Sunnyvale, California, USA ☐ Other, specify: ☐ Not reported Model number(s): Surgical approaches: ☐ Intra-peritoneal ☐ Extra-peritoneal ☐ Not reported Location of the operator console: ☐ In the same room ☐ An adjacent room ☐ Off-site, specify ☐ Not reported Nerve sparing for erectile function: ☐ Unilateral, n/N ☐ Bilateral, n/N: ☐ Non- nerve sparing ☐ Not reported Lymph node dissection: ☐ No ☐ Yes, details: ☐ Not reported Additional information:
Intervention 2: **Laparoscopic prostatectomy** Trade name, manufacturer, and model number of laparoscopic equipment: Surgical approaches: ☐ Intra-peritoneal ☐ Extra-peritoneal ☐ Not reported Nerve sparing for erectile function: ☐ Unilateral, n/N ☐ Bilateral, n/N: ☐ Non- nerve sparing ☐ Not reported Lymph node dissection: ☐ No ☐ Yes, details: ☐ Not reported Additional information:
Intervention 3: **Open prostatectomy** Nerve sparing for erectile function: ☐ Unilateral, n/N ☐ Bilateral, n/N: ☐ Non- nerve sparing ☐ Not reported Lymph node dissection: ☐ No ☐ Yes, details: ☐ Not reported Additional information:

Safety outcomes				
Peri-operative	Timing, e.g. 6wks, 1mo, 3mo, 1 year after surgery	Intervention 1: **robotic**	Intervention 2: **laparoscopic**	Intervention 3: **open**
Equipment failure, n/N (%)				
Converted to other intervention, e.g. open operation, n/N (%), specify the route				
Blood transfusion requirement, n/N (%)	--			
Operating time, minutes, n, mean (SD) / median (range)				
Hospital stay (recovery time), days, n, mean (SD) /median (range)				
Re-admission, days, n, mean (SD) /median (range)				
Need critical care, number of patients (n/N),also number of days, mean (SD) /median (range)				
Bladder neck stenosis / anastomotic stricture, n/N (%)				
Duration of catheterisation, days, n, mean (SD) /median (range)				
Anastomotic leak, n/N (%)				
Hernia into port sites or incision sites, n/N (%)				
Infection, n/N (%), specify site				
Organ injury, e.g. bowel, blood vessels, n/N (%), specify				
Ileus, n/N (%)				
Deep vein thrombosis, n/N (%)				
Pulmonary embolism, n/N (%)				
Other peri-operative outcomes, n/N (%), specify:				
Dysfunction				
Any dysfunction including urinary, faecal, or erectile, n/N (%)				
Urinary incontinence ☐ > 1 thin pad per day, n/N (%) ☐ Other measures, e.g. subjective measure, specify				
Erectile dysfunction, ☐ International Index of Erectile Dysfunction ☐ Other measures, specify, and validated or not				
Faecal incontinence, n/N (%), specify measure and validated or not:				

Efficacy outcomes				
	Timing, e.g. 6wks, 1mo, 3mo, 1 year after surgery	Intervention 1: **robotic**	Intervention 2: **laparoscopic**	Intervention 3: **open**
Positive margin in resected specimen, n/N (%), specify definition:				
Pathology stage, pT1/pT2/pT3, specify staging method, e.g. digital rectal examination, MRI				
Pathological Gleason Score ≤ 6, n *7, n* *8-10, n*				
PSA recurrence, n/N (%), specify definition, e.g. two successive PSA levels ≥ 0.4 ng/ml):				
Local recurrence, n/N (%)				
Port site recurrence, n/N (%)				--
Metastatic disease, n/N (%)				
Required further treatment & death				
Further cancer treatment, n/N (%) in total				
Curative treatment, n/N (%)				
Resolved or died, n/N (%)				
Palliative treatment, n/N (%)				
Resolved or died, n/N (%)				
Curative and palliative treatment, n/N (%)				
Resolved or died, n/N (%)				
Treatment of urinary incontinence, n/N (%)	**			
Resolved or persistent, n/N (%)				
Treatment of faecal incontinence, n/N (%)				
Resolved or persistent, n/N (%)				
Treatment of erectile dysfunction, n/N (%)				
Resolved or persistent, n/N (%)				
Death in total, n/N (%), specify causes				
Quality of life outcomes				
Time to return to full activity, n, mean (SD) / median (range)				
Quality of life (QoL): ☐ Generic QoL, specify measure (validated) used: ☐ Disease-specific QoL, specify measure (validated) used: ☐ Other validated measures specify:				

Procedural outcomes			
	Intervention 1: **robotic**	Intervention 2: **laparoscopic**	Intervention 3: **open**
Procedures done in the centre each year, mean (SD) / median (range)			
Surgeon competence (learning curve), by surgeon and by centre	--	--	--
Number of surgeons			
Number of procedures conducted before this study			
Number of procedures conducted during this study			
Time taken to perform the procedure at the end this study, minutes, mean (SD) / median (range)			
Additional information, e.g. description about the experience of the surgeons			
Conclusion as reported by the authors of the study			
Additional information and comments			

Appendix 4

Risk of bias form

Cochrane risk of bias table (non-randomised studies)

Laparoscopic versus robotic prostatectomy for localised prostate cancer

Assessor initial: Date evaluated:

Study ID:

Item			Judgement[a]	Description (quote from paper or describe key information)
1. Sequence generation				
2. Allocation concealment				
3a. Confounding[b]	Outcome 1 (perioperative safety)	Confounders balanced[b]		
	Surgeon experience			
	Comorbidity (ASA/Charlson score)			
	Prostate size			
3b. Confounding[b]	Outcome 2 (urinary dysfunction)	Confounders balanced[b]		
	Surgeon experience			
	Age			
	Neurovascular bundle excision			
	Anastomotic stricture			
3c. Confounding[b]	Outcome 3 (erectile dysfunction)	Confounders balanced[b]		
	Preoperative dysfunction/status			
	Neurovascular bundle excision			
	Surgeon experience			
	Age/comorbidity			
3d. Confounding[b]	Outcome 4 (efficacy)	Confounders balanced[b]		
	Gleason score balanced at baseline			
	Surgeon experience			
	PSA score balanced at baseline			
	Clinical[c] tumour stage/nodal stage balanced at baseline			
4a. Blinding?	Outcome 1 (perioperative safety)			
4b. Blinding?	Outcome 2 (urinary dysfunction)			
4c. Blinding?	Outcome 3 (erectile dysfunction)			
4d. Blinding?	Outcome 4 (efficacy)			

Item		Judgement[a]	Description (quote from paper or describe key information)
5a. Incomplete outcome data addressed?	Outcome 1 (perioperative safety)		
5b. Incomplete outcome data addressed?	Outcome 2 (urinary dysfunction)		
5c. Incomplete outcome data addressed?	Outcome 3 (erectile dysfunction)		
5d. Incomplete outcome data addressed?	Outcome 4 (efficacy)		
6a. Free of selective reporting?	Outcome 1 (perioperative safety)		
6b. Free of selective reporting?	Outcome 2 (urinary dysfunction)		
6c. Free of selective reporting?	Outcome 3 (erectile dysfunction)		
6d. Free of selective reporting?	Outcome 4 (efficacy)		
7. Free of other bias?			
8. A priori protocol?[d]			
9. A priori analysis plan?[e]			

a For all items, record 'unclear' if inadequate reporting prevents a judgement being made.
b Confounders listed by order of importance (high to low importance) based on list of confounders considered important at the outset and defined in the protocol for the review (and assessment against worksheet – optional). Low risk: four balanced = low risk, three balanced, one unbalanced = low risk, three balanced, one unclear = low risk, two balanced, one unbalanced, one unclear = low risk, two balanced, two unclear = low risk. High risk: four unbalanced = high risk, three unbalanced, one balanced = high risk, three unbalanced, one unclear = high risk, two unbalanced, two balanced = high risk, two unbalanced, one balanced, one unclear = high risk, two unbalanced, two unclear = high risk. Unclear: four unclear = unclear, three unclear, one balanced = unclear, three unclear, one unbalanced = unclear. Note: if confounders are imbalanced but adjusted for in the analysis, the imbalance is no longer a serious concern for risk of bias.
c Or pathological stage balanced in absence of clinical stage information.
d Did the researchers write a protocol defining the study population, intervention and comparator, primary and other outcomes, data collection methods, etc. *in advance of* starting the study?
e Did the researchers have an analysis plan defining the primary and other outcomes, statistical methods, subgroup analyses, etc. *in advance of* starting the study?

General decision rules

- When a paper does not report details of confounders/other source of bias this should be judged as unclear.
- When a paper does not report considered outcomes this should be judged as not applicable.
- Allocation concealment should be judged as high risk of bias if groups are allocated by factors such as surgeon decision, patient preference. Allocation by hospital/institution = low risk. When no details are given, judge as unclear.
- Surgeon experience: assume that surgeons performing open prostatectomy are experienced unless stated otherwise.
- Absence of blinding is likely to have a low risk of bias for perioperative and efficacy outcomes.
- Free of other bias: default is low risk unless there is a fundamental flaw with the study (e.g. inadequate follow-up time for dysfunction outcomes, data not presented for learning curve effects if these are likely to influence outcomes).
- Judging overall direction of bias for individual outcomes: if confounding is judged unbalanced, outcome should be judged as high risk of bias.

Risk of bias tool (non-randomised studies)

Studies for which risk of bias tool is intended

Only suitable for 'cohort-like' studies, individually or cluster allocated. Include secondary analyses of clinical databases providing that the analysis is clearly structured as a comparison of control and intervention participants. Refer to Chapter 13, tables 13.2.a and b [Barnaby C, Reeves, Jonathan J, Deeks, Julian PT, Higgins, *et al.* on behalf of the Cochrane Non-Randomised Studies Methods Group. Chapter 13: Including non-randomized studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011)]:

Table 13.2.a: individually allocated study designs:

- RCT – randomised controlled trial
- Q-RCT – quasi-randomised controlled trial
- NRCT – non-randomised controlled trial
- CBA – controlled before-and-after study (not common use of this label, see CChBA below)
- PCS – prospective cohort study
- RCS – retrospective cohort study.

Table 13.2.b: cluster-allocated study designs:

- ClRCT – cluster randomised controlled trial
- ClQ-RCT – cluster quasi-randomised controlled trial
- ClNRCT – cluster non-randomised controlled trial
- CITS – controlled interrupted time series
- CChBA – controlled cohort before-and-after study.[217]

Assessment of risk of bias

Issues when using modified risk of bias tool to assess cohort-like non-randomised studies:

- use existing principle: score judgement and provide information (preferably direct quote) to support judgement
- additional item on confounding
- 5-point scale for *some* items (distinguish 'unclear' from intermediate risk of bias
- keep in mind the general philosophy – assessment is *not* about whether researchers could have done better but about the risk of bias; the assessment tool must be used in a standard way whatever the difficulty/circumstances of investigating the research question of interest and whatever the study design used
- use of 5-point scale is uncharted territory; very interested to know whether this makes things easier or more difficult for reviewers
- anchors?: '1/no/low risk' of bias should correspond to a high-quality RCT; '5/high risk' of bias should correspond to a risk of bias which means that the findings should not be considered (too risky, too much bias, more likely to mislead than inform).

1. Sequence generation
   - low/high/unclear risk of bias item
   - always high risk of bias (not random) for a non-randomised study

- might argue that this item redundant for non-randomised studies as it is always high – but important to include in risk of bias table ('level playing field' argument).

2. Allocation concealment
   - low/high/unclear risk of bias item
   - potentially *low* risk of bias for a *non-randomised study*, for example quasi-randomised (so high risk of bias to sequence generation) but concealed (reviewer judges that the people making decisions about including participants did not know how allocation was being carried out, e.g. odd/even date of birth/hospital number).

3. Risk of bias from confounding (additional item for non-randomised studies; assess for each outcome)
   - assumes a *prespecified* list of potential confounders defined in the protocol
   - low(1)/2/3/4/high(5)/unclear risk of bias item
   - judgement needs to factor in:
     - proportion of confounders (from prespecified list) that were considered
     - whether most important confounders (from prespecified list) were considered
     - resolution/precision with which confounders were measured
     - extent of imbalance between groups at baseline
     - care with which adjustment was carried out (typically a judgement about the statistical modelling carried out by authors)
   - low risk of bias requires that all important confounders are balanced at baseline (*not primarily/not only* a statistical judgement *or* measured 'well' *and* 'carefully' controlled for in the analysis).

We have provided an optional 'worksheet' to help reviewers focus on the task (rows = confounders and columns = factors to consider).

4. Risk of bias from lack of blinding (*assess for each outcome*, as per existing risk of bias tool)
   - low(1)/2/3/4/high(5)/unclear risk of bias item
   - judgement needs to factor in:
     - nature of outcome (subjective/objective; source of information)
     - who was/was not blinded and the risk that those who were not blinded could introduce *performance or detection* bias
     - see Chapter 8 [Higgins JP, Altman D, Sterne J, Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Chapter 8: Assessing risk of bias in included studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011)].

5. Risk of bias from incomplete outcome data (*assess for each outcome*, as per existing risk of bias tool)
   - low(1)/2/3/4/high(5)/unclear risk of bias item
   - judgement needs to factor in:
     - reasons for missing data
     - whether amount of missing data is balanced across groups, with similar reasons
     - see Chapter 8 [Higgins JP, Altman D, Sterne J, Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Chapter 8: Assessing risk of bias in included studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011)].

6. Risk of bias from selective reporting (*assess for each outcome*; note: different to existing Chapter 8 recommendation) [Higgins JP, Altman D, Sterne J, Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Chapter 8: Assessing risk of bias in included studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011)]
   - low(1)/2/3/4/high(5)/unclear risk of bias item
   - judgement needs to factor in:
     - existing risk of bias guidance on selective outcome reporting
     - see Chapter 8 [Higgins JP, Altman D, Sterne J, Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Chapter 8: Assessing risk of bias in included studies. In Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration, 2011. URL: www.cochrane-handbook.org (accessed March 2011).]
     - also, extent to which analyses (and potentially other choices) could have been manipulated to bias the findings reported, for example choice of method of model fitting, potential confounders considered/included
     - look for evidence that there was a protocol in advance of carrying out any analysis/obtaining the data (difficult unless explicitly reported); non-randomised studies very different from RCTs – RCTs must have a protocol in advance of starting to recruit [for Research Ethics Committe (REC)/Institutional Review Board (IRB)/other regulatory approval] but non-randomised studies need not (especially older studies)
     - hence, separate yes/no items asking reviewers whether they think that the researchers had a prespecified protocol and analysis plan?

Appendix 5

List of included studies

Al-Shaiji 2010

Al-Shaiji TF, Kanaroglou N, Thom A, Prowse C, Comondore V, Orovan W, *et al.* A cost-analysis comparison of laparoscopic radical prostatectomy versus open radical prostatectomy: the McMaster Institute of Urology experience. *Can Urol Assoc J* 2010;**4**:237–41.

Anastasiadis 2003

Anastasiadis AG, Salomon L, Katz R, Hoznek A, Chopin D, Abbou CC. Radical retropubic versus laparoscopic prostatectomy: a prospective comparison of functional outcome. *Urology* 2003;**62**:292–7.

Artibani 2003

Artibani W, Grosso G, Novara G, Pecoraro G, Sidoti O, Sarti A, *et al.* Is laparoscopic radical prostatectomy better than traditional retropubic radical prostatectomy? An analysis of peri-operative morbidity in two contemporary series in Italy. *Eur Urol* 2003;**44**:401–6.

Ball 2006

Ball AJ, Gambill B, Fabrizio MD, Davis JW, Given RW, Lynch DF, *et al.* Prospective longitudinal comparative study of early health-related quality-of-life outcomes in patients undergoing surgical treatment for localized prostate cancer: a short-term evaluation of five approaches from a single institution. *J Endourol* 2006;**20**:723–31.

Barocas 2010

Barocas DA, Salem S, Kordan Y, Herrell SD, Chang SS, Clark PE, *et al.* Robotic assisted laparoscopic prostatectomy versus radical retropubic prostatectomy for clinically localized prostate cancer: comparison of short-term biochemical recurrence-free survival. *J Urol* 2010;**183**:990–6.

Kordan Y, Barocas DA, Altamar HO, Clark PE, Chang SS, Davis R, *et al.* Comparison of transfusion requirements between open and robotic-assisted laparoscopic radical prostatectomy. *BJU Int* 2010;**106**:1036–40.

Chan RC, Barocas DA, Chang SS, Herrell SD, Clark PE, Baumgartner R, *et al.* Effect of a large prostate gland on open and robotically assisted laparoscopic radical prostatectomy. *BJU Int* 2008;**101**:1140–4.

Bhayani 2003

Bhayani SB, Pavlovich CP, Hsu TS, Sullivan W, Su LM. Prospective comparison of short-term convalescence: laparoscopic radical prostatectomy versus open radical retropubic prostatectomy. *Urology* 2003;**61**:612–16.

Bolenz 2010

Bolenz C, Gupta A, Hotze T, Ho R, Cadeddu JA, Roehrborn CG, *et al.* The influence of body mass index on the cost of radical prostatectomy for prostate cancer. *BJU Int* 2010;**106**:1188–93.

Bolenz C, Gupta A, Hotze T, Ho R, Cadeddu JA, Roehrborn CG, *et al.* Cost comparison of robotic, laparoscopic and open radical prostatectomy. *Eur Urol Suppl* 2009;**8**:364.

Brown 2004

Brown JA, Garlitz C, Gomella LG, McGinnis DE, Diamond SM, Strup SE. Perioperative morbidity of laparoscopic radical prostatectomy compared with open radical retropubic prostatectomy. *Urol Oncol* 2004;**22**:102–6.

Carlsson 2010

Carlsson S, Nilsson AE, Schumacher MC, Jonsson MN, Volz DS, Steineck G, *et al.* Surgery-related complications in 1253 robot-assisted and 485 open retropubic radical prostatectomies at the Karolinska University Hospital, Sweden. *Urology* 2010;**75**:1092–7.

Dahl 2009

Dahl DM, Barry MJ, McGovern FJ, Chang Y, Walker-Corkery E, McDougal WS. A prospective study of symptom distress and return to baseline function after open versus laparoscopic radical prostatectomy. *J Urol* 2009;**182**:956–65.

Dahl DM, He W, Lazarus R, McDougal WS, Wu CL. Pathologic outcome of laparoscopic and open radical prostatectomy. *Urology* 2006;**68**:1253–6.

Doumerc 2010

Doumerc N, Yuen C, Savdie R, Rahman MB, Rasiah KK, Pe BR, *et al.* Should experienced open prostatic surgeons convert to robotic surgery? The real learning curve for one surgeon over 3 years. *BJU Int* 2010;**106**:378–84.

Drouin 2009

Drouin SJ, Vaessen C, Hupertan V, Comperat E, Misrai V, Haertig A, *et al.* Comparison of mid-term carcinologic control obtained after open, laparoscopic, and robot-assisted radical prostatectomy for localized prostate cancer. *World J Urol* 2009;**27**:599–605.

Ficarra 2009

Ficarra V, Novara G, Fracalanza S, D'Elia C, Secco S, Iafrate M, *et al.* A prospective, non-randomized trial comparing robot-assisted laparoscopic and retropubic radical prostatectomy in one European institution. *BJU Int* 2009;**104**:534–9.

Fornara 2004

Fornara P, Zacharias M. [Minimal invasiveness of laparoscopic radical prostatectomy: reality or dream?] *Aktuel Urol* 2004;**35**:395–405.

Fracalanza 2008

Fracalanza S, Ficarra V, Cavalleri S, Galfano A, Novara G, Mangano A, *et al.* Is robotically assisted laparoscopic radical prostatectomy less invasive than retropubic radical prostatectomy? Results from a prospective, unrandomized, comparative study. *BJU Int* 2008;**101**:1145–9.

Ghavamian 2006

Ghavamian R, Knoll A, Boczko J, Melman A. Comparison of operative and functional outcomes of laparoscopic radical prostatectomy and radical retropubic prostatectomy: single surgeon experience. *Urology* 2006;**67**:1241–6.

Gosseine 2009

Gosseine PN, Mangin P, Leclers F, Cormier L. [Pure laparoscopic versus robotic-assisted laparoscopic radical prostatectomy: comparative study to assess functional urinary outcomes.] *Prog Urol* 2009;**19**:611–17.

Greco 2010

Greco F, Wagner S, Hoda M, Kawan F, Inferrera A, Lupo A, *et al.* Laparoscopic vs open retropubic intrafascial nerve-sparing radical prostatectomy: surgical and functional outcomes in 300 patients. *BJU Int* 2010;**106**:543–7.

Guazzoni 2006

Guazzoni G, Cestari A, Naspro R, Riva M, Centemero A, Zanoni M, *et al.* Intra- and peri-operative outcomes comparing radical retropubic and laparoscopic radical prostatectomy: results from a prospective, randomised, single-surgeon study. *Eur Urol* 2006;**50**:98–104.

Hu 2006

Hu JC, Nelson RA, Wilson TG, Kawachi MH, Ramin SA, Lau C, *et al.* Perioperative complications of laparoscopic and robotic assisted laparoscopic radical prostatectomy. *J Urol* 2006;**175**:541–6.

Jacobsen 2007

Jacobsen NE, Moore KN, Estey E, Voaklander D. Open versus laparoscopic radical prostatectomy: a prospective comparison of postoperative urinary incontinence rates. *J Urol* 2007;**177**:615–19.

Joseph 2005

Joseph JV, Vicente I, Madeb R, Erturk E, Patel HR. Robot-assisted vs pure laparoscopic radical prostatectomy: are there any differences? *BJU Int* 2005;**96**:39–42.

Joseph 2007

Joseph JV, Salomon L, Capello SA, Patel HR, Abbou CC. Laparoscopic or robot-assisted extraperitoneal radical prostatectomy: 1554 cases from two high volume institutions performed extraperitoneally. *J Urol* 2007;**177**:525–6.

Jurczok 2007

Jurczok A, Zacharias M, Wagner S, Hamza A, Fornara P. Prospective non-randomized evaluation of four mediators of the systemic response after extraperitoneal laparoscopic and open retropubic radical prostatectomy. *BJU Int* 2007;**99**:1461–6.

Kim 2007

Kim Y-J. Comparison of perioperative outcomes of extraperitoneal laparoscopic radical prostatectomy (ELRP) versus open radical retropubic prostatectomy (RRP): single surgeon's initial experience. *Kor J Urol* 2007;**48**:131–7.

Krambeck 2009

Krambeck AE, DiMarco DS, Rangel LJ, Bergstralh EJ, Myers RP, Blute ML, *et al.* Radical prostatectomy for prostatic adenocarcinoma: a matched comparison of open retropubic and robot-assisted techniques. *BJU Int* 2009;**103**:448–53.

Lama 2009

Lama MK, Salinas NRO, Martinez JMF, Gribbell RAO, Cabrera OS, Sudy CAF. Prospective study and comparative of surgical and oncologic outcome between laparoscopic and retropubical radical prostatectomy. *Actas Urol Esp* 2009;**33**:167–71.

Loeb 2010

Loeb S, Epstein JI, Ross AE, Schultz L, Humphreys EB, Jarow JP. Benign prostate glands at the bladder neck margin in robotic vs open radical prostatectomy. *BJU Int* 2010;**105**:1446–9.

Malcolm 2010

Malcolm JB, Fabrizio MD, Barone BB, Given RW, Lance RS, Lynch DF, *et al.* Quality of life after open or robotic prostatectomy, cryoablation or brachytherapy for localized prostate cancer. *J Urol* 2010;**183**:1822–8.

Martorana 2004

Martorana G, Manferrari F, Bertaccini A, Malizia M, Palmieri F, Severini E, *et al.* Laparoscopic radical prostatectomy: oncological evaluation in the early phase of the learning curve comparing to retropubic approach. *Arch Ital Urol Androl* 2004;**76**:1–5.

Menon 2002

Menon M, Tewari A, Baize B, Guillonneau B, Vallancien G. Prospective comparison of radical retropubic prostatectomy and robot-assisted anatomic prostatectomy: the Vattikuti Urology Institute experience. *Urology* 2002;**60**:864–8.

Miller 2007

Miller J, Smith A, Kouba E, Wallen E, Pruthi RS. Prospective evaluation of short-term impact and recovery of health related quality of life in men undergoing robotic assisted laparoscopic radical prostatectomy versus open radical prostatectomy. *J Urol* 2007;**178**:854–8.

Nadler 2010

Nadler RB, Casey JT, Zhao LC, Navai N, Smith ZL, Zhumkhawala A, *et al.* Is the transition from open to robotic prostatectomy fair to your patients? A single-surgeon comparison with 2-year follow-up. *J Robotic Surg* 2010;**3**:201–7.

Namiki 2005

Namiki S, Egawa S, Baba S, Terachi T, Usui Y, Terai A, *et al.* Recovery of quality of life in year after laparoscopic or retropubic radical prostatectomy: a multi-institutional longitudinal study. *Urology* 2005;**65**:517–23.

Namiki 2006

Namiki S, Egawa S, Terachi T, Matsubara A, Igawa M, Terai A, *et al.* Changes in quality of life in first year after radical prostatectomy by retropubic, laparoscopic, and perineal approach: multi-institutional longitudinal study in Japan. *Urology* 2006;**67**:321–7.

Ou 2009

Ou YC, Yang CR, Wang J, Cheng CL, Patel VR. Comparison of robotic-assisted versus retropubic radical prostatectomy performed by a single surgeon. *Anticancer Res* 2009;**29**:1637–42.

Poulakis 2007

Poulakis V, Witzsch U, de Vries R, Dillenburg W, Becht E. Laparoscopic radical prostatectomy in men older than 70 years of age with localized prostate cancer: comparison of morbidity, reconvalescence, and short-term clinical outcomes between younger and older men. *Eur Urol* 2007;**51**:1341–8.

Raventos Busquets 2007

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Appendix 6

List of excluded studies: comparative studies in which number of patients for each baseline clinical stage was unclear

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Appendix 7

Characteristics of the included studies

TABLE 47 Characteristics of the included RCT ($n = 1$)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Guazzoni 2006[90] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting:** hospital **Country**: Italy **Recruitment/ treatment dates**: not reported **Prospective/ retrospective data collection**: prospective **Randomisation method**: consecutive and age-matched patients randomised using computer-generated randomisation table **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: consecutive and age-matched patients who were diagnosed with clinically localised prostate cancer (cT1–cT2); patients who are aged < 70 years, with PSA < 20 ng/dl, Gleason score ≤ 7 **Exclusion criteria**: those with previous hormone blockade therapy or any previous prostatic bladder neck, urethral or pelvic surgery and total prostate volume ≥ 60 ml; patients without an indwelling catheter A: 60 patients; B: 60 patients; Patients enrolled, *n*: 120 Patients analysed, *n*: A 60, B 60 Age (years), mean (SD): A 62.29 (8.2), B 2.9 (7.4) PSA (ng/ml), mean (SD): A 6.9 (2.9), B 6.5 (3) ***Clinical stage,* n *(%)*** T1: A 45 (75), B 50 (83) T2: A 15 (25), B 10 (17) Digital rectal examination, TRUS, abdominal computed tomography scan and bone scan used for staging	**A. Laparoscopic prostatectomy**: performed according to Montsouris technique; the urethra–vesicle anastomosis was performed with 8-10, 3-0 interrupted sutures performed intracorporeally after insertion of a metal bougie to expose the urethral stump; transperitoneal route was used **Nerve sparing**: Unilateral: 11/60 (18.3%) Bilateral: 25/60 (41.7%) Pelvic lymphadenectomy: 24/60 (40.0%) **B. Open prostatectomy**: performed by anatomic technique; a xenon head light and 2.5 magnification loops were used. The urethra–vesicle anastomosis was performed with 8-10, 3-0 interrupted sutures with a 5/8 needle **Nerve sparing**: Unilateral: 8/60 (13.3%) Bilateral: 31/60 (51.7%) Pelvic lymphadenectomy: 27/60 (45.0%) **For both A and B**: Lymph node dissection was performed when total serum PSA level was ≥ 10 ng/ml and/or Gleason score = 7 Nerve sparing was performed whenever possible according to preoperative parameters such as age, clinical stage and preoperative potency (recorded by the IIEF questionnaire and penile power Doppler ultrasound evaluation) (data not reported)	**Safety**: open conversion, surgical complications, operating time, discharge time, catheterisation, blood loss, mobilisation, oral feeding **Efficacy**: margins, pT stage **Quality of life**: pain

TABLE 48 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic vs open prostatectomy) [*n* = 4 (3 primary, 1 secondary)]

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Ball 2006[99] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: January 2000–April 2005 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 6 months **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients with newly diagnosed clinically localised prostate cancer **Exclusion criteria**: not reported ***Patients,* n** Enrolled: A 82, B 124, C 135 1 month: A 76, B 93, C 82 3 months: A 56, B 102, C 122 6 months: A 22, B 112, C 91 Age (years), mean (SD): A 60 (7), B 61 (7), C 59 (6) PSA (ng/ml), mean (SD): A 6.0 (2.4), B 7.2 (7.1), C 7.8 (5.6) ***Clinical stage,* n** T1: A 66, B 100, C 116 T2: A 15, B 24, C 19 T3: A 1, B 0, C 0 ***Biopsy Gleason score,* n** ≤6: A 59, B 94, C 85 7: A 15, B 22, C 37 8–10: A 8, B 8, C 13	**A. Robotic prostatectomy**: trade name of robot: da Vinci **B. Laparoscopic prostatectomy**: used a well-described technique, reference given **C. Open prostatectomy**: used a standard radical retropubic technique **Nerve sparing for erectile function**: Non-nerve sparing, *n* (%): A 18 (22), B 67 (54), C 40 (30) Unilateral, *n* (%): A 9 (11), B 23 (19), C 30 (22) Bilateral, *n* (%): A 54 (66), B 34 (27), C 65 (48) Unknown, *n* (%): A 1 (1), B 0, C 0	**Efficacy**: pT stage **Dysfunction**: urinary incontinence, erectile dysfunction
Author, year: Bolenz 2010[100] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: not reported **Country**: USA **Recruitment/treatment dates**: September 2003–April 2008 **Prospective/retrospective data collection**: not reported **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: TG	**Inclusion/exclusion criteria:** not reported Patients, *n*: A 262, B 211, C 156 Age (years), median: A 62, B 59, C 61 BMI <30 kg/m²: A 62 (56–66), B 59 (54–63), C 61.5 (57–66) BMI >30 kg/m²: A 60 (57–65), B 56.5 (52–63), C 60.5 (54–64) ***PSA (ng/ml), median (range)*** BMI <30 kg/m²: A 5.2 (4.1–7), B 5 (4.2–6.5), C 5.6 (4.4–7.2) BMI >30 kg/m²: A 5.4 (4.3–7), B 5.1 (4–7.2), C 4.7 (4.1–5.9) BMI, body mass index. Biopsy Gleason scores for total sample: ≤6: 341 7: 236 8–10: 48	**A. Robotic prostatectomy**: nerve sparing **B. Laparoscopic prostatectomy**: nerve sparing **C. Open prostatectomy**: nerve sparing	**Safety**: blood transfusion

TABLE 48 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic vs open prostatectomy) [*n* = 4 (3 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics				Intervention characteristics	Outcomes
Author, year: Bolenz 2009;[102] secondary to Bolenz 2010[100]	**Inclusion/exclusion criteria:** not reported				**A. Robotic prostatectomy**: nerve sparing 85%, lymph node dissection 11%	**Safety**: operating time, hospital stay
Language: English		**A**	**B**	**C**	**B. Laparoscopic prostatectomy**: nerve sparing 96%, lymph node dissection 22%	
Publication type: conference abstract	Patients, *n*	264	220	162	**C. Open prostatectomy**: nerve sparing 90%, lymph node dissection 100%	
Number of study centres: 1	Age (years), median	61	59	61		
Setting: not reported	BMI (kg/m^2), median	27.8	27.3	27.2		
Country: USA	PSA (ng/ml), median	5.3	5	5.3		
Recruitment/treatment dates: September 2003–April 2008	***Clinical stage,*** **n**					
Prospective/retrospective data collection: not reported	T1c	198	193	107		
	T2a	9	20	17		
Patients recruited consecutively: not reported	T2b	7	2	10		
	T2c	47	0	22		
Length of follow-up: not reported	Not provided	2	0	1		
	Unknown	1	5	5		
Source of funding: not reported	Biopsy Gleason score 8–10 (%)	6.10	8.40	9.40		
	Prostate size (ml)	46	46	45		
	BMI, body mass index. Clinical stage data obtained via correspondence with lead author.					

continued

TABLE 48 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic vs open prostatectomy) [*n* = 4 (3 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Drouin 2009[101] **Language**: English **Publication type**: full text **Number of study centres**: not reported **Setting**: hospital **Country**: France **Recruitment/treatment dates**: January 2000–August 2004 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: months, mean (range): total: 49.7 (18–103); A: 40.9 (18–60); B: 48.4 (18–84); C: 57.7 (18–103) **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients treated for prostate cancer with surgery **Exclusion criteria**: evidence of lymph node involvement during preoperative work-up or in case of clinical signs of non-localised disease	**A. Robotic prostatectomy**: robot trade name: da Vinci system; approaches: transperitoneal; 34/71 had lymph node dissection **B. Laparoscopic prostatectomy**: approaches: transperitoneal; 42/85 had lymph node dissection **C. Open prostatectomy**: 58/83 had lymph node dissection	**Safety**: surgical complications, open conversion, operating time, catheterisation, blood loss **Efficacy**: margins, pT stage, PSA recurrence **Death**

	A	B	C
Patients, *n*	71	85	83
Age (years), mean (range)	60.4 (46–70)	61.8 (39–73)	60.5 (45–81)
BMI (kg/m^2), mean(range)	22.6 (22–25)	23 (22–25.2)	23.3 (22.6–24.8)
PSA (ng/ml), mean (range)	7.8 (3–24)	8.9 (3.4–37)	9.2 (1.2–60)
***Clinical stage,* n**			
T1a–b	0	0	2
T1c	50	55	38
T2a–b	17	22	28
T2c	4	8	15
***Biopsy Gleason score,* n**			
≤ 6	60	62	59
7	11	21	24
8–10	0	2	0

BMI, body mass index.

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) ($n = 8$)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Gosseine 2009[91] **Language**: French **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: France **Recruitment/treatment dates**: March 2004–April 2007 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: 3 years **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: not reported **Exclusion criteria**: not reported	**A. Robotic prostatectomy**: trade name of robot: da Vinci system **B. Laparoscopic prostatectomy:**	**Safety**: surgical complications, operating time, hospital stay, catheterisation, blood loss **Dysfunction**: urinary incontinence

	A	B
Patients, *n*	122	125
Age (years), mean (SD)	60.6 (6.1)	61.7 (6.8)
BMI (kg/m^2), mean (SD)	26.7 (3.4)	27.2 (3.5)
Previous TURP, *n*	2	4
PSA (ng/ml), mean (SD)	7.37 (4.3)	7.87 (5.09)
Clinical stage,* n *(%)		
T1	70 (57.4)	78 (62.4)
T2	52 (42.6)	47 (37.6)
Biopsy Gleason score,* n *(%)		
≤ 6	73 (59.8)	86 (68.8)
7	42 (34.4)	36 (28.8)
8–10	7 (5.8)	3 (2.4)

Nerve sparing for erectile function:

	A	B
Non-nerve sparing, *n* (%)	30 (25)	45 (36)
Unilateral, *n* (%)	16 (13)	13 (10.4)
Bilateral, *n* (%)	76 (62)	64 (5.12)
Bladder neck preservation, *n* (%)	97 (79)	53 (42)
Not reported *n* (%)	0	3 (2.4)

BMI, body mass index; TURP, transurethral resection of the prostate.

continued

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) ($n = 8$) (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Hu 2006[92] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: US **Recruitment/treatment dates**: A: June 2003–June 2004; B: October 2000–January 2003 **Prospective/ retrospective data collection**: mixture **Patient recruited consecutively, Y/N**: no **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients had radical prostatectomies with laparoscopic or robotic procedures **Exclusion criteria**: patients with neoadjuvant hormonal therapy	**A. Robotic prostatectomy**: trade name of robot: da Vinci system; approaches: trans-peritoneal **B. Laparoscopic prostatectomy**: approaches: trans-peritoneal (both Montsouris technique); nerve sparing	**Safety**: surgical complications, operation time **Death** **Learning curve**: operating time

	A	B
Patient enrolled	671	517
Patient analysed	322	358
Age, mean (range)	62.1 (41-84)	63.7 (40-83)
BMI, median (range)	27.5 (17.8-51.5)	27.4 (17.9-43.8)
Previous abdominal surgery	37/322 (11.5%)	39/358 (10.9%)
PSA, ng/ml		
0–4	66 (20.6%)	55 (15.4%)
4–10	213 (66.4%)	247 (69%)
10	42 (13.1%)	56 (15.6%)
Clinical stage,* n *(%)		
T1a	1 (0.3)	6 (1.7)
T1b	0	2 (0.6)
T1c	231 (74.5)	261 (72.9)
T2a	59 (19.0)	72 (20.%)
T2b	11 (3.5)	4 (1.1)
T2c	7 (2.3)	10 (2.8)
T3a	1 (0.3)	1 (0.3)
T3b	0	2 (0.6)
Biopsy Gleason score,* n *(%)		
1–5	5 (1.6)	9 (2.5)
6–7	289 (93.5)	322 (90.2)
8–10	15 (4.9)	26 (7.3)

	A	B
Unilateral, *n* (%)	27 (8.4)	23 (6.4)
Bilateral, *n* (%)	259 (80.4)	237 (66.2)
Non-sparing, *n* (%)	35 (0.9)	87 (24.3)

All patients (A and B) had bilateral pelvic lymph node dissection

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) ($n = 8$) (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Joseph 2007[94] **Language**: English **Publication type**: conference abstract **Number of study centres**: 2 **Setting**: hospital **Country**: France/USA **Recruitment/treatment dates**: A: 2003–6 at the University of Rochester Medical Centre; B: 2002–6 at Henri Mondor Hospital of Creteil **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: none **Systematic reviewer**: XJ	**Inclusion criteria**: patients underwent prostatectomy **Exclusion criteria**: not reported A: 754 patients enrolled, *n*; Age (years), mean (range): 60.0 (40–78); BMI (kg/m^2), mean (range): 28.5 (17.7–56.2); PSA (ng/ml), mean (range): 6.6 (0.1–39.0) B: 800 patients enrolled, *n*; Age (years), mean (range): 64.9 (43–77); BMI (kg/m^2), mean (range): 27.2 (16.5–44.8); PSA (ng/ml), mean (range): 10.1 (1.5–99) ***Clinical stage,* n *(%)*** T1a–b: A 0, B 14 (1.8) T1c: A 452 (75.2), B 643 (80.4) T2: A 148 (24.6), B 141 (17.8) T3: A 1 (0.2), B 0 Not reported: A 153, B 2 Biopsy Gleason score, mean (range): A 6.3 (4–9), B 6.2 (4–9) Prostate size (g), mean (range): A 55.4 (21–141), B 55.6 (22–192) BMI, body mass index.	**A. Robotic prostatectomy** **B. Laparoscopic prostatectomy**: approaches: extraperitoneal **Lymph node dissection:** Yes, *n* (%): A 281 (37.3), B 322 (40.3) No (%): A (62.6), B (59.7)	**Efficacy**: margins, pathological Gleason score
Author, year: Joseph 2005[93] (considered separate to Joseph 2007[94] but may include patient overlap for US patients) **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: not reported **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: last 50 patients in a series with localised prostate cancer who had laparoscopic radical prostatectomy or robot-assisted prostatectomy **Exclusion criteria**: first 50 cases in each laparoscopic and robot-assisted series Patients enrolled, *n*: A 50, B 50 Age (years), mean (95% CI): A 59.6 (1.6), B 61.8 (1.6) PSA (ng/ml), mean (95% CI): A 7.3 (1.2), B 6.0 (0.83) ***Clinical stage,* n** T1c: A 43, B 34 T2a: A 6, B 14 T2b: A 1, B 2 Biopsy Gleason score, mean: A 6 (0.15), B 6 (0.14) Prostate size (g), mean: A 53 (5.3), B 51 (4.1)	**A. Robotic prostatectomy** **B. Laparoscopic prostatectomy** **Nerve sparing:** Unilateral, *n* (%): A 1 (2), B 10 (20) Bilateral, *n* (%): A 46 (92), B 24 (48) Non-sparing, *n* (%): A 3(6), B 16 (32)	**Dysfunction**: urinary incontinence, erectile dysfuntion, potency

continued

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) ($n = 8$) (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Menon 2002[95] **Language**: English **Publication type**: full text **Number of study centres**: one **Setting**: hospital **Country**: France **Recruitment/treatment dates**: October 2000–October 2001 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: mean (SD): A: 3 (1.3) months; B: 8.5 (3.2) months Length of follow-up for functional outcomes, mean: A: 1.5 months; B: 6.5 months Follow-up carried out with telephone survey by third party **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: patients with clinically localised prostate cancer undergoing prostatectomy; patients medically fit to undergo surgery, weighing < 250 lb (those weighing > 250 lb were recommended for open radical prostatectomy), waist size < 45 inches, body mass index < 35 kg/m^2; patients with previous abdominal surgery were included **A** / **B** Patients enrolled, *n*: 50 / 48 Patients analysed, *n*: 40 / 40 Age (years), mean (SD): 60.7 (7.6) / 62.8 (7.0) BMI (kg/m^2), mean (SD): 27.7 (3.2) / 27.7 (2.5) PSA (ng/ml), mean (SD): 5.7 (3.2) / 6.9 (4.4) ***Clinical stage,* n *(%)*** T1c: 28 (70) / 26 (65) T2: 12 (30) / 14 (35) BMI, body mass index. Number of patients undergoing open prostatectomy during the study = 115	**A. Robotic prostatectomy**: first 22 patients were operated using Montsouris technique; later 18 patients were operated using Vattikuti Institute technique **B. Laparoscopic prostatectomy**: performed using classical Montsouris technique	**Equipment failure** **Safety**: surgical complications, operating time, discharge, blood loss **Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence **Death (none)** **Learning curve:** operating time

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) ($n = 8$) (*continued*)

Study details	Participant characteristics			Intervention characteristics			Outcomes
Author, year: Rozet 2007[96] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: France **Recruitment/treatment dates**: May 2003–May 2005 **Prospective/ retrospective data collection**: not reported **Patient recruited consecutively, Y/N**: yes for group A **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients underwent robotic or laparoscopic prostatectomy			**A. Robotic prostatectomy**: robot trade name: da Vinci system; approaches: extra-peritoneal **B. Laparoscopic prostatectomy**: approaches: extra-peritoneal nerve sparing			**Safety**: surgical complications, operating time, catheterisation, blood loss, blood transfusion **Efficacy**: margins, pT stage, pathological Gleason score **Death** **Learning curve**: operating time
		A	**B**		**A**	**B**	
	Patient enrolled, *n*	133	758 (operated at the same period)	Unilateral, *n* (%)	35 (27.8)	30 (23.8)	
	Patient analysed, *n*	133	133 (match-pair)	Bilateral, *n* (%)	91 (72.2)	96 (76.2)	
	Age, mean (range)	62.0 (49–76)	62.5 (47–74)				
	BMI, mean (range)	24.8 (18.8–35.5)	25.3 (19.3–32.7)	**Lymph node dissection:**			
	Previous abdominal/ pelvic surgery	51	51		**A**	**B**	
	PSA, ng/ml, mean (range)	7.6 (0.9–38.0)	7.8 (3.2–19.0)	No, *n* (%)	131 (98.5)	130 (97.7)	
	Clinical stage,* n *(%)			Yes, *n* (%)	2 (1.5)	3 (2.3)	
	T1b	0	1 (0.8)				
	T1c	76 (57.1)	90 (67.7)				
	T2a	51 (38.3)	39 (29.3)				
	T2b	6 (4.5)	2 (1.5)				
	T3a	0	1 (0.8)				
	Biopsy Gleason score, mean (range)						
		6.3 (4.0–9.0)	6.3 (4.0–9.0)				
	≤ 6	101 (76%)	93 (70%)				
	7	29 (21.8%)	37 (27.8%)				
	8–10	3 (2.2%)	3 (2.2%)				

continued

TABLE 49 Characteristics of the included studies: non-randomised comparative studies (robotic vs laparoscopic prostatectomy) (*n* = 8) (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Sundaram 2004[97] **Language**: English **Publication type**: conference abstract **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: not reported **Prospective/ retrospective data collection**: not reported **Patients recruited consecutively**: yes in robotic group, not reported for laparoscopic group **Length of follow-up**: mean: 3 months **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion and exclusion criteria:** not reported A: Patients, *n* = 10; Age (years), mean (range) 59.5 (53–69); PSA (ng/ml), mean (range) 5.2 (3–7.9) B: Patients, *n* = 10; Age (years), mean (range) 58.7 (50–66); PSA (ng/ml), mean (range) 5.3 (4.7–6) ***Clinical stage,* n** T1c: A 9, B 7 2a: A 1, B 3	**A. Robotic prostatectomy** **B. Laparoscopic prostatectomy**	**Safety**: operating time, hospital stay, surgical complications, blood loss **Efficacy**: margins **Dysfunction**: urinary incontinence
Author, year: Trabulsi 2008[98] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: A: October 2005–August 2006 B: March 2000–December 2005 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: men with clinically localised prostate cancer treated with either robotic or laparoscopic prostatectomy A: Patients, *n* = 50; Age (years), mean (range) 57.7 (37–60); BMI (kg/m^2), mean (range) 28.4 (20.4–36.6); PSA (ng/ml), mean (range) 5.5 (1.1–21.1) B: Patients, *n* = 190; Age (years), mean (range) 58.6 (43–74); BMI (kg/m^2), mean (range) 26.8 (18.8–51.8); PSA (ng/ml), mean (range) 6.5 (0.4–46) ***Clinical stage,* n *(%)*** T1c: A 41 (82), B 145 (76) T2a: A 9 (18), B 40 (21) Not reported: A 0, B 5 ***Biopsy Gleason score,* n *(%)*** ≤ 6: A 36 (72), B 136 (72) 3 + 4: A 8 (16), B 31 (16) 4 + 3: A 4 (8), B 6 (3) ≥ 8: A 2 (4), B 3 (2) Prostate size (g), mean (range): A 41 (16–102), B 43.3 (14–156)	**A. Robotic prostatectomy**: used da Vinci system; surgical approaches intraperitoneal; lymph nodes dissected when indicated (in intermediate- and high-risk patients): 14 (28%) **B. Laparoscopic prostatectomy**: surgical approaches transperitoneal; lymph nodes dissection: same indication as above: 51 (27%)	**Safety**: open conversion, blood loss **Efficacy**: margins, pT stage, pathological Gleason score

BMI, body mass index.

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)]

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Barocas 2010[103] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: medical centre **Country**: USA **Recruitment/treatment dates**: June 2003–January 2008 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**, median [interquartile range (IQR)]: total: 10 (2–23) months; A: 8 (2–20) months; B: 17 (8–34) months **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients undergoing radical prostatectomy for clinically localised prostate cancer **Exclusion criteria**: patients with earlier treatment, missing data, lymph node involvement	**A. Robotic prostatectomy**: trade name of robot: da Vinci system **B. Open prostatectomy**: performed by standard techniques with small modifications described by Walsh and Partin[218]	**Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence

	A	B
Patients, *n*	1413	491
Age (years), mean (SD)	61 (7.3)	62 (7.3)
PSA (ng/ml), median (IQR)	5.4 (4.3–7.4)	5.8 (4.6–8.4)
Clinical stage,* n *(%)		
T1a	3 (0.21)	3 (0.61)
T1b	1 (0.07)	0
T1c	1086 (77.3)	342 (69.94)
T2a	267 (19)	89 (18.2)
T2b	37 (2.63)	42 (8.59)
T2c	4 (0.28)	12 (2.45)
T3a	7 (0.5)	0
T3b	0	1 (0.2)
Missing	8 patients were missing clinical stage; 2 patients were missing procedure type	
Biopsy Gleason score,* n *(%)		
≤ 6	986 (69.9)	327 (66.6)
7	353 (25.0)	116 (23.5)
8–10	72 (5.1)	48 (9.8)
Missing	2	0

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Kordan 2010[120] (secondary to Barocas 2010[103]) **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: university medical centre **Country**: USA **Recruitment/treatment dates**: June 2003–July 2006 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer:** TG	**Inclusion criteria**: clinically localised prostate cancer **Exclusion criteria**: not reported	**A. Robotic prostatectomy** **B. Open prostatectomy**	**Safety**: blood transfusion, blood loss

	A	B
Patients, *n*	830	414
Age (years), mean (SD)	60.5 (7.2)	61.5 (7.5)
BMI (kg/m^2), mean (SD)	28.2 (4.2)	28.0 (4.6)
PSA (ng/ml), median (IQR)	5.5 (4.4–7.3)	6.0 (4.6–9.1)
Clinical stage (clinically palpable > cT2), *n* (%)	204 (24.8)	128 (31.2)
Biopsy Gleason score,* n *(%)		
≤ 6	578 (69.8)	261 (63.0)
7	211 (25.5)	104 (15.1)
8–10	39 (47.1)	49 (11.8)
Not reported	2	0
Prostate size (ml) (range)	46 (37–58)	41 (31–52)

BMI, body mass index.

Author, year: Chan 2008[119] (secondary to Barocas 2010[103]) **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: May 2003–August 2006 **Prospective/retrospective data collection**: not reported **Patients recruited consecutively**: yes **Length of follow-up**: none **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: patient with clinically localised carcinoma of the prostate Data reported based on prostate size (large vs small). Here we have extracted the combined data wherever possible. When mean (range) were reported, only ranges have been extracted	**A. Robotic prostatectomy**: performed using a five-port technique **Nerve sparing**: Unilateral: 8/28 Bilateral: 86/522 Non-nerve sparing: 25/110 **B. Open prostatectomy**: performed via an infra-umbilical midline incision **Nerve sparing**: Unilateral: 12/30 Bilateral: 52/183 Non-nerve sparing: 52/127	**Safety**: open conversion, operating time, hospital stay **Learning curve**: operating time

	A	B
Patients, *n*	660	340
Age (years), range	36–78	40–81
PSA (ng/ml), range	0.18–76	0.5–51.7
Clinical stage,* n *(%)		
T1	497 (75)	225 (66)
T2	160 (24)	111 (33)
T3	3 (1)	4 (1)
Biopsy Gleason score,* n *(%)		
≤ 6	459 (70)	212 (62)
7	173 (26)	87 (26)
8–10	28 (4)	41 (12)
Prostate size (g), range	15–181	0.7–224

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Carlsson 2010[104] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Sweden **Recruitment/treatment dates**: January 2002–August 2007 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: median: A: 19 months; B: 30 months **Source of funding**: Swedish Cancer Society, Avtal om läkarutbildning och forskning (Agreement on Medical Education and Research; ALF) and the Johanna Hagstrand and Sigfrid Linnér Foundation **Systematic reviewer**: XJ	**Inclusion criteria**: patients underwent robotic or retropubic prostatectomy for clinically localised prostate cancer	**A. Robotic prostatectomy** **B. Open prostatectomy**: modification of Walsh 'anatomical radical retropubic prostectomy[218] **Both A and B**: a limited lymph node dissection performed if indicated (Gleason score 4 + 4 = 8 or PSA > 20 ng/ml)	**Safety**: surgical complications **Further treatment**: urinary incontinence **Death**

	A	B
Patients, *n*	1253	485
Age (years), median (range)	62 (35–78)	63 (47–77)
PSA (ng/ml), median (range)	6.0 (4–9)	6.0 (4–10)
Clinical stage,* n *(%)		
cT1	770 (61.5)	251 (51.8)
cT2	435 (34.7)	183 (37.8)
cT3	48 (3.8)	50 (10.4)
Not reported	0	1
Biopsy Gleason score, median (range)	6.3 (0.4–50)	7.4 (0.1–135)
Prostate size (ml), median (range)	38.0 (16–206)	38.0 (16–130)

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Doumerc 2010[105] **Language**: English **Publication type**: full text paper **Number of study centres**: not reported **Setting**: referral institution **Country**: Australia **Recruitment/treatment dates**: February 2006–December 2008 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up, mean (SD)**: A: 11.2 (9.4) months; B: 17.2 (9.7) months **Source of funding**: NIH Grant 5R01DK077116 **Systematic reviewer:** TG	**Inclusion criteria**: clinically localised prostate cancer **Exclusion criteria**: patients with factors considered to increase surgical difficulty, e.g. morbid obesity, prostate size > 100 ml, large middle lobe, previous TURP, a history of laparoscopic hernia mesh repair, multiple abdominal operations, high-volume tumour	**A. Robotic prostatectomy**: described by Patel;[219] transperitoneal surgical approach; trade name and manufacturer of robot not reported **B. Open prostatectomy**: performed via infra-umbilical incision **Lymph node dissection:**	**Safety**: surgical complications, operating time, hospital stay, catheterisation, blood loss **Efficacy**: margins, pT stage, pathological Gleason score **Death**

	A	B
Patients, *n*	212	502
Age (years), mean (range)	61.3 (41–76)	60.1 (40–78)
PSA (ng/ml), mean (range)	7.1 (0.7–41)	8.3 (0.9–64)
Clinical stage,* n *(%)		
T1a	4 (2)	5 (1)
T1b	2 (1)	5 (1)
T1c	99 (47)	201 (40)
T2a	59 (28)	111 (22)
T2b	16 (7)	70 (14)
T2c	32 (15)	95 (19)
T3	0	15 (3)
Gleason score* n *(%)		
≤ 6	73 (34)	126 (25)
7	128 (61)	321 (64)
8–10	12 (5.6)	55 (11)
Prostate size (ml), mean (range)	50 (16–140)	53.2 (20–145)

Data for robotic Gleason scores as reported by study authors.

	A	B
No lymph node, *n* (%)	158/212 (74.5)	239/502 (47.6)
Negative, *n* (%)	54/54 (100)	247/263 (94)
1 positive, *n* (%)	0	11/263 (4)
> 1 positive, *n* (%)	0	5/263 (2)

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Ficarra 2009[106] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Italy **Recruitment/treatment dates**: February 2006–April 2007 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: 1 year **Source of funding**: partially funded by the Italian Ministry for University and Research **Systematic reviewer**: XJ	**Inclusion criteria**: all patients undergoing robotic or open prostatectomy for clinically localised prostate cancer **Exclusion criteria**: not reported **A**: Patients, *n* 103; Age (years), median (IQR) 61 (57–67); BMI (kg/m²), median (IQR) 26 (24–28); PSA (ng/ml), median (IQR) 6.4 (4.6–9) **B**: Patients, *n* 105; Age (years), median (IQR) 65 (61–69); BMI (kg/m²), median (IQR) 26 (24–28); PSA (ng/ml), median (IQR) 6 (5–10) ***Clinical stage*, n (%)** **A**: T1c 77 (75); T2a-b 22 (21); T2c 4 (4) **B**: T1c 66 (63); T2a-b 32 (30); T2c 7 (7) ***Biopsy Gleason score*, n (%)** **A**: n = *97*; ≤6 71 (73); 7 18 (19); 8–10 8 (8) **B**: n = *104*; ≤6 67 (64); 7 29 (28); 8–10 8 (8) **A**: Prostate size (ml), median (IQR) 37.5 (30–48) **B**: Prostate size (ml), median (IQR) 40 (30–47) BMI, body mass index.	**A. Robotic prostatectomy**: trade name of robot: da Vinci system; approaches: extraperitoneal; 64 (62%) had bilateral nerve sparing; lymph node dissected in patients with high risk of lymph node involvement **B. Open prostatectomy**: approaches: extraperitoneal; 41 (39%) had bilateral nerve sparing; same indication as above for lymph node dissection	**Safety**: surgical complications, operating time, hospital stay, catherisation, blood loss **Efficacy**: margins, pT stage **Dysfunction**: urinary incontinence, erectile dysfunction
Author, year: Fracalanza 2008[107] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Italy **Recruitment/treatment dates**: May 2006–October 2006 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: none **Source of funding**: Italian ministry for University and Research **Systematic reviewer**: PS	**Inclusion criteria**: patients with clinically localised prostate cancer (cT1-2) **A**: Patients, *n* 35; Age (years), mean (range) 62 (56–68); BMI (kg/m²), mean (SD) 25.5 (2.7); PSA (ng/ml), median (range) 6.2 (4.2–10.2) **B**: Patients, *n* 26; Age (years), mean (range) 68.5 (59–71); BMI (kg/m²), mean (SD) 26.4 (3.7); PSA (ng/ml), median (range) 6.2 (4.5–9.1) ***Biopsy Gleason score*, n (%)** **A**: ≤6 14 (40); 7 13 (37); 8–9 8 (23) **B**: ≤6 6 (23); 7 16 (62); 8–9 4 (15) **A**: Prostate size (ml), median (range) 40 (30–60); Charlson score, mean (SD) 4 (3–4) **B**: Prostate size (ml), median (range) 36 (30–40); Charlson score, mean (SD) 4.5 (3.7–5) BMI, body mass index.	**A. Robotic prostatectomy**: trade name: da Vinci system; performed with transperitoneal approach with an antegrade prostatic dissection; lymph node dissection carried out in men with a high risk of lymph node involvement **B. Open prostatectomy**: performed according to the Walsh technique;[218] all patients had lymph node dissection, including external iliac and obturatory lymph nodes	**Safety**: surgical complications, operating time, hospital stay, blood loss, surgical incision, time to mobilisation, oral feeding **Efficacy**: margins, pT stage **Learning curve**: operating time

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Krambeck 2009[108] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: clinic **Country**: USA **Recruitment/treatment dates**: August 2002–December 2005 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: yes in the robotic group, no in the open group. **Length of follow-up**: median 1.3 years **Source of funding**: not reported **Systematic reviewer:** XJ	**Inclusion criteria**: patients undergoing clinically localised prostate cancer **Exclusion criteria**: not reported **A** = Robotic prostatectomy **B** = Open prostatectomy Patients, *n*: A 294; B 588 Age (years), median (range): A 61.0 (38.0–76.0); B 61.0 (41.0–77.0) PSA (ng/ml), median (range): A 4.9 (0.5–33.5); B 5.0 (0.6–39.7) ***Clinical stage,* n *(%)*** T1a/b: A 0; B 4 (0.7) T1c: A 214 (72.8); B 418 (71.1) T2a: A 75 (25.5); B 130 (22.1) T2b: A 4 (1.4); B 28 (4.8) T3/4: A 1 (0.3); B 8 (1.4) ***Biopsy Gleason score,* n *(%)*** ≤6: A 214 (72.8); B 441 (75.0) 7: A 70 (23.8); B 133 (22.6) 8–9: A 10 (3.4); B 14 (2.3)	**A. Robotic prostatectomy**: robot trade name: da Vinci system; all patients had pelvic lymphadenectomy **B. Open prostatectomy**: all patients had pelvic lymphadenectomy **Nerve sparing:** **A** = Robotic prostatectomy **B** = Open prostatectomy Unilateral, *n* (%): A 20 (6.8); B 26 (4.4) Bilateral, *n* (%): A 221 (75.1); B 509 (86.6)	**Safety**: surgical complications, operating time, hospital stay **Efficacy**: margins, pathological Gleason score, PSA recurrence, local recurrence, metastatic recurrence **Dysfunction**: urinary incontinence, erectile dysfunction **Death** **Learning curve**: operating time
Author, year: Loeb 2010[109] **Language**: English **Publication type**: full text **Number of study centres**: not reported **Setting**: medical institution **Country**: USA **Recruitment/treatment dates**: 2005–8 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer:** TG	**Inclusion criteria:** not reported **Exclusion criteria:** not reported **A** = Robotic prostatectomy **B** = Open prostatectomy Patients, *n*: A 152; B 137; Total 289 Age (years), mean (SD): A –; B –; Total 58.1 (5.6) PSA (ng/ml), mean (SD): A –; B –; Total 5.4 (2.9) ***Clinical stage,* n *(%)*** T1c: A –; B –; Total 220 (76.1) T2: A –; B –; Total 67 (23.1) T3: A –; B –; Total 1 (0.4) Missing: A –; B –; Total 1 (0.4) ***Gleason score,* n *(%)*** ≤6: A –; B –; Total 199 (68.9) 7: A –; B –; Total 73 (25.2) 8–10: A –; B –; Total 17 (5.9)	**A. Robotic prostatectomy**: various techniques but the prostatic dissection was always antegrade with division of the bladder neck from anterior and posterior **B. Open prostatectomy**: performed in the standard anatomical fashion described by Latiff and Gomez[220]	**Efficacy**: margins, PSA recurrence

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Malcolm 2010[110] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: prostate centre/ institution **Country**: USA **Recruitment/treatment dates**: February 2000–December 2008 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: A: 20 months; B: 31.5 months **Source of funding**: not reported; three authors declared financial interest with In Touch Health Inc., Endocare Inc., Intuitive Surgical Inc., Dendreon Crop, southwest Oncology Group, ContraVac and Theralogix **Systematic reviewer:** CR	**Inclusion criteria**: undergoing operative treatment for localised prostate cancer. Included in the analysis if a baseline and at least one follow-up questionnaire were completed (149 excluded) **Exclusion criteria**: patients were excluded from the analysis if multimodal treatment was administered. 195 patients with a UCLA-PCI function/bother score < 30 at baseline excluded from stat analysis A: Patients, *n* = 447; Age (years), mean (SD) = 59 (6) B: Patients, *n* = 135; Age (years), mean (SD) = 59 (7) ***Clinical stage,* n *(%)*** ≤T1c: A 340 (76); B 112 (83) T2a: A 68 (15); B 17 (13) T2b: A 32 (7); B 6 (4) Unknown: A 7 (2); B 0 ***Biopsy Gleason score,* n *(%)*** ≤6: A 269 (60); B 93 (69) 7: A 154 (34); B 34 (25) ≥8: A 24 (5); B 8 (6) PSA (ng/ml), median (IQR): A 5.2 (3.9–6.8); B 5.7 (4.7–7.3)	**A. Robotic prostatectomy**: nerve-sparing techniques used where clinically appropriate as determined by the surgeon **B. Open prostatectomy**: nerve-sparing techniques used where clinically appropriate as determined by the surgeon; retropubic or perineal route **Nerve sparing:** Spared, *n* (%): A 366 (82); B 95 (70) Not spared, *n* (%): A 81 (18); B 40 (30)	**Dysfunction**: urinary function, sexual function
Author, year: Miller 2007[111] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital institution **Country**: USA **Recruitment/treatment dates**: July 2002–August 2006 **Prospective/retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 6 weeks **Source of funding**: not reported **Systematic reviewer:** XJ	**Inclusion criteria**: patients with clinically localised (cT1-2) prostate cancer **Exclusion criteria**: not reported A: Patients, *n* = 42; Age (years), mean = 61.1 B: Patients, *n* = 120; Age (years), mean = 60.6	**A. Robotic prostatectomy**: robot trade name: da Vinci system (four robotic and two assistant ports in a manner similar to that of Menon *et al.*[221]) **B. Open prostatectomy**: anatomical retropubic radical prostectomy via a 10–12 cm infra-umbilical midline incision **For both A and B**: nerve sparing was performed when oncologically appropriate and in patients who were potent preoperatively	**Safety**: blood loss **Quality of life**

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Nadler 2010[112] **Language**: English **Publication type**: full text paper **Number of study centres**: 1 **Setting**: not reported **Country**: USA **Recruitment/treatment dates**: A: October 2005–October 2006; B: July 2002–February 2006 **Prospective/retrospective data collection**: both **Patients recruited consecutively**: yes **Length of follow-up**: 2 years **Source of funding**: not reported **Systematic reviewer:** CR	**Inclusion criteria:** not reported **Exclusion criteria:** not reported A: 50 patients; B: 50 patients Age (years), mean (range): A: 59.7 (44–77); B: 60 (40–75) BMI (kg/m²), mean (range): A: 28.6 (23.3–42); B: 28.2 (21–42.6) PSA (ng/ml), mean (range): A: 6.5 (1.5–18.8); B: 8.5 (1.9–95.6) ***Clinical stage,* n *(%)*** T1: A: 41 (82); B: 41 (82) T2: A: 9 (18); B: 9 (18) Biopsy Gleason score, mean (range): A: 6.42 (6–9); B: 6.66 (6–10) Prostate size (ml), mean (range): A: 49.4 (27.2–109.1); B: 62.8 (14.9–135.8) ***American Urological Association risk stratification,* n *(%)*** Low: A: 30 (60); B: 28 (56) Moderate: A: 14 (28); B: 12 (24) High: A: 6 (12); B: 10 (20)	**A. Robotic prostatectomy**: four-arm, five-port technique **B. Open prostatectomy**: performed as described by McCarthy and Catalona[222] **Nerve sparing:** Bilateral, *n* (%): A: 38 (76); B: 43 (86) Unilateral, *n* (%): A: 8 (16); B: 0 Non-nerve sparing: A: 4; B: 7 **Lymph node dissection:** A: 29/50 (58%) B: 50/50 (100%) Bilateral, *n* (%): A: 16 (55); B: 45 (90) Unilateral, *n* (%): A: 13 (45); B: 5 (10)	**Safety**: surgical complications, operating time, hospital stay, blood loss **Efficacy**: margins, pT stage, PSA recurrence **Dysfunction**: urinary continence, potency
Author, year: Ou 2009[113] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Taiwan, Province of China **Recruitment/treatment dates**: April 2004–April 2007 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: yes **Length of follow-up**: 15 months **Source of funding**: not reported **Systematic reviewer:** XJ	**Inclusion criteria**: patients undergoing prostatectomy Patients, *n*: A: 30; B: 30 Age (years), mean (SD): A: 67.3 (6.2); B: 70.0 (6.1) BMI (kg/m²), mean (SD): A: 24.2 (3.2); B: 24.1 (3.3) PSA (ng/ml), mean (SD): A: 16.5 (18.8); B: 15.9 (14.1) ***Clinical stage,* n** T1: A: 15; B: 9 T2: A: 15; B: 19 T3: A: 0; B: 2 Biopsy Gleason score, mean (SD): A: 6.1 (0.9); B: 6.2 (1.6)	**A. Robotic prostatectomy**: performed as described by Patel[219] with minor modification; 22/30 (73.3%) patients had bilateral lymph node dissection **B. Open prostatectomy**: performed using Walsh's technique;[218] 30/30 (100%) patients had bilateral lymph node dissection **Nerve sparing**: Unilateral, *n* (%): A: 5 (16.7); B: 1 (3.3) Bilateral, *n* (%): A: 11 (36.7); B: 1 (3.3) Non-nerve sparing, *n* (%): A: 14 (46.7); B: 28 (93.3)	**Safety**: open conversion, surgical complications, operating time, hospital stay, catheterisation, blood loss **Efficacy**: margins, pathological Gleason score, PSA recurrence **Dysfunction**: urinary incontinence, erectile dysfunction **Learning curve**: operating time

BMI, body mass index.

BMI, body mass index.

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Rocco 2009[114] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: institution **Country**: Italy **Recruitment/treatment dates**: A: November 2006–December 2007; B: May 2004–February 2007 **Prospective/retrospective data collection**: A: prospective; B: retrospective **Patients recruited consecutively**: yes in laparoscopic group **Length of follow-up**: 1 year **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients had robotic or laparoscopic prostatectomy **Exclusion criteria**: A: 120 patients; Age (years), median (range): 63 (47–76); PSA (ng/ml), median (range): 6.9 (0.4–23.0) B: 240 patients; Age (years), median (range): 63 (46–77); PSA (ng/ml), median (range): 6.7 (0.7–22.0) ***Clinical stage,* n *(%)*** T1c: A 82 (69%); B 145 (6%) T2a: A 36 (31%); B 93 (39%) Missing: A 2; B 2 Biopsy Gleason score, median (range): A 6 (4–9); B 6 (4–10)	**A. Robotic prostatectomy:** Patel technique[219] **B. Open prostatectomy**: Walsh technique[218]	**Safety**: operating time, hospital stay, catheterisation, blood loss **Efficacy**: margins, pT stage, pathological Gleason score **Dysfunction**: urinary incontinence, erectile dysfunction
Author, year: Schroeck 2008[115] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: not reported **Country**: USA **Recruitment/treatment dates**: August 2003–January 2007 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: yes **Length of follow-up**, mean: A: 1.09 years; B: 1.37 years **Source of funding**: not reported **Systematic reviewer:** CR	**Inclusion criteria:** not reported **Exclusion criteria:** conversion to open procedure A: 362 patients; Age (years), median (range): 59.2 (54.5–63.8); BMI (kg/m^2), median (range): 27.8 (25.7–29.9); PSA (ng/ml), median (range): 5.4 (4.1–7.1) B: 435 patients; Age (years), median (range): 60.3 (55.3–64.7); BMI (kg/m^2), median (range): 27.7 (25.5–30.4); PSA (ng/ml), median (range): 5.3 (4.1–7.2) ***Clinical stage,* n** T1: A 281; B 296 T2: A 57; B 101 T3: A 0; B 12 Not reported: A 2; B 2 ***Biopsy Gleason score,* n** ≤6: A 254; B 241 7: A 89; B 127 8–10: A 9; B 42 Not reported: A 10; B 25 Prostate size (ml), median (range): A 42.9 (34.3–55); B 41.3 (24.4–52)	**A. Robotic prostatectomy**: robot trade name: da Vinci system; performed using Vattikuti Institute technique; lymph node dissection 271/362 (74.9%) **B. Open prostatectomy**: lymph node dissection 313/435 (72%)	**Safety**: blood loss **Efficacy**: margins, pathological Gleason score, PSA recurrence

BMI, body mass index.

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Tewari 2003[116] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: October 1999–December 2002 **Prospective/retrospective data collection:** prospective **Patients recruited consecutively**: yes for open group, not reported for robotic group **Length of follow-up**, mean: A: 236 days; B: 556 days **Systematic reviewer:** XJ	**Inclusion criteria**: patients with clinically localised prostate cancer, patients who had a 10-year life expectancy and had prostate cancer of Gleason score ≥ 6	**A. Robotic prostatectomy**: robot trade name: da Vinci system (robotically assisted Vattikuti Institute prostatectomy) **B. Open prostatectomy**: conducted using the anatomical technique **For A and B**: some patients had lymph node dissection	**Safety**: open conversion, surgical complications, hospital stay, catheterisation, blood loss **Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence **Dysfunction**: urinary incontinence, erectile dysfunction **Quality of life** **Pain** **Death** (none)

	A	B
Patients, *n*	200	100
Age (years), mean (range)	59.9 (40–72)	63.1 (42.8–72)
BMI (kg/m^2), mean (range)	27.7 (19–38)	27.6 (17–41)
Previous abdominal and hernia surgery	20%	19%
PSA (ng/ml), mean (range)	6.4 (0.6–41)	7.3 (1.9–35)
Clinical stage (%, as reported by study authors)		
T1a	0.5	0
T1c	49	59
T2a	10	10
T2b	39	35
T3a	1.5	4
Biopsy Gleason score (%)		
≤ 6	67	52
7	28	35
8–10	6	13
Mean score	6.5	6.6
Prostate size (ml), mean (range)	58.8 (18–140)	48.4 (24.2–70)

BMI, body mass index.

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Truesdale 2010[117] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: academic institution **Country**: USA **Recruitment/treatment dates**: January 2005–November 2009 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer:** CR	**Inclusion criteria**: patients who had undergone open or robot-assisted radical prostatectomy with concurrent pelvic lymph node dissection for histologically proven, clinically localised prostate cancer **Exclusion criteria:** not reported	**A. Robotic prostatectomy**: pelvic lymph node dissection carried out; positive lymph node 1/99 (1%) **B. Open prostatectomy**: pelvic lymph node dissection carried out; positive lymph node 19/217 (8.8%) Overall lymph node positivity rate 6.3%	**Safety**: operating time, blood loss **Efficacy**: pT stage, pathological Gleason score

	A	B
Patients, *n*	99	217
Age (years), mean (SD)	59.2 (7.1)	61.7 (6.8)
BMI (kg/m^2), mean (SD)	24.6 (8.3)	23.1 (9.1)
PSA (ng/ml), mean (SD)	7.04 (7.5)	8.35 (7.62)
Clinical stage,* n *(%)		
T2a	57 (57.6)	155 (71.4)
T2b	4 (4)	12 (5.5)
T2c	38 (38.4)	50 (23)
Biopsy Gleason score,* n *(%)		
≤ 6	28 (28.3)	63 (29)
7	34 (34.3)	95 (43.8)
8–10	37 (3.4)	59 (27.2)
D'Amico risk,* n *(%)		
Low	43 (43.4)	64 (29.5)
Intermediate	36 (36.4)	94 (43.3)
High	20 (20.2)	59 (27.2)

BMI, body mass index.

continued

TABLE 50 Characteristics of the included studies: non randomised comparative studies (robotic vs open prostatectomy) [*n* = 18 (17 primary, 2 secondary)] (*continued*)

Study details	Participant characteristics			Intervention characteristics	Outcomes
Author, year: White 2009[118] **Language**: English **Publication type:** full text **Number of study centres:** 1 **Setting**: community urological practice **Country:** USA **Recruitment/treatment dates:** December 2005–March 2008 **Prospective/retrospective data collection**: retrospective; laparoscopic procedures were conducted before the initiation of the robotic programme **Patients recruited consecutively**: yes in robotic group, no in the laparoscopic group **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer:** XJ	**Inclusion criteria**: patients had clinically localised carcinoma of the prostate			**A. Robotic prostatectomy**: technique as described by Menon *et al.*[223] **B. Open prostatectomy**: performed in the traditional fashion **For both A and B**: nerve sparing was performed in all patients, but not reported whether unilateral or bilateral	**Safety**: open conversion **Efficacy**: margins, pT stage, pathological Gleason score
		A	**B**		
	Patients, *n*	50	50[a]		
	Age (years), mean	62	64.7		
	PSA (ng/ml), mean	4.63	5.04		
	Clinical stage,* n *(%)				
	T1	40 (80)	38 (76)		
	T2	10 (20)	12 (24)		
	T3	0	0		
	Biopsy Gleason score,* n *(%)				
	≤ 6	39 (78)	40 (80)		
	7	10 (20)	9 (18)		
	8–10	1 (2)	1 (2)		
	Matched to the robotic group according to clinical stage, baseline PSA level, age, Gleason score.				

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)]

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Al-Shaiji 2010[121] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: health centre **Country**: Canada **Recruitment/ treatment dates**: November 2004–November 2005 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: yes **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: TG	**Inclusion criteria**: those diagnosed with organ-confined prostate cancer **Exclusion criteria**: not reported	**A: Laparoscopic prostatectomy**: not reported **B. Open prostatectomy**: not reported	**Safety**: blood loss, operating time, hospital stay
Author, year: Anastasiadis 2003[122] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: France **Recruitment/ treatment dates**: May 1998–December 2001 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**, median: A: 15.1 months; B: 15.5 months **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: men with localised prostate cancer **Exclusion criteria**: patients using vacuum erection devices, pharmacological injection therapy or transurethral alprostadil were not included in the questionnaire group	**A. Laparoscopic prostatectomy**: performed with a descending technique **B. Open prostatectomy**: performed with an ascending technique For both interventions the indication for preserving one bundle [laparoscopic *n* = 33 (14.3%); open *n* = 4 (5.7%)] or both bundles [laparoscopic *n* = 77 (33.4%); open *n* = 28 (40.0%)] depended on pre- and intraoperative factors. If all biopsies from one lobe were positive that bundle was usually sacrificed, prioritising cancer control before sexual function	**Safety**: catheterisation, surgical complications **Efficacy**: margins, pT stage, pathological Gleason score **Dysfunction**: urinary continence

	A	B
Patients, *n*	70	70
Age (years), mean (range) SD	60 (48–73) 5.84	62 (46–75) 6.33
PSA level, **n**		
0–10 ng/ml	67	56
> 10 ng/ml	3	14
Clinical stage, **n**		
T1c	55	41
T2a	14	24
T2b	1	3
T2c	0	2
Biopsy Gleason score, **n**		
< 7	34	33
7	32	30
> 7	4	7

	A	B
Patients, *n*	230	70
Age (years), mean (range) SD	64.1 (46–77) 6.4	64.8 (50–75) 6.4
PSA (ng/ml), mean (range) SD	10.7 (1.2–80) 8.8	11.2 (1.2–70) 9.7
Clinical stage, **n** ***(%)***		
T1a–b	10 (4.3)	2 (2.8)
T1c	156 (67.8)	50 (71.4)
T2a	58 (25.2)	17 (24.3)
T2b	6 (2.6)	1 (1.4)
Biopsy Gleason score, mean (range) SD	5.8 (2–9) 1.2	6.1 (3–10) 1.1

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Artibani 2003[123] **Language**: English **Publication type**: full text **Number of study centres**: 2 **Setting**: hospital **Country**: Italy **Recruitment/treatment dates**: January 2001–December 2001 **Prospective/retrospective data collection**: not reported **Patients recruited consecutively**: yes **Length of follow-up**: median (range): A: 10 (4–16) months; B: 10 (4–18) months **Source of funding**: not reported **Additional information**: two groups of patients were from two different hospitals in the same city **Systematic reviewer**: XJ	**Inclusion criteria**: patients undergoing prostatectomy A: 71; B: 50 Age (years), mean (SD): A: 63 (5.8); B: 64 (6.6) PSA (ng/ml), mean (SD): A: 15.7 (17); B: 11 (9) ***Clinical stage,* n *(%)*** T1b: A: 1 (1.5); B: 4 (8) T1c: A: 20 (28); B: 26 (52) T2a: A: 34 (48); B: 15 (30) T2b: A: 10 (14); B: 4 (8) T3: A: 6 (8.5); B: 1 (2) Biopsy Gleason score, mean (SD): A: 5.8 (1.3); B: 5.7 (1.2)	**A. Laparoscopic prostatectomy**: surgical approaches: extraperitoneal **B. Open prostatectomy** **Nerve sparing**: Unilateral, *n* (%): A: 9 (12.7); B: 0 Bilateral, *n* (%): A: 9 (12.7); B: 0 Non-nerve sparing, *n* (%): A: 53 (74.6); B: 50 (100) **Lymph node dissection**: A: not carried out if PSA < 10 ng/ml and biopsy Gleason score < 7 B: all had lymph node dissection	**Safety**: hospital stay, catheterisation, surgical complications **Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence **Dysfunction**: urinary incontinence, erectile dysfunction
Author, year: Bhayani 2003[124] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: urological institute/medical centre **Country**: USA **Recruitment/treatment dates**: July 2001–June 2002 **Prospective/retrospective data collection**: retrospective **Patients recruited consecutively**: unclear **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: all patients undergoing laparoscopic and open radical prostatectomy for localised prostate cancer **Exclusion criteria**: not reported A: 33; B: 24 Age (years), mean (SD): A: 57.4 (6.3); B: 60.5 (6.4) PSA (ng/ml), mean (SD): A: 6.74 (3.8); B: 8.6 (9.1) ***Clinical stage,* n** T1a: A: 0; B: 1 T1c: A: 21; B: 14 T2a: A: 11; B: 8 T2b: A: 1; B: 1 Biopsy Gleason score, mean (SD): A: 6.06 (0.25); B: 6.13 (0.44)	**A. Laparoscopic prostatectomy**: performed using the Guillonneau and Vallancien technique[222] **B. Open prostatectomy**: performed using the Walsh technique[218]	**Safety**: open conversion, operating time, hospital stay, surgical complications, catheterisation, blood loss **Efficacy**: pT stage

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Brown 2004[125] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: urological institution **Country**: USA **Recruitment/ treatment dates**: March 2000–March 2002 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: not reported **Exclusion criteria**: patients requiring conversion to open procedure and patients receiving neoadjuvant hormonal therapy or with metastatic disease A: Patients, *n* = 60; Age (years), mean (median) 58.8 (58.5); PSA (ng/ml), mean (median) 6.4 (6) B: Patients, *n* = 60; Age (years), mean (median) 59 (59); PSA (ng/ml), mean (median) 5.6 (5.1) ***Clinical stage,* n** T1a–b: A 0, B 1 T1c: A 47, B 45 T2a: A 13, B 11 T2b: A 0, B 3 ***Biopsy Gleason score,* n** ≤ 6: A 47, B 41 7: A 13, B 18 8–10: A 0, B 1	**A. Laparoscopic prostatectomy**: performed using the Guillonneau and Vallancien technique.[224] Simultaneous bilateral pelvic lymph node dissection performed in 11 patients **B. Open prostatectomy**: performed in the standard fashion with simultaneous modified bilateral pelvic lymph node dissection. Unilateral or bilateral nerve sparing was performed when indicated	**Safety**: operating time, hospital stay, readmission, surgical complications **Efficacy**: margins, pT stage **Learning curve**: operating time
Author, year: Dahl 2009[126] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/ treatment dates**: 16 June 2003–22 July 2004 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: 12 months **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients 40–70 years old scheduled to undergo open or laparoscopic radical prostatectomy for clinical stage T1–2 N0M0 prostate cancer by any one of three experienced surgeons **Exclusion criteria**: not reported ***n*** At baseline: A 104, B 102 6 months: A 75, B 78 12 months: A 78, B 73 Age (years), mean: A 59.5, B 59.9 ***PSA (ng/ml),* n *(%)*** 0–2.5: A 12 (12), B 11 (11) 2.6–4.0: A 20 (19), B 26 (25) 4.1–7.0: A 42 (40), B 40 (39) 7.1–100: A 17 (16), B 14 (14) > 100: A 13 (13), B 11 (11)	**A. Laparoscopic prostatectomy** **B. Open prostatectomy** **Nerve sparing:** Unilateral, *n* (%): A 5 (5), B 4 (4) Bilateral, *n* (%): A 98 (94), B 98 (96) Non-nerve sparing, *n* (%): A 1 (1), B 0	**Safety**: surgical complications **Dysfunction**: urinary incontinence, erectile dysfunction **Further treatment**: cancer treatment

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Dahl 2006[147] (secondary to Dahl 2009[126]) **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/ treatment dates**: 2001–5 **Prospective/ retrospective data collection**: not reported **Patients recruited consecutively**: yes **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: patients who underwent radical prostatectomy **Exclusion criteria**: not reported From He 2006[225] (secondary to Dahl 2006): **Baseline characteristics**: PSA: 10 ng/ml in > 90% of patients; T1c: 89% **Quote**: 'similar distributions of clinical stages, preoperative PSA levels and Gleason scores on biopsy were seen between two groups'	**A. Laparoscopic prostatectomy**: *n* = 286; performed using modified Guillonneau and Vallancien technique[224] **B. Open prostatectomy**: *n* = 714	**Efficacy**: margins, pT stage, pathological Gleason score
Author, year: Fornara 2004[127] **Language**: German **Publication type**: full text **Number of study centres**: 1 **Setting**: institution **Country**: Germany **Recruitment/treatment dates**: January 2003–April 2004 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported? **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: Clinically localised prostate cancer **Exclusion criteria**: unknown **A** / **B** Patients, *n*: 32 / 32 Age (years), mean (range): 62.9 (42–74) / 64.8 (57–74) PSA (ng/ml), mean (range): 7.9 (3.6–20.8) / 7.25 (4.4–17.3) ***Clinical stage,*** **n** T1a: 2 / 1 T1c: 16 / 15 T2a: 12 / 12 T2b: 2 / 4 Biopsy Gleason score, median (range): 5.7 (3–7) / 5.3 (3–7) Prostate weight (g), median (range): 37 (18–72) / 62.3 (20–120)	**A. Laparoscopic prostatectomy**: pre-peritoneal **B. Open prostatectomy**: ascending technique Both A and B involved removal of the prostate gland and seminal vesicles All patients had lymph node dissection prior to prostatectomy	**Safety**: surgical complications, operating time, hospital stay, catheterisation, blood loss **Efficacy**: margins, pT stage, pathological Gleason score

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Ghavamian 2006[128] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: university hospital **Country**: USA **Recruitment/ treatment dates**: A: 2001–2; B:1999–2001 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: unclear **Length of follow-up**: at least 18 months **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: clinically localised prostate cancer with low comorbidities and a greater than 10-year life expectancy **Exclusion criteria**: not reported **A**: Patients, *n* 70; Age (years), mean (range) SD 60.8 (43–72) 6.1; PSA (ng/ml), mean (range) SD 7.6 (3–16.5) 8.0 ***Clinical stage,* n *(%)***: T1c 54 (77.1); T2a–b 7 (10); T2c 9 (12.86); Biopsy Gleason score, mean (SD) 6.4 (0.8) ***Biopsy Gleason score,* n *(%)***: 5–6 49; 7 19; 8–10 2; Prostate volume (ml), mean (range) 40.8 (20–114) **B**: Patients, *n* 70; Age (years), mean (range) SD 57.8 (44–72) 7.3; PSA (ng/ml), mean (range) SD 9.9 (2.3–33.7) 7.1 ***Clinical stage,* n *(%)***: T1c 49 (70); T2a–b 9 (12.85); T2c 12 (17.1); Biopsy Gleason score, mean (SD) 6.7 (1.3) ***Biopsy Gleason score,* n *(%)***: 5–6 43; 7 21; 8–10 6; Prostate volume (ml), mean (range) 53.2 (19–135)	**A. Laparoscopic prostatectomy**: performed using the Stolzenburg *et al.*[226] and Bollens *et al.*[227] technique. Extraperitoneal *n* = 40; transperitoneal *n* = 30. Nerve sparing performed when appropriate. Lymphadenectomy performed when PSA > 10 ng/nl or Gleason score ≥ 7 **B. Open prostatectomy**: performed using modified Walsh technique.[218] Nerve sparing performed when appropriate. Lymphadenectomy performed when PSA > 10 ng/nl or Gleason score ≥ 7	**Safety**: open conversion, surgical complications, operating time, hospital stay, blood loss **Dysfunction**: urinary incontinence, erectile dysfunction
Author, year: Greco 2010[129] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: clinic **Country**: Italy **Recruitment/treatment dates**: January 2005–November 2007 **Prospective/ retrospective data collection:** prospective **Patients recruited consecutively**: yes **Length of follow-up**: 1 year **Source of funding**: not reported **Systematic reviewer**: TG	**Inclusion criteria:** PSA < 10 ng/ml, Gleason score ≤ 7 and only two positive of at least 12 biopsy cores **Exclusion criteria**: not reported **A**: Patients, *n* 150; Age (years), mean (range) 60.5 (45–76); BMI (kg/m^2), mean (range) 32 (26–38); PSA (ng/ml), mean (range) 6.3 (2.4–10) ***Clinical stage,* n**: T1a 18; T1b 23; T1c 106; T2a 3; Biopsy Gleason score, mean (range) 5 (3–7); Prostate size (ml), mean (range) 45 (18–72) **B**: Patients, *n* 150; Age (years), mean (range) 61.5 (49–74); BMI (kg/m^2), mean (range) 29 (25–53); PSA (ng/ml), mean (range) 6.95 (3.4–10) ***Clinical stage,* n**: T1a 15; T1b 20; T1c 110; T2a 5; Biopsy Gleason score, mean (range) 5 (3–7); Prostate size (ml), mean (range) 54 (20–88)	**A. Laparoscopic prostatectomy**: nerve sparing **B. Open prostatectomy**: nerve sparing	**Safety**: open conversion, surgical complications, operating time, catheterisation, blood loss **Efficacy**: margins, pT stage **Dysfunction**: urinary incontinence, erectile dysfunction

BMI, body mass index.

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Jacobsen 2007[130] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Canada **Recruitment/treatment dates**: October 1999–July 2002 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 12 months **Source of funding**: the Northern Alberta Urology Foundation and Alberta Heritage Foundation for Medical Research **Systematic reviewer**: XJ	**Inclusion criteria**: all men with clinically localised prostate cancer scheduled for radical prostatectomy (open, retropubic or laparoscopic) at the University of Alberta between October 1999 and July 2002 **Exclusion criteria**: previous pelvic radiotherapy, a stated subjective complaint of incontinence at baseline or a neurological impairment known to affect bladder function	**A. Laparoscopic prostatectomy**: approaches: transperitoneal. No lymph node dissection **B. Open prostatectomy**: approaches: transperitoneal. Lymph node dissection was conducted when indicated **Additional information**: patients with risk factors for lymphatic metastases (PSA ≥ 20 ng/ml, clinical stage ≥ T3, Gleason score 8–10) were offered an open procedure in lieu of a laparoscopic procedure	**Efficacy**: margins, pT stage, pathological Gleason score **Dysfunction**: urinary incontinence **Quality of life**

	A (first half)	A (second half)	B
Patients, *n*	67		172
Lost to follow-up at 1 year, *n* (%)	10 (12)		24 (13)
Patients, *n*	29	28	148
Age (years), mean (SD)	62.3 (6.4)	60.9 (6.6)	63.7 (5.7)
BMI (kg/m^2), mean (SD)	26.87 (2.4)	27.54 (2.8)	28.1 (4.0)
PSA, mean (SD)	6.9 (2.0)	7.2 (3.0)	9.8 (8.2)
Clinical stage,* n *(%)			
T1b	0	0	2 (2)
T1c	15 (56)	16 (57)	61 (49)
T2a	8 (29)	8 (29)	41 (33)
T2b	3 (11)	0	8 (6)
T2c	1 (4)	4 (14)	12 (10)
T3a	0	0	1 (0.8)
Biopsy Gleason score, mean (SD)	6.5 (0.51)	6.4 (0.64)	6.4 (0.77)

BMI, body mass index.

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Jurczok 2007[131] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: university hospital **Country**: Germany **Recruitment/treatment dates**: January 2003–April 2006 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: clinical locally confined prostate carcinoma that had been confirmed histologically **Exclusion criteria**: not reported **A**: 163 patients; age (years), median (range) 62.9 (42–74); PSA (ng/ml), median (range) 7.9 (2.4–10.2) **B**: 240 patients; age (years), median (range) 64.8 (52–76); PSA (ng/ml), median (range) 7.25 (4.4–11.3) ***Clinical stage,* n** T1a: A 0, B 6 T1c: A 79, B 75 T2a: A 14, B 12 T2b: A 7, B 7 Not reported: A 63, B 140 Biopsy Gleason score, median: A 5.7, B 5.3 Prostate size (ml), mean (range): A 37 (18–72), B 42.3 (20–120)	**A. Laparoscopic prostatectomy**: pre-peritoneal technique with pelvic lymphadenectomy **B. Open prostatectomy**: ascending retropubic technique as described by Walsh[218] with pelvic lymphadenectomy	**Safety:** open conversion, surgical complications, operating time, hospital stay, catheterisation, blood loss **Efficacy:** margins, pT stage, pathological Gleason score
Author, year: Kim 2007[132] **Language**: Korean **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Republic of Korea **Recruitment/ treatment dates**: A: 2005–6, B: 2003–6 **Prospective/ retrospective data collection**: uncertain **Patients recruited consecutively**: uncertain **Length of follow-up**: uncertain **Source of funding**: uncertain **Systematic reviewer**: PS	**Inclusion criteria**: uncertain **Exclusion criteria**: uncertain **A**: 30 patients; age (years), mean (SD) 66.7 (4.4); BMI (kg/m^2), mean (SD) 24.4 (2.3); PSA (ng/ml), mean (SD) 11.1 (12.5) **B**: 45 patients; age (years), mean (SD) 63.2 (9.2); BMI (kg/m^2), mean (SD) 24.5 (2.7); PSA (ng/ml), mean (SD) 9.3 (10.4) ***Clinical stage,* n *(%)*** T1c: A 21 (70), B 30 (66.7) T2: A 9 (30), B 15 (33.3) Biopsy Gleason score, mean (SD): A 6.5 (0.9), B 6.5 (0.8)	**A. Laparoscopic prostatectomy**: extraperitoneal: all **B. Open prostatectomy** **Nerve sparing:** A: unilateral = 3/30; bilateral = 7/30; non-nerve sparing = 20/30 B: unilateral = 7/45; bilateral = 25/45; non-nerve sparing = 13/45	**Safety**: surgical complications, operating time, hospital stay, catheterisation **Efficacy**: margins, pT stage, pathological Gleason score

BMI, body mass index.

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Lama 2009[133] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Chile **Recruitment/ treatment dates**: January 2003–March 2007 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 3 years **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients having localised prostate cancer, no previous prostate surgery, prostate < 100 g, a Gleason score < 8 and complete data to obtain an adequate follow-up of at least 1 year were recruited **A** / **B** Patients, *n*: 56 / 59 Age (years), mean: 64.4 / 63.5 PSA (ng/ml), mean (range): 7.94 (1.8–35) / 8.85 (2.5–34) ***Clinical stage,*** **n** T1c: 39 / 40 T2a: 15 / 14 T2b: 1 / 5 T2c: 1 / 0 Biopsy Gleason score, mode (range): 5 (3–7) / 5 (3–7)	**A. Laparoscopic prostatectomy** **B. Open prostatectomy**	**Safety**: surgical complications, operating time, hospital stay, catheterisation **Efficacy**: margins, PSA recurrence **Dysfunction**: urinary incontinence, erectile dysfunction **Learning curve**: operating time
Author, year: Martorana 2004[134] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Italy **Recruitment/ treatment dates**: March 2002–November 2003 **Prospective/ retrospective data collection**: not reported **Patients recruited consecutively**: yes **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer:** CR	**Inclusion criteria**: not reported **Exclusion criteria**: not reported **A** / **B** Patients, *n*: 50 / 50 Age (years), median (SD): 64.6 (7.54) / 66.9 (5.46) PSA (ng/ml), median (SD): 10.85 (9.02) / 13.62 (10.53) ***Clinical stage,*** **n** T1: 27 / 20 T2: 22 / 27 T3: 1 / 3 Biopsy Gleason score, median (SD): 5.56 (1.28) / 5.68 (1.35)	**A: Laparoscopic prostatectomy**: performed according to the Montsouris technique[222] **B. Open prostatectomy**	**Safety**: open conversion, surgical complications, operating time, hospital stay, catheterisation **Efficacy**: margins, pT stage, pathological Gleason score **Learning curve**: operating time

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Namiki 2005[135] **Language**: English **Publication type**: full text **Number of study centres**: 4 **Setting**: hospital **Country**: Japan **Recruitment/treatment dates**: January 2002–April 2003 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: not reported **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: newly diagnosed prostate cancer T1–T3N0M0 **Exclusion criteria**: PSA failure > 0.1 ng/ml within 12 months following surgery	**A. Laparoscopic prostatectomy**: performed using the Guillonneau and Vallancien technique[224] with minor modifications **B. Open prostatectomy**: performed using the Walsh technique[218]	**Efficacy**: pT stage, pathological Gleason score **Dysfunction**: urinary function, sexual function **Quality of life**

	A	B
Patients, *n*	45	121
Age (years), mean, median, SD (range)	64.7, 64, 5.8 (54–75)	66.5, 67, 5.8 (49–78)
Comorbidities, **n**		
Diabetes	5	7
Cardiovascular	3	9
Other cancer	4	10
Hypertension	9	33
Gastrointestinal	5	23
PSA (ng/ml), mean, median, SD (range)	8.3, 7.3, 4.5 (2.3–26)	8.9, 7.3, 5.8 (2–54)
Clinical stage, **n**		
T1	27	61
T2	18	55
T3	0	5
Biopsy Gleason score, **n**		
≤ 6	19	48
7	26	73

	A	B
Unilateral, *n* (%)	21 (47)	71 (59)
Bilateral, *n* (%)	3 (6)	20 (16)
Non-nerve sparing, *n* (%)	21 (47)	30 (25)

Indications for nerve sparing depended on preoperative and intraoperative factors, prioritising cancer control

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Namiki 2006[136] **Language**: English **Publication type**: full text **Number of study centres**: 4 **Setting**: hospital **Country**: Japan **Recruitment/ treatment dates**: April 2003–March 2004 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 1 year **Source of funding**: study supported by a grant from the Suzuki Urological Foundation and the Japanese Ministry of Health and Welfare **Systematic reviewer:** CR	**Inclusion criteria**: patients with localised prostate cancer **Exclusion criteria**: only patients with preoperative health-related quality-of-life data and data from at least two later time points were included in the analysis	**A. Laparoscopic prostatectomy** **B. Open prostatectomy**: B1: retropubic B2: perineal	**Efficacy**: pathological Gleason score **Dysfunction**: urinary function, sexual function **Quality of life**

	A	B1	B2
Patients, *n*	64	218	65
Age (years), mean, median, SD (range)	64.7, 64, 5.8 (54–77)	67.1, 67, 5.6 (49–78)	68.6, 70, 5.5 (56–78)
PSA (ng/ml), mean, median, SD (range)	10.1, 8.9, 6.3 (2.3–32)	11.8, 8.4, 10.6 (2.8–67)	7.9, 6.8 4.4 (2.5–25.4)
Clinical stage, n			
T1	33	97	46
T2	28	91	18
T3	3	30	1
Biopsy Gleason score, n			
≤ 6	20	47	18
7	44	171	47

	A	
Unilateral, *n* (%)	28 (44)	105 (37)
Bilateral, *n* (%)	3 (5)	39 (1)
Non-nerve sparing, *n* (%)	33 (51)	139 (49)

Indications for nerve sparing depended on preoperative and intraoperative factors, prioritising cancer control

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Poulakis 2007[137] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Germany **Recruitment/ treatment dates**: A: January 2004 – not reported; B: July 2000 – not reported **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: not < 6 months **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: patients who underwent extra peritoneal laparoscopy and pelvic lymphadenectomy since January 2004 for clinically localised prostate cancer **Exclusion criteria**: patients with follow-up of < 6 months	**A. Laparoscopic prostatectomy**: group 1: ≥ 71 years; group 2: ≤ 59 years **Nerve sparing**: Unilateral: group 1: 13 (18%); group 2: 41 (31%) Bilateral: group 1: 2 (2.8%); group 2: 30 (22.7%) **B. Open prostatectomy**: historical cohort from July 2000 **Nerve sparing**: Unilateral: 11 (5.7%) Bilateral: 3 (4.3%) Only group 1 was compared with the cohort who underwent open prostatectomy	**Safety**: surgical complications, operating time, hospital stay, catherisation, blood loss, mobilisation, oral feeding **Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence **Dysfunction**: urinary incontinence **Death** (**none**)

	A		
	Group I	**Group II**	**B**
Patients, *n*	72	132	70
Age (years), mean (SD)	74.1 (2.3)	57.3 (2.2)	74 (1.9)
BMI (kg/m^2), mean (SD)	29 (4)	27 (5)	30 (5)
Previous abdominal or pelvic surgery, *n* (%)	18 (25)	41 (31)	17 (24.3)
PSA (ng/ml), mean (SD)	13.5 (6.4)	9.1 (7.1)	13.7 (6.8)
***Clinical stage*, n[a]**			
Total	51	133	53
T1c	6	33	6
T2a/b	27	64	30
T2c	18	36	17
Biopsy Gleason score, median (range)	7 (5–9)	6 (5–9)	7 (5–9)
Prostate size (ml), mean (SD)	51 (14)	47 (16)	53 (15)
Comorbidity, mean (range)	2 (1–2)	1 (1–3)	2 (1–2)

BMI, body mass index.
a Data as reported by study authors.

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Raventos Busquets 2007[138] **Language**: Spanish **Publication type**: full text **Number of study centres**: not reported **Setting**: hospital **Country**: Spain **Recruitment/ treatment dates**: January 2004–January 2006 **Prospective/ retrospective data collection**: not reported **Patients recruited consecutively**: yes **Length of follow-up**: none **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria:** not reported **Exclusion criteria:** not reported A: 105 patients; B: 75 patients Age (years), mean, (SD): A 65 (5.9); B 65.6 (6.7) PSA (ng/ml), mean, (SD): A 7.1 (2.2); B 9.28 (NR) ***Clinical stage,* n *(%)***: A / B T1: 78 (74) / 58 (76.9) T2: 27 (26) / 17 (23.1) ***Biopsy Gleason score,* n *(%)***: A / B ≤6: 55 (52.6) / 40 (53) >6: 50 (47.4) / 35 (47) NR, not reported.	**A. Laparoscopic prostatectomy**: extraperitoneal procedure: 20/105 **B. Open prostatectomy**: 41% did not undergo lymph node dissection	**Safety**: operating time, hospital stay **Efficacy**: margins, pT stage **Learning curve**: Operating time
Author, year: Remzi 2005[139] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: not reported **Country**: Austria **Recruitment/ treatment dates**: January 2002–October 2003 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: at least 12 months, mean 14.9 months **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: histologically confirmed adenocarcinoma of the prostate and clinically ≤T2 **Exclusion criteria**: A1: 39 patients; A2: 41 patients; B: 41 patients Age (years), mean (SD): A1 61 (11); A2 59 (12); B 60 (14) PSA (ng/ml), mean (SD): A1 5.5 (3.7); A2 8.1 (6.1); B 6.9 (4.4) Gleason score, mean (SD): A1 5.1 (1.2); A2 5.5 (1.3); B 4.7 (1.5) Prostate size (ml), mean (SD): A1 37 (16); A2 32 (14); B 44 (18)	**A. Laparoscopic prostatectomy**: cutting and dissection performed using a harmonic scalpel and bipolar forceps. A voice-controlled robotic arm (AESOP) was used for camera guidance A1: transperitoneal approach performed using Guillonneau and Vallancien technique;[224] 37/39 (95%) had staging lymphadenectomy A2: extraperitoneal approach performed using Bollens *et al.* technique;[227] 41/41(100%) had staging lymphadenectomy **B. Open prostatectomy**: 29/41 (71%) had staging lymphadenectomy **Nerve sparing**: Nerve sparing, *n* (%): A 46 (57.5); B 29 (71) Non-nerve sparing, *n* (%): A 34 (42.5); B 12 (29)	**Safety**: open conversion, operating time, hospital stay, surgical complications, catheterisation, blood loss **Efficacy**: margins, pT stage, pathological Gleason score **Dysfunction**: urinary continence **Quality of life**: postoperative pain

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Salomon 2002[140] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: France **Recruitment/ treatment dates**: 1988–2001 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**, mean (range): B1: 4.7 (0.27–13.9) years; B2: 5.4 (1.7–8.6) years; A: 1.3 (0.1–3.5) years **Source of funding**: not reported **Systematic reviewer**: CR	**Inclusion criteria**: PSA < 10 ng/ml **Exclusion criteria**: not reported Patients, *n*: A 155; B 151 Age (years), mean: A 63.5; B B1: 63.8; B2: 65.9 PSA (ng/ml), mean: A 6.6; B B1: 5.5; B2: 6.5 ***Clinical stage*, n** T1a–b: A 7; B 15 T1c: A 106; B 71 T2a: A 40; B 57 T2b: A 2; B 8 Biopsy Gleason score, mean: A 5.7; B B1: 5.6; B2: 5.7	**A. Laparoscopic prostatectomy** **B. Open prostatectomy** B1: retropubic *n* = 86 B2: perineal *n* = 65 **Lymphadenectomy**: B1: all B2: preoperative Gleason score ≥ 7 A: preoperative Gleason score ≥ 7	**Safety**: blood transfusion, operating time, hospital stay, catheterisation, surgical complications **Efficacy**: margins, pT stage, pathological Gleason score, PSA recurrence
Author, year: Silva 2007[141] **Language**: English **Publication type**: full text **Number of study centres**: 2 **Setting**: hospital/private practice **Country**: Brazil **Recruitment/ treatment dates**: A: May 2000–August 2004; B: June 1999–October 2003 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: yes **Length of follow-up**: none **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: patients with PSA ≤ 15 ng/ml, Gleason score ≤ 7 in the prostate biopsy, patients with maximum clinical stage of T2 **Exclusion criteria**: Patients, *n*: A 90; B 89 Age (years), median (range): A 63 (46–78); B 63 (46–76) PSA (ng/ml), median: A 7.36; B 7.99 Variance for values not specified.	**A. Laparoscopic prostatectomy** **B. Open prostatectomy** Detail of interventions not reported	**Efficacy**: margins, pT stage, pathological Gleason score

continued

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Soderdahl 2005[142] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: medical centre **Country**: USA **Recruitment/ treatment dates**: 2001–3 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: 12 months **Source of funding**: US Army and the Department of Defence **Systematic reviewer**: XJ	**Inclusion criteria**: patients with newly diagnosed clinically localised prostate cancer **Exclusion criteria**: not reported **A** / **B** Patients, *n*: 116 / 186 Complete survey data, *n*: 93 / 86 Age (years), median: 61 / 59 PSA (ng/ml), median: 5.71 / 6 ***Clinical stage (%)*** T1c: 81.70 / 84.90 T2: 18.30 / 15.10 ***Gleason score,* n *(%)*** ≤6: 74 (79.6) / 58 (67.4) 7: 16 (17.2) / 22 (25.6) 8–10: 3 (3.2) / 6 (7.0)	**A. Laparoscopic prostatectomy** **B. Open prostatectomy** **Nerve sparing**: **A** / **B** Unilateral, *n* (%): 16 (17) / 23 (27) Bilateral, *n* (%): 20 (22) / 38 (44) Non-nerve sparing, *n* (%): 57 (61) / 25 (29)	**Efficacy**: pT stage **Dysfunction**: urinary function, sexual function
Author, year: Soric 2004[143] **Language**: Croatian **Publication type**: full text **Number of study centres**: 1 **Setting**: medical centre **Country**: Croatia **Recruitment/ treatment dates** January 2004–January 2005 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: unclear **Length of follow-up**: **Source of funding:** not reported **Systematic reviewer**: CR	**Inclusion criteria**: patients with localised prostate cancer (T1–T2), <71 years **Exclusion criteria**: **A** / **B** Patients, *n*: 26 / 26 Age (years), mean (range): 62 (52–70) / 64 (50–70) PSA (ng/ml), mean (range): 10.54 (1.25–27) / 14.65 (4.9–60) Clinical stage T1–T2, *n*: 26 / 26 Gleason score, mean (range): 5.5 (3–7) / 5.5 (4–7) Comorbidity,[a] *n*: 0 / 26 a Abdominal surgery, abdominal or pelvic radiotherapy, adipose patients and patients with anaesthetic contraindications.	**A. Laparoscopic prostatectomy** **B. Open prostatectomy**	**Safety**: open conversion, surgical complications, operating time, hospital stay, catheterisation **Efficacy**: margins, pT stage, pathological Gleason score

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
Author, year: Terakawa 2008[144] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: Japan **Recruitment/treatment dates**: January 2000–April 2007 **Prospective/ retrospective data collection**: retrospective **Patients recruited consecutively**: not reported **Length of follow-up**: none **Source of funding**: not reported **Systematic reviewer**: PS	**Inclusion criteria**: patients who underwent both systematic TRUS-guided needle biopsy of the prostate and radical prostatectomy without any neoadjuvant therapies **Exclusion criteria**: **A**: 137 patients; age (years), mean (SD) 67.3 (5.8); PSA (ng/ml), mean (SD) 10.9 (8.5); *Clinical stage,* n *(%)*: T1c 51 (37), T2 86 (63); Biopsy Gleason score, mean (SD) 6.5 (0.9) **B**: 220 patients; age (years), mean (SD) 69.1 (5.9); PSA (ng/ml), mean (SD) 12.9 (15.1); *Clinical stage,* n *(%)*: T1c 74 (34), T2 146 (66); Biopsy Gleason score, mean (SD) 6.4 (1.3) Digital rectal examination, transrectal ultrasonography, PSA assay, TRUS-guided needle biopsy, pelvic computerised tomography and bone scan were used for staging.	**A. Laparoscopic prostatectomy** **Nerve sparing**: Unilateral: 13 (9.5%) Bilateral: 17 (12.4%) Surgical procedure described elsewhere **B. Open prostatectomy** **Nerve sparing**: Unilateral: 19 (8.6%) Bilateral: 17 (7.7%) Surgical procedure described elsewhere	**Efficacy**: margins, pT stage
Author, year: Touijer 2007[145] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: hospital **Country**: USA **Recruitment/treatment dates**: January 2003–June 2005 **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: yes **Length of follow-up**: none **Source of funding**: National Cancer Institute **Systematic reviewer**: PS	**Inclusion criteria**: men with clinically localised (cT1–cT3a) adenocarcinoma of the prostate **Exclusion criteria**: those receiving hormone therapy before surgery (*n* = 36/1213 excluded) **A**: Patients enrolled, *n* 1213; Patients analysed, *n* 485; Age (years), median (IQR) 60 (55–65); PSA (ng/ml), median (IQR) 5.3 (4.0–7.5); *Clinical stage,* n *(%)*: T1c 348 (71.7), T2 125 (25.8), T3 12 (2.5); *Biopsy Gleason score,* n *(%)*: 6 307 (63), 7 151 (31), 8–9 27 (6); Partin probability of non-organ-confined disease, median (IQR) 0.37 (0.33–0.51 **B**: Patients analysed, *n* 692; Age (years), median (IQR) 59 (54–64); PSA (ng/ml), median (IQR) 5.3 (4.1–7.1); *Clinical stage,* n *(%)*: T1c 451 (65), T2 213 (31), T3 28 (4); *Biopsy Gleason score,* n *(%)*: 6 405 (59), 7 228 (33), 8–9 57 (8); Partin probability of non-organ-confined disease, median (IQR) 0.45 (0.33–0.62) Magnetic resonance imaging (MRI) was used for clinical staging.	**A. Laparoscopic prostatectomy**: *n* = 485. Performed using modified Montsouris technique[222] **Nerve sparing**: Unilateral preservation: 6% Bilateral preservation: 89% Bilateral resection: 5% **B. Open prostatectomy**: *n* = 692. Standard technique **Nerve sparing**: Unilateral preservation: 6% Bilateral preservation: 91% Bilateral resection: 3%	**Efficacy**: margins, pT stage, pathological Gleason score

TABLE 51 Characteristics of the included studies: non-randomised comparative studies (laparoscopic vs open prostatectomy) [*n* = 27 (26 primary, 1 secondary)] (*continued*)

Study details	Participant characteristics	Intervention characteristics	Outcomes
			continued
Author, year: Wagner 2007[146] **Language**: English **Publication type**: full text **Number of study centres**: 1 **Setting**: institution **Country**: USA **Recruitment/ treatment dates**: not reported **Prospective/ retrospective data collection**: prospective **Patients recruited consecutively**: not reported **Length of follow-up**: mean: total: > 2 years; A: 26 months; B: 27 months **Source of funding**: not reported **Systematic reviewer**: XJ	**Inclusion criteria**: patients undergoing prostatectomy **Exclusion criteria**: not reported	**A. Laparoscopic prostatectomy**: Montsouris technique[222] was used **B. Open prostatectomy**: anatomical approach of Walsh[218] was used **Nerve sparing**:	**Safety**: operating time, surgical complications, blood loss **Efficacy**: margins, pT stage **Dysfunction**: urinary incontinence, erectile dysfunction

	A	B
Patients, *n*	75	75
Age (years), mean (SD)	58 (6.9)	59 (6.9)
BMI (kg/m^2), mean (SD)	27 (3.0)	29 (4.5)
PSA (ng/ml), mean (SD)	6.2 (4.22)	8.1 (6.27)
Clinical stage,* n *(%)		
T1c	47 (63)	45 (60)
T2a	21 (28)	24 (32)
T2b–2c	7 (9)	6 (8)
T3	0	0
Biopsy Gleason score,* n *(%)		
≤ 6	61 (81)	48 (64)
7	12 (16)	23 (31)
8–10	2 (3)	4 (5)

	A	B
Unilateral, *n* (%)	22 (29)	9 (12)
Bilateral, *n* (%)	47 (63)	62 (83)

BMI, body mass index.
Author admitted there was a selection bias.

Appendix 8

Detailed risk of bias assessment for the included studies

TABLE 52 Risk of bias assessment

Study	Sequence generation	Allocation concealment	Confounding				Blinding	
			Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction
Al-Shaiji 2010[121]	×	?	?				?	
Anastasiadis 2003[122]	×	?	✓	✓	✓	✓	✓	✓
Artibani 2003[123]	×	?	?	?	×	✓	✓	✓
Ball 2006[99]	×	?		✓	✓			✓
Barocas 2010[103]	×	?				✓		
Bhayani 2003[124]	×	×	✓			✓	✓	
Bolenz 2010[100]	×	?	✓				✓	
Brown 2004[125]	×	?	✓			✓	✓	
Carlsson 2010[104]	×	×	×				✓	
Chan 2008[119]	×	×	?				✓	
Dahl 2006[147]	×	?				✓		
Dahl 2009[126]	×	?	✓	✓	✓	✓	✓	×
Doumerc 2010[105]	×	×	×	?		×	?	?
Drouin 2009[101]	×	?	×			✓	✓	
Ficarra 2009[106]	×	×	✓	×	×	✓	✓	✓
Fracalanza 2008[107]	×	×	×			×	✓	
Ghavamian 2006[128]	×	?	?	✓	✓	✓	✓	✓
Greco 2010[129]	×	×	?	✓	✓	✓	✓	✓
Guazzoni 2006[90]	✓	?	✓			✓	✓	
Hu 2006[92]	×	?	?				✓	
Jacobsen 2007[130]	×	?		×		×		✓
Joseph 2005[93]	×	?	?	×	×	?	✓	✓
Jurczok 2007[131]	×	?	✓			✓	✓	
Malcolm 2010[110]	×	?		✓	✓			×
Martorana 2004[134]	×	?	×			×	✓	
Menon 2002[95]	×	?	×	×	×	✓	✓	×
Miller 2007[111]	×	?	?				✓	
Nadler 2010[112]	×	?	×	×	×	?	✓	✓

		Incomplete outcome data				Free of selective reporting				
Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Other bias
		?				?				?
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×
✓	✓	?	?	✓	✓	✓	✓	✓	✓	✓
✓			×	×			?	?		?
	✓				?				✓	?
	✓	✓			✓	✓			✓	✓
		✓				✓				?
	✓	✓			✓	✓			✓	?
		✓				✓				×
		✓				✓				✓
	✓				✓				✓	✓
×	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	?	✓	×		✓	✓	?		✓	?
	✓	✓			✓	✓			✓	✓
×	×	✓	✓	×	×	✓	✓	✓	✓	✓
	✓	✓			✓	✓			✓	✓
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	?
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	✓	✓			✓	✓			✓	✓
		✓				✓				×
	✓		?		✓		✓		✓	?
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	?
	✓	✓			✓	✓			✓	✓
×			?	?			✓	✓		×
	?	✓			✓	✓			✓	?
×	✓	✓	×	×	✓	✓	✓	×	✓	×
		✓				✓				✓
✓	✓	✓	?	?	✓	✓	✓	?	?	?

continued

TABLE 52 Risk of bias assessment (*continued*)

Study	Sequence generation	Allocation concealment	Confounding				Blinding	
			Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction
Namiki 2005[135]	×	?		?	✓			✓
Namiki 2006[136]	×	×		×	×			✓
Ou 2009[113]	×	×	?	?	?	✓	✓	?
Poulakis 2007[137]	×	?	✓	×	✓	✓	✓	✓
Remzi 2005[139]	×	×	×	?		✓	✓	?
Rocco 2009[114]	×	×	✓	✓	✓	✓	✓	✓
Rozet 2007[96]	×	×	✓			✓	✓	
Salomon 2002[140]	×	?	?			✓	✓	
Schroeck 2008[115]	×	×	×			✓	✓	
Silva 2007[141]	×	?				✓		
Soderdahl 2005[142]	×	?		×	×			×
Terakawa 2008[144]	×	×				✓		
Tewari 2003[116]	×	×	✓	✓	?	✓	✓	×
Touijer 2007[145]	×	✓				✓		
Trabulsi 2008[98]	×	?	?			✓	✓	
Truesdale 2010[117]	×	?	?			✓	✓	
Wagner 2007[146]	×	?	×	✓	?	✓	✓	?
White 2009[118]	×	?				✓		

✓, low risk of bias; ?, unclear risk of bias; ×, high risk of bias.
Grey shading indicates that this outcome was not assessed as it was not reported by the study authors.

		Incomplete outcome data				Free of selective reporting				
Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Perioperative safety	Urinary dysfunction	Erectile dysfunction	Efficacy	Other bias
✓			?	?			✓	✓		?
✓			×	×			✓	✓		✓
?	✓	✓	?	?	✓	✓	✓	✓	✓	×
?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	✓	?	?		✓	✓	✓		✓	?
×	×	✓	×	×	✓	✓	✓	✓	✓	✓
	✓	✓			✓	✓			✓	✓
	✓	✓			✓	✓			✓	✓
	✓	✓			✓	✓			✓	✓
	✓				✓				✓	?
×			×	×			✓	✓		✓
	✓				✓				?	?
×	✓	✓	×	×	?	✓	?	?	×	?
	✓				✓				✓	?
	✓	✓			✓	×			?	✓
	✓	✓			✓	✓			✓	✓
?	✓	✓	×	×	✓	✓	×	×	✓	?
	✓				✓				✓	✓

Appendix 9

Data tables

TABLE 53 Summary of outcomes: safety (perioperative)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Equipment failure					
Hu 2006[92]	Robot malfunction (unresponsive and refractory to troubleshooting measures)	2/333 (0.6)	0		First case converted to laparoscopic radical prostatectomy and second case occurred after second robot replacement
Menon 2002[95]	Reported as excluded from analysis and not as equipment failure	Not reported	8; initial problems with the voice recognition system of the AESOP camera holder		'The problem was corrected after the first 4 cases. Inclusion of these 8 patients in analysis would have increased the average operative times for laparoscopic prostatectomy by 10 mins'
Converted to other intervention					
Bhayani 2003[124]	Converted to other intervention		3/36 (8.3)	0/24	
Chan 2008[119]	Converted to other intervention	6/660 (0.9), to open			Secondary report of primary study Barocas 2010[104]
Drouin 2009[101]	Converted to other intervention	0/71	1/85 (1.2)	0/83	
Ghavamian 2006[78]	Converted to other intervention		0/70	0/70	
Greco 2010[129]	Converted to other intervention		0/150	0/150	
Guazzoni 2006[90]	Converted to other intervention		0/60		RCT
Hu 2006[92]	Converted to other intervention	0/322	3/358 (0.8), first 3, to open		
Jurczok 2007[131]	Converted to other intervention		0/163	0/240	
Martorana 2004[134]	Converted to other intervention		0/50	0/50	
Menon 2002[95]	Converted to other intervention	0/40, to open	1/40 (2.5), to open		
Namiki 2005[135]	Converted to other intervention		0/45	0/121	
Ou 2009[113]	Converted to other intervention	2/30 (6.7)		0/30	
Remzi 2005[139]	Converted to other intervention		1/80 (1.3)	0/41	
Rozet 2007[96]	Converted to other intervention	4/133 (3.0)	0/133		
Soric 2004[143]	Converted to other intervention		3/26 (11.5)	0/26	
Tewari 2003[116]	Converted to other intervention	0/200		0/100	
Trabulsi 2008[98]	Converted to other intervention	0/50	7/197 (3.6)		
White 2009[118]	Converted to other intervention	0/50		Not reported	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Blood transfusion					
Al-Shaiji 2010[121]	Blood transfusion		3/70 (4.3)	42/70 (60.0)	
Anastasiadis 2003[122]	Blood transfusion during surgery		6/230 (2.6)	6/70 (8.6)	
Artibani 2003[123]	Blood transfusion		45/71 (63)	17/50 (34.0)	
Bolenz 2010[100]	Blood transfusion	12/262 (4.6)	4/211 (1.9)	32/156 (20.5)	
Brown 2004[125]	Blood transfusion		1/60 (1.7)	31/60 (51.7)	
Carlsson 2010[104]	Blood transfusion	58/1253 (4.6)		112/485 (23.1)	
Chan 2008[119]	Blood transfusion	5/660 (0.8)		11/340 (3.2)	
Doumerc 2010[105]	Blood transfusion	2/212 (0.9)		10/502 (2.0)	
Drouin 2009[101]	Blood transfusion	4/71 (5.6)	5/85 (5.9)	8/83 (9.6)	
Ficarra 2009[106]	Blood transfusion	2/103 (1.9)		15/105 (14.3)	
Fornara 2004[127]	Blood transfusion		2/32 (6.3)	6/32 (18.8)	
Fracalanza 2008[107]	Blood transfusion				
	During surgery	6/35 (17.1)		9/26 (34.6)	
	After surgery	1/35 (2.9)		3/26 (11.5)	
Ghavamian 2006[128]	Blood transfusion		5/70 (7.1)	22/70 (31.4)	
Gosseine 2009[91]	Blood transfusion	4/122 (3.3)	8/125 (6.4)		
Greco 2010[129]	Blood transfusion		3/150 (2.0)	9/150 (6.0)	
Guazzoni 2006[90]	Blood transfusion				RCT
	Homologous		0/60	5/60 (8.3)	
	Autologous		8/60 (13.3)	27/60 (45.0)	
Hu 2006[92]	Blood transfusion	5/322 (1.6)	8/358 (2.2)		
Joseph 2007[94]	Blood transfusion	10/754 (1.3)	35/800 (4.4)		Abstract
Jurczok 2007[131]	Blood transfusion		5/163 (3)	22/240 (9)	*n*/*N* calculated from reported percentages
Kim 2007[132]	Blood transfusion		7/30 (23.3)	10/45 (22.2)	
Kordan 2010[120]	Blood transfusion	7/830 (0.8)		14/414 (3.4)	Secondary to Barocas 2010[104]
Krambeck 2008[108]	Blood transfusion	15/294 (5.1)		77/588 (13.1)	
Lama 2009[133]	Blood transfusion		7/56 (12.5)	23/59 (39.0)	
Martorana 2004[134]	Blood transfusion		1/50 (2.0)	5/50 (10.0)	
Menon 2002[95]	Blood transfusion	0/40	1/40 (2.5)		
Nadler 2010[112]	Blood transfusion	10/50 (20.0)		45/50 (90.0)	
Ou 2009[113]	Blood transfusion	4/30 (13.3)		18/30 (60.0)	
Poulakis 2007[137]	Blood transfusion (unit)		Group I: 2/72 (2.7) Group II: 3/132 (2.3)	13/70 (18.6)	Groups I and II split by age (data not combined)
Rozet 2007[96]	Blood transfusion	13/133 (9.8)	4/133 (3.0)		
Salomon 2002[140]	Blood transfusion		3/155 (1.9)	31/151 (20.5)	
Soric 2004[143]	Blood transfusion (ml), mean		130	240	
Tewari 2003[116]	Blood transfusion	0/200		67/100 (67.0)	
Operating time, minutes (convert hours to minutes: hours x 60 = minutes)					
Al-Shaiji 2010[121]	Operating time, mean (range)		232 (132–348)	170 (108–330)	
Bhayani 2003[124]	Operating time, mean (SD)		348 (72)	168 (33)	
Bolenz 2009[102] (secondary to Bolenz 2010[100])	Operating time, median	198	235	225	

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Brown 2004[125]	Operating time, mean (median)		348 (330)	Not reported	From time of skin incision to time of completion of wound closure
Chan 2008[119]	Operating time, range	63–483		82–245	Range reported from two groups of different prostate size
Doumerc 2010[105]	Operating time, mean (range)	192 (119–525)		148 (75–330)	
Drouin 2009[101]	Operating time, mean (SD)	199.6 (36.6)	257.3 (94.3)	208.5 (76)	
Ficarra 2009[106]	Operating time, median	185		135	
Fornara 2004[127]	Operating time, median (range)		220 (180–360)	140 (120–190)	
Fracalanza 2008[107]	Operating time, mean (SD)	195.6 (45)		127.2 (31.7)	Robotics: insertion of the Veress needle to the suture of the last laparoscopic port; open: from skin incision to suture
Ghavamian 2006[128]	Operating time, mean (SD)		246.4 (46.1)	181.8 (18.7)	Skin incision to closure
Gosseine 2009[1]	Operating time, mean	237	241		
Greco 2010[129]	Operating time, mean (range)		165 (90–240)	120 (60–180)	
Guazzoni 2006[90]	Operating time, mean (SD)		N235 (49.9)	170 (34.2)	RCT Total time in the operating room from entry to exit
Hu 2006[92]	Operating time, median (range)	186 (114–528)	246 (150–768)		
Joseph 2007[94]	Operating time, mean (range)	194 (91–486)	179 (75–450)		Abstract Skin incision to closure
Jurczok 2007[131]	Operating time, median (range)		180 (120–240)	120 (80–190)	
Kim 2007[132]	Operating time, mean (SD)		335.9 (93.7)	201.9 (62.8)	
Krambeck 2008[108]	Operating time, median (25th–75th percentile)	236 (204–285)		204 (162–268)	
Lama 2009[133]	Operating time, mean (SD)		203 (52)	151 (30)	
Martorana 2004[134]	Operating time, mean (range)		358 (180–565)	159 (115–225)	
Menon 2002[95]	Operating time, mean (SD)	274 (94.3)	258 (80.3)		Start of dissection to closure
Nadler 2010[112]	Operating time, mean (range)	341 (175–591)		235 (152–352)	
Ou 2009[113]	Operating time, mean (SD)	205 (103)		213 (37)	
Poulakis 2007[137]	Operating time, mean (SD)		Group I: 144 (36) Group II: 144 (30)	150 (30)	Two age groups
Raventos Busquets 2007[138]	Operating time, mean (SD)		172.3 (43.7)	145.1 (32.9)	
Remzi 2005[139]	Operating time, mean (SD)		Transperitoneal: 279 (70) Extraperitoneal: 217 (51)	195 (72)	
Rocco 2009[114]	Operating time, median (range)	215 (165–450)		160 (90–240)	Skin incision to closure
Rozet 2007[96]	Operating time, mean (range)	166 (90–300)	160 (90–270)		

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
					continued
Salomon 2002[140]	Operating time, mean, SD, (range)		266, 73 (120–510)	Retropubic: 181, 46 (120–360) Perineal: 163, 58 (80–325)	Total operative time included pelvic lymphadenectomy
Soric 2004[143]	Operating time, mean (range)		302 (183–513)	272 (197–304)	
Sundaram 2004[97]	Operating time, mean (range)	290 (210–340)	394 (240–480)		Abstract
Truesdale 2010[117]	Operating time, mean (SD)	153.4 (51.3)		204 (32.9)	
Wagner 2007[146]	Operating time, mean (SD)		282 (53.4)	162 (39.0)	
Hospital stay, days					
Al-Shaiji 2010[121]	Hospital stay, mean, SD, (range)		3.4, 1.84 (2–12)	5.6, 1.49 (2–10)	
Artibani 2003[123]	Hospital stay, mean, SD, (range)		7.2, 3.4 (2–19)	10.2, 2 (7–15)	
Bhayani 2003[124]	Hospital stay, mean (SD)		2.97 (0.55)	3.04 (0.21)	
Bolenz 2009[102]	Hospital stay, median	2	1	2	
Brown 2004[125]	Hospital stay, mean, median (range)		2.8, 2 (6–15)	3, 3 (2–5)	
Chan 2008[119]	Hospital stay, range	0.6–8.8		0.7–3.6	Range reported from two groups of different prostate size
Doumerc 2010[105]	Hospital stay, mean (range)	2.8 (2–7)		505 (3–10)	
Ficarra 2009[106]	Hospital stay, median (range)	6 (5–8)		7 (6–9)	
Fornara 2004[127]	Hospital stay, mean		12.4	11.2	
Fracalanza 2008[107]	Hospital stay, median (range)	5 (9–6)		8 (5–9)	
Ghavamian 2006[128]	Hospital stay, mean		2	3	
Gosseine 2009[91]	Hospital stay, mean (SD)	9 (2.1)	10.2 (3.2)		
Jurczok 2007[131]	Hospital stay, median		9.4	11.2	
Kim 2007[132]	Hospital stay, mean (SD)		6.7 (3.7)	6.9 (2.6)	
Krambeck 2008[108]	Hospital stay (days), *n*/*N* (%)				
	1	86/294 (29.3)		114/588 (19.4)	
	2	176/294 (59.9)		400/588 (68.0)	
	3–6	31/294 (10.5)		65/588 (11.1)	
	≥7	1/294 (0.3)		9/588 (1.5)	
Lama 2009[133]	Hospital stay, mean (SD)		7.3 (4.7)	10.7 (9.2)	
Martorana 2004[134]	Hospital stay, mean		5 (3–39)	6.9 (4–17)	
Nadler 2010[112]	Hospital stay, mean (range)	2.5 (1.12)		2.8 (2–6)	
Ou 2009[113]	Hospital stay, mean (SD)	7.3 (2.3)		8.37 (2.2)	
Poulakis 2007[137]	Hospital stay, mean (SD)		Group I: 9 (2) Group II: 9 (3)	11 (3)	Groups I and II are two age groups (data not combined)
Raventos Busquets 2007[138]	Hospital stay, mean (SD)		4.8 (1.3)	5.79 (1.67)	
Remzi 2005[139]	Hospital stay, mean (SD)		Transperitoneal: 7 (2) Extraperitoneal: 7 (2)	10 (4)	
Rocco 2009[114]	Hospital stay, mean (range)	3 (2–12)		6 (3–16)	
Rozet 2007[96]	Hospital stay, mean (range)	5.4 (3–26)	4.9 (3–20)		

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]	Notes
Salomon 2002[140]	Hospital stay, mean, SD (range)		6.8, 3 (4–21)	Retropubic: 12.1, 7.6 (5–55) Perineal: 7.9, 4.1 (2–22)	
Soric 2004[143]	Hospital stay, mean		12	12	
Sundaram 2004[97]	Hospital stay, mean (range)	1.3 (1–3)	2.2 (1–3)		Abstract
Tewari 2003[116]	Hospital stay, mean (range)	1.2 (< 1–5)		3.5 (3–6)	
Proportion of included men discharged from hospital within the stated interval					
Guazzoni 2006[90]	Discharged on day 6 with or without catheter		54/60 (90.0)	52/60 (86.7)	RCT Delayed discharge was due to fever, persistent lymphorrhea and rectal damage
Menon 2002[95]	Discharge home < 1day	32/40 (80.0)	26/40 (65.0)		
Readmission					
Brown 2004[125]	Readmission due to surgical complications		0/60	1/60 (1.7)	Because of deep-vein thrombosis
Need critical care					
No studies					
Bladder neck stenosis/anastomotic stricture					
Bhayani 2003[124]	Bladder neck contracture		0/33	6/24 (25.0)	
Brown 2004[125]	Bladder neck contracture		0/60	2/60 (3.3)	
Carlsson 2010[104]	Bladder neck contracture (30 days–15 months)	3/1253 (0.2)		22/485 (4.5)	
Dahl 2009[126]	Bladder neck contracture		2/104 (2.0)	0/102	
Ficarra 2009[106]	Stenosis of the urethrovesical anastomosis	3/103 (3.0)		6/105 (5.7)	
Ghavamian 2006[128]	Bladder neck contracture		1/70 (1.4)	3/70 (4.3)	
Hu 2006[93]	Bladder neck contracture	2/322 (0.6)	8/358 (2.2)		
Krambeck 2008[108]	Bladder neck contracture, 1 year	3/248 (1.2)		23/492 (4.7)	
	Stricture, 1 year	8/286 (2.8)		6/492 (1.2)	
Lama 2009[133]	Bladder neck stenosis		5/56 (8.9)	1/59 (1.7)	
Nadler 2010[112]	Bladder neck contracture	2/50 (4.0)		7/50 (14.0)	
Ou 2009[113]	Mild vesicourethral anastomosis stricture	1/30 (3.3)		0/30	
Remzi 2005[139]	Anastomotic stricture		3/80 (3.8)	4/41 (9.8)	
Wagner 2007[146]	Bladder neck contracture		2/75 (2.7)	12/75 (16.0)	
Catheterisation, days					
Anastasiadis 2003[122]	Catheterisation, mean		5.8	7.8	
Artibani 2003[123]	Catheterisation, mean, SD (range)		8, 2.8 (4–18)	8.4, 0.9 (7–12)	
Bhayani 2003[124]	Catheterisation, mean (SD)		14 (6.9)	19 (1.22)	
Doumerc 2010[105]	Catherisation, mean (range)	6.3 (6–21)		7.9 (6–20)	
Drouin 2009[101]	Catheterisation, mean (range)	8.1 (3–31)	8.9 (3–91)	14.7 (6–28)	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Ficarra 2009[106]	Catheterisation, median (range)	5 (4–7)		6 (5–12)	
Fornara 2004[127]	Catheterisation, mean		17.9	13.2	
Gosseine 2009[91]	Catheterisation, mean	5.5	6.5		
Greco 2010[129]	Catheterisation, mean		7	9	
Guazzoni 2006[90]	5-day catheterisation, *n*/*N* (%)		52/60 (86.7)	40/60 (66.7)	RCT Patients requiring 5 days of catherisation
Joseph 2007[94]	Catheterisation, mean (range)	10.2 (7–21)	6.1 (1–48)		Abstract
Jurczok 2007[131]	Catheterisation, median or mean		8.9	10.2	
Kim 2007[132]	Catheterisation, mean (SD)		10.7 (7.8)	12.1 (6.7)	
Lama 2009[133]	Catheterisation, mean (SD)		8.8 (3.9)	14.9 (6.2)	
Martorana 2004[134]	Catheterisation, mean (range)		13 (6–36)	15 (11–21)	
Ou 2009[113]	Catheterisation, mean (SD)	7.7 (2.1)		9.2 (2.9)	
Poulakis 2007[137]	Catheterisation, mean (SD)		Group I: 7 (3) Group II: 7 (2)	22 (6)	Groups I and II are two age groups (data not combined)
Remzi 2005[139]	Catheterisation, mean (range)		Transperitoneal: 7.2 (6–23) Extraperitoneal: 6.1 (4–24)	10.9 (8–35)	
Rocco 2009[114]	Catheterisation, mean (range)	6 (4–30)		7 (4–35)	
Rozet 2007[96]	Catheterisation, mean (range)	9.2 (6–29)	9.0 (7–31)		
Salomon 2002[140]	Catheterisation, mean, SD (range)		5.7, 4.8 (2–30)	Retropubic: 12.1, 8.1 (4–45) Perineal: 11.3, 4.6 (3–30)	
Soric 2004[143]	Catheterisation, mean		10	8	
Tewari 2003[116]	Catheterisation, mean (range)	7 (1–18)		15.8 (7–28)	
Anastomotic leak					
Brown 2004[125]	Anastomotic leak		9/60 (15.0)	2/60 (3.3)	
Carlsson 2010[104]	Anastomotic leak	13/1253 (1.0)		8/485 (1.6)	< 30 days postoperatively
Dahl 2009[126]	Anastomotic leak		2/104 (1.9)	0/102	> 200 ml/day
Drouin 2009[101]	Anastomotic leak	0/71	2/85 (2.4)	1/83 (1.2)	
Ghavamian 2006[128]	Anastomotic leak		2/70 (2.9)	3/70 (4.3)	
Guazzoni 2006[90]	Anastomotic leak		8/60 (13.3)	20/60 (33.3)	RCT
Joseph 2007[94]	Urine leak at cystogram	12/754 (1.6)	112/800 (14.0)		Abstract
Kim 2007[132]	Anastomotic leak		5/30 (16.7)	Not reported	> 14 days; managed by prolonged catheterisation
Martorana 2004[134]	Anastomotic leak		1/50 (2.0)	2/50 (4.0)	
Nadler 2010[112]	Anastomotic leak	2/50 (4.0)		2/50 (4.0)	
Ou 2009[113]	Mild vesicourethral anastomosis leaking	0/30		2/30 (6.7)	
Remzi 2005[139]	Anastomotic leak		8/80 (10.0)	6/41 (14.6)	
Rozet 2007[96]	Anastomotic leak	1/133 (0.8)	1/133 (0.8)		
Salomon 2002[140]	Anastomotic leak		4/155 (2.6)	2/151 (1.3)	
Sundaram 2004[97]	Anastomotic leak	0/10	1/10 (10.0)		Abstract

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Hernia (port/incision sites)					
Menon 2002[95]	Hernia port/incision site	Not reported	1/40 (2.5)		
Nadler 2010[112]	Inguinal hernia	0/50		1/50 (2.0)	
Tewari 2003[116]	Wound dehiscence/hernia	2/200 (1.0)		1/100 (1.0)	
Infection					
Artibani 2003[123]	Fever		15	7	
	Wound infection		0	1	
	Port site infection		1	0	
	Subtotal		16/71 (22.5)	8/50 (16.0)	
Brown 2004[125]	Superficial wound infection		0/60	2/60 (3.3)	
Carlsson 2010[104]	Infection	18		44	All occurred < 30 days postoperatively
	Pneumonia	0		4	
	Infected lymphocele	1		3	
	Wound infection	6		29	
	Subtotal	25/1253 (2.0)		80/485 (16.0)	
Dahl 2009[126]	Wound infection		1/104 (1.0)	0/102	
Drouin 2009[101]	Urinary infection	1/71 (1.4)	0/85	6/83 (7.2)	
Fornara 2004[127]	Wound infection		0/32	2/32 (6.3)	
Ghavamian 2006[128]	Urinary tract infection		1/70 (1.4)	1/70 (1.4)	
Hu 2006[92]	Cellulitis	6	12		
	Orchitis	1	1		
	Clostridium difficile enterocolitis	0	1		
	Pneumonia	0	1		
	Bacterial peritonitis	0	1		
	Subtotal	7/322 (2.2)	16/358 (4.5)		
Jurczok 2007[131]	Wound infection		5/163 (3.1)	8/240 (3.4)	*n*/*N* calculated from reported percentages
Krambeck 2008[108]	Sepsis, 1 month	0		1	
	Urinary tract infection, 1 month	3		6	
	Abdominal abscess, 1 year	0		2	
	Subtotal	3/248 (1.2)		9/249 (3.6)	
Rozet 2007[96]	Wound abscess	1	0		
	Infected pelvic haematoma	3	2		
	Urinary infection	6	1		
	Urinary sepsis	2	2		
	Subtotal	12/133 (9.0)	5/133 (3.8)		
Salomon 2002[140]	Wound infection		2/155 (1.3)	12/151 (7.9)	
	Sepsis		0/155	2/151 (1.3)	
	Subtotal		2/155 (1.3)	14/151 (9.3)	
Tewari 2003[116]	Postoperative fever/pneumonia	0/200		4/100 (4.0)	
Organ injury					
Artibani 2003[123]	Rectal injury		2	0	
	Transient peripheral nerve injury		2	0	
	Subtotal		4/71 (5.6)	0/50	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Bhayani 2003[124]	Epigastric artery injury		1/33 (3.0)	0/24	
Brown 2004[125]	Ureteral injury		2/60 (3.3)	0/60	One required reoperation
Carlsson 2010[104]	Rectal injury	2		8	
	Small bowel injury	1		0	
	Ureteral injury	1		0	
	Femoral nerve injury	2		0	
	Obturator nerve injury	0		2	
	Subtotal	6/1253 (0.5)		10/485 (2.1)	
Doumerc 2010[105]	Bowel injury	1/212 (0.5)		0/502	
Drouin 2009[101]	Rectal injury	0/71	1/85 (1.2)	1/83 (1.2)	
Ficarra 2009[106]	Colon lesion	1		0	
	Rectal lesion	1		0	
	Subtotal	2/103 (1.9)		0/105	
Fornara 2004[127]	Rectal lesion		1/32 (3.1)	0/32 (0)	
Ghavamian 2006[128]	Bladder injury		1/70 (1.4)	0/70	
	Inferior epigastric injury		1/70 (1.4)	0/70	
	Subtotal		2/70 (2.9)	0/70	
Greco 2010[129]	Rectal injury		2/150 (1.3)	1/150 (0.7)	
Guazzoni 2006[90]	Rectal injury		1/60 (1.7)	Not reported	RCT Rectal injury repaired with interrupted sutures intraoperatively
Hu 2006[92]	Artery injury	0	3		
	Nerve injury	0	4		
	Intraoperative heocolonic injury	2	1		
	Intraoperative urethral injury	1	1		
	Intraoperative rectal injury	0	7		
	Rectourethral fistulas	0	7		
	Subtotal	3/322 (0.9)	23/358 (6.4)		
Kim 2007[132]	Rectal injury		1/30 (3.3)	Not reported	Managed by laparoscopic repair
	Epigastric vessel injury		1/30 (3.3)		Managed by simple closure
Lama 2009[133]	Rectal perforation		0/56	1/59 (1.7)	
Martorana 2004[134]	Epigastric vessel injury		1/50 (2.0)	0/50	
	Bladder wall lesion		1/50 (2.0)	0/50	
	Subtotal		2/50 (4.0)	0/50	
Ou 2009[113]	Bladder injury and vesicourethral anastomosis tear	1		0	
	Urinary bladder injury	1		0	
	Rectal injury	0		1	
	Subtotal	2/30 (6.7)		1/30 (3.3)	
Remzi 2005[139]	Rectal injury		1/80 (1.3)	1/41 (2.4)	Repaired intraoperatively
Salomon 2002[140]	Ureteral injury		1/155 (0.6)	0/151	
	Rectal injury		3/155 (1.9)	3/151 (2.0)	
	Subtotal		4/155 (2.6)	3/151 (2.0)	

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Soric 2004[143]	Ureter wound		2/26 (7.7)	Not reported	
Tewari 2003[116]	Rectal injuries	0/200		1/100 (1.0)	
Ileus					
Artibani 2003[123]	Ileus		1/71 (1.4)	0/50	
Brown 2004[125]	Prolonged ileus		2/60 (3.3)	3/60 (5.0)	
Ficarra 2009[106]	Ileus	1/103 (1.0)		1/105 (1.0)	
Ghavamian 2006[128]	Ileus		2/70 (2.9)	1/70 (1.4)	
Hu 2006[92]	Ileus	9/322 (2.8)	19/358 (5.3)		
Krambeck 2008[108]	Ileus, 1 month	5/286 (1.7)		10/564 (1.8)	
Martorana 2004[134]	Ileus		1/50 (2.0)	0/50	
Menon 2002[95]	Ileus	1/40 (2.5), transient	1/40 (2.5), paralytic		
Nadler 2010[112]	Ileus	2/50 (4.0)		0/50	
Remzi 2005[139]	Ileus		1/80 (1.3)	0/41	
Salomon 2002[140]	Ileus		4/155 (2.6)	0/151	
Tewari 2003[116]	Ileus	3/200 (1.5)		3/100 (3.0)	
Deep-vein thrombosis					
Brown 2004[125]	Deep-vein thrombosis		0/60	2/60 (3.3)	
Ghavamian 2006[128]	Deep-vein thrombosis		1/70 (1.4)	1/70 (1.4)	
Hu 2006[92]	Deep-vein thrombosis	2/322 (0.6)	0/358		
Krambeck 2008[108]	Deep-vein thrombosis	1/248 (0.4)		6/492 (1.2)	
Lama 2009[133]	Deep-vein thrombosis		0/56	1/59 (1.7)	
Nadler 2010[112]	Deep-vein thrombosis	0/50		1/50 (2.0)	
Salomon 2002[140]	Deep-vein thrombosis		1/155 (0.6)	2/151 (1.3)	
Tewari 2003[116]	Deep-vein thrombosis	1/200 (0.5)		1/100 (1.0)	
Pulmonary embolism					
Carlsson 2010[104]	Pulmonary embolism	2/1253 (0.2)		5/485 (1.0)	
Dahl 2009[126]	Pulmonary embolism		1/104 (1.0)	0/102	
Krambeck 2008[108]	Pulmonary embolism	0/248		5/492 (1.0)	
Rozet 2007[96]	Pulmonary embolism	0/133	1/133 (0.8)		
Salomon 2002[140]	Pulmonary embolism		1/155 (0.6)	1/151 (0.7)	
Blood loss (ml)					
Al-Shaiji 2010[121]	Blood loss, mean, SD (range)		241.4, 167.0 (50–1200)	849.6, 646.7 (100–3500)	
Bhayani 2003[124]	Blood loss (estimated), mean (SD)		533 (212)	1473 (768)	
Doumerc 2010[105]	Blood loss estimated				Numbers of patients with mean estimated blood loss
	< 499	208/212 (98.1)		349/502 (69.5)	
	500–999	4/212 (1.9)		147/502 (29.3)	
	> 1000	0/212		6/502 (1.2)	
Drouin 2009[101]	Blood loss, mean, SD (range)	310.7, 205.5 (80–1800)	558, 574 (110–1100)	821.2, 582.3 (210–2200)	
Ficarra 2009[106]	Blood loss (intraoperative), median	300		500	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Fornara 2004[127]	Blood loss, median		200	550	
Fracalanza 2008[107]	Blood loss, median (range)	300 (200–400)		500 (250–650)	
Ghavamian 2006[128]	Blood loss (estimated), mean (SD)		275.8 (43.1)	563.2 (54.5)	
Gosseine 2009[91]	Blood loss, mean	551	538		
Greco 2010[129]	Blood loss, mean (range)		450 (150–750)	650 (400–900)	
Guazzoni 2006[90]	Blood loss, mean (SD)		257.3 (177)	853.3 (485)	RCT
Hu 2006[92]	Blood loss (estimated), median (range)	250 (50–1600)	200 (0–1500)		
Joseph 2007[94]	Blood loss (estimated), mean (range)	190.0 (20–1400)	768 (100–2000)		Abstract
Jurczok 2007[131]	Blood loss (estimated), median (range)		200 (100–700)	550 (200–1900)	
Kordan 2010[120]	Blood loss (estimated), median (range)	100 (50–200)		450 (300–600)	Secondary to Barocas 2010[104]
Menon 2002[95]	Blood loss, mean (SD)	256 (164.4)	391 (278.9)		
Miller 2007[111]	Blood loss (estimated operative), mean	232.1	490.4		
Nadler 2010[112]	Blood loss, mean (range)	533 (200–1500)		1540 (500–5000)	
Ou 2009[113]	Blood loss, mean (SD)	314 (284)		912 (370)	
Poulakis 2007[137]	Blood loss (estimated intraoperative), mean (SD)		Group I: 205 (81) Group II: 190 (84)	486 (185)	Groups I and II two age groups (data not combined)
Remzi 2005[139]	Blood loss, mean (SD)		Transperitoneal: 290 (254) Extraperitoneal: 189 (140)	385 (410)	
Rocco 2009[114]	Blood loss, median (range)	200 (50–2000)		800 (150–5000)	
Rozet 2007[96]	Blood loss (operative), mean (range)	609 (100–3000)	512 (70–1800)		
Schroeck 2008[115]	Blood loss (estimated), median (range)	150 (100–173)		800 (500–1200)	
Sundaram 2004[97]	Blood loss (estimated), mean (range)	295 (50–500)	620 (250–2000)		Abstract
Tewari 2003[116]	Blood loss (estimated), mean (range)	153 (25–750)		910 (200–5000)	
Trabulsi 2008[98]	Blood loss (estimated), median (range)	287 (50–1500)	370 (50–3200)		
Truesdale 2010[117]	Blood loss (estimated), mean (SD)	157.7 (105.1)		940.5 (615.0)	
Wagner 2007[146]	Blood loss (estimated), mean (SD)		305 (164.2)	1331 (709.8)	
Surgical incision					
Fracalanza 2008[107]	Length of surgical incision (cm), median (range)	3.5 (3–4)		15 (12–17)	

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Other perioperative complications					
Anastasiadis 2003[122]	Surgical complications		22/230 (9.6)	9/70 (12.9)	Including anastomotic leak, wound infection, rectal injury, temporary ileus, haematoma % complications for open reported as 13.1% in paper (9.17 patients)
Artibani 2003[123]	Acute urinary retention		1	2	
	Pelvic haematoma		1	0	
	Cardiovascular complications		3	0	
	Subtotal		5/71 (7.0)	2/50 (4.0)	
Bhayani 2003[124]	*Major complications*				
	Hydroureteronephrosis		1	0	
	Dislodged catheter requiring replacement		1	0	
	Bladder neck contracture requiring operative bladder neck incision		0	3	
	Subtotal		2/33 (6.0)	3/24 (12.5)	
	Minor complications:				
	Calf myositis		1	0	
	Obturator nerve palsy		1	0	
	Postoperative hydrocele		1	0	
	Epigastric artery injury		1	0	
	Inadvertent cystotomy		1	0	
	Subtotal		5/33 (15.2)	0/24	
	Overall subtotal		7/33 (21.2)	3/24 (12.5)	
Brown 2004[125]	Ulnar neuropathy		1/60	0/60	
	Rectus haematoma		1/60	0/60	
	Subtotal		2/60 (1.7)	0/60	
Carlsson 2010[104]	Myocardial infarction, < 30 days postoperatively	1/1253 (0.1)		2/485 (0.4)	
	Surgical reintervention, < 30 days postoperatively	24/1253 (1.9)		14/485 (2.9)	
Dahl 2009[126]	Lymphocele		4	0	
	Hematuria		5	1	
	Hematoma leading to contracture		1	0	
	Fatal cardiac arrest		0	1	
	Genital femoral nerve irritation		3	0	
	Meatal stricture		1	0	
	Urinary retention		1	1	
	Seroma		1	0	
	Vasovagal syncope		1	0	
	Chronic pain in abdomen		0	1	
	Subtotal		17/104 (16.3)	4/102 (3.9)	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Doumerc 2010[105]	Bleeding	2/212 (0.9)		0/502	
	Severe pain	1/212 (0.5)		0/502	
	Pelvic haematoma	0/212		1/502 (0.2)	
	Subtotal	3/212 (1.4)		1/502 (0.2)	
Drouin 2009[101]	Retention	1	3	3	
	Postoperative bleeding	4	0	0	
	Lymphocele	0/	0	1	
	Subtotal	5/71 (7.0)	3/85 (3.5)	4/83 (4.8)	
Ficarra 2009[106]	Postoperative bleeding	7		7	
	Cardiovascular complications	0		2	
	Wound dehiscence	0		1	
	Surgical re-exploration	4 (due to bleeding)		0	
	Subtotal	11/103 (10.7)		10/105 (9.5)	
Fornara 2004[127]	Lymphocele		0/32	1/32 (3.1)	
Fracalanza 2008[107]	Fever	2/35 (5.7)		4/26 (15.4)	'no other complications'
Ghavamian 2006[128]	Clot retention		1	1	
	Lymphocele		2	2	
	Neuropraxia		1	0	
	Subtotal		4/70 (5.7)	3/70 (4.3)	
Gosseine 2009[91]	Surgical complications	5/122 (4.1)	8/125 (6.4)		
Guazzoni 2006[90]	Fever		1	3	RCT
	Persistent lymphorrhea		4	5	
	Acute urinary retention after removal of catheter		1	1	
	Subtotal		6/60 (10.0)	9/60 (15.0)	
Hu 2006[92]	Myocardial infarction	0	0		
	Cerebrovascular accidents	0	0		
	Lymphocele	3	3		
	Urine retention	13	20		
	Urine leak	24	48		
	Clot retention	1	1		
	Intra-abdominal drain retraction	1	0		
	Acute tubular necrosis	0	1		
	Subtotal	42/322 (13.0)	73/358 (20.4)		
Joseph 2007[94]	Urinary retention	12/754 (1.6)	48/800 (6.0)		Abstract
Jurczok 2007[131]	Rectal lesion		3/163 (1.8)	4/240 (1.6)	*n*/*N* calculated from reported percentages
	Lymphocele		5/163 (3.2)	7/240 (2.9)	
	Revision		2/163 (1.2)	6/240 (2.5)	
Kim 2007[132]	Subcutaneous emphysema		4/30 (13.3)	Not reported	Conservative management

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Krambeck 2008[108]	Urinary retention, 1 month	8/286		7/564	
	Ureteric obstruction, 1 month	0/286		1/564	
	Haemorrhage/haematoma, 1 month	10/286		10/564	
	Renal failure, 1 month	0/286		1/564	
	Drug reaction, 1 month	2/286		7/564	
	Lymphocele, 1 year	1/248		5/492	
	Lymphoedema, 1 year	0/248		0/492	
	Myocardial infarction, 1 month	0/286		0/564	
	Respiratory failure, 1 month	2/286		3/564	
	Stroke, 1 month	3/286		3/564	
	Subtotal	26/248 (10.5)		37/492 (7.5)	
Lama 2009[133]	Urinary retention		1	5	
	Urinary leakage		0	2	
	Bleeding		1	3	
	Seroma		1	0	
	Perioperative hypercapnia		0	1	
	Embolic stroke		0	1	
	Subtotal		3/56 (5.4)	12/59 (20.3)	
Martorana 2004[134]	Uteral stretching		1	0	
	Lymphoceles		0	2	
	Subtotal		1/50 (2.0)	2/50 (4.0)	
Menon 2002[95]	Entrapment of ureter in vesicourethral anastomotic stitch	0/40	1/40 (2.5)		
Nadler 2010[112]	Pneumonia	1		0	
	Gastric ulcer	1		0	
	Subtotal	2/50 (4.0)		0/50	
Ou 2009[113]	Intraoperative bleeding	1		0	
	Lymph leakage for 3 weeks	1		0	
	Subtotal	2/30 (6.7)		0/30	

continued

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]		Open, *n*/*N* (%)[a]	Notes
Poulakis 2007[137]			Group I	Group II		
	Early complications (first 30 days after surgery):					Data not combined
	Minor/moderate complications					Major, moderate and minor complications defined
	Dehiscence/rupture of wound		0	1	7	
	Haematoma/haemorrhage		2	2	7	
	Urinary retention		0	2	1	Medical comorbidity assessed with a scoring algorithm placing patients into four groups (but not defined)
	Prolonged urinary leakage (> 2 weeks)		1	0	3	
	Lymphocele		2	2	2	
	Gastrointestinal symptoms including peritonitis and ileus		0	0	7	
	Delirium		6	0	4	
	Fever > 39ºC (urosepsis)		1	1	1	
	Subtotal		12/72 (16.7)	8/132 (7)	32/70 (43)	
	Major complications					
	Respiratory insufficiency		2	0	2	
	Cardiovascular including arrhythmias and myocardial infarction		1	1	3	
	Thrombophlebitis/pulmonary emboli/stroke		1	1	2	
	Subtotal		4/72 (5.6)	2/132 (1.5)	7/70 (10.0)	
	Late complications (30 days after surgery)					
	Bladder neck contraction		0	0	3	
	Wound hernia		0	1	3	
	Subtotal		0/72	1/132 (0.8)	6/70 (8.6)	
Remzi 2005[139]	Haemorrhage		1/80 (1.3)		3/41 (7.3)	
Rozet 2007[96]	Cardiac complications	0	0			
	Postoperative bleeding	6	1			
	Retention	1	3			
	Renal insufficiency	2	0			
	Subtotal	9/133 (6.8)	4/133 (3.0)			
Salomon 2002[140]	Lymphorrhea		2		6	
	Pelvic haematoma		2		2	
	Postoperative neuropathy		0		2	
	Subtotal		4/155 (2.6)		10/151 (6.7)	
Soric 2004[143]	Blood vessel damage		1/26 (3.8)		Not reported	
	Nerve damage		1/26 (3.8)		Not reported	
	Bladder neck sclerosis		2/26 (7.7)		Not reported	
Sundaram 2004[97]	Transient urinary retention for 3 weeks after the catheter was removed	1/10 (10.0)	0/10			Abstract

TABLE 53 Summary of outcomes: safety (perioperative) (*continued*)

Study	Outcome reported as	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]	Notes
Tewari 2003[116]	Lymphocele	0		2	
	Obturator neuropathy	0		2	
	Myocardial infarction	0		1	
	Postoperative bleeding/re-exploration	1		4	
	Subtotal	1/200 (0.5)		9/100 (9.0)	
Early postoperative results					
Mobilisation					
Fracalanza 2008[107]	Mobilisation (days), mean (SD)	1 (0)		1.2 (0.4)	
Guazzoni 2006[91]	First flatus				RCT
	Day 1		21/60 (35.0)	11/60 (18.3)	
	Day 2		37/60 (61.7)	45/60 (75.0)	
	Day 3		2/60 (3.3)	4/60 (6.7)	
	Mobilisation				
	Day 1		55/60 (91.7)	49/60 (81.7)	
	Day 2		5/60 (8.3)	11/60 (18.3)	
	Day 3		–	–	
	Free ambulation				
	Day 1		14/60 (23.3)	6/60 (10.0)	
	Day 2		46/60 (76.7)	54/60 (90.0)	
	Day 3		–	–	
Poulakis 2007[137]	Time to full mobilisation (days), mean (SD)		Group I: 3.7 (1.2) Group II: 3.2 (1.0)	5.1 (1.7)	Groups I and II two age groups (data not combined)
Oral feeding					
Fracalanza 2008[107]	Resumption of oral feeding (days), mean (SD)	1 (0.3)		1.8 (0.7)	
Guazzoni 2006[90]	Oral solid intake				RCT
	Day 1		–	–	
	Day 2		55/60 (91.7)	58/60 (96.7)	
	Day 3		5/60 (8.3)	2/60 (3.3)	
Poulakis 2007[137]	Time to first oral intake (days), mean (SD)		Group I: 1.1 (0.5) Group II: 0.9 (0.6)	2.3 (0.9)	Groups I and II two age groups (data not combined)
Poulakis 2007[137]	Duration of parenteral fluid administration (days), mean (SD)		Group I: 2.2 (0.9) Group II: 1.9 (0.8)	3.1 (1.2)	Groups I and II two age groups (data not combined)

a Data presented as *n* (%) unless indicated otherwise.

TABLE 54 Summary of outcomes: dysfunction

Study	Measures	Timing	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]	Notes
Urinary incontinence						
Artibani 2003[123]	Incontinence (any amount of urinary leakage)	>12 months		12/20 (60.0)	5/14 (35.7)	
	Incontinence (need protection system)	>12 months		8/20 (40.0)	3/14 (21.4)	
Ball 2006[99]	Urinary function (UCLA-PCI), mean (SD)	6 months				Both validated measures
	Baseline		88 (18)	86 (24)	88 (20)	
	% baseline score		69 (31)	69 (40)	75 (40)	
	Urinary bother (UCLA-PCI), mean (SD)	6 months				
	Baseline		85 (24)	81 (30)	85 (26)	
	% baseline score		78 (45)	75 (40)	74 (40)	
	AUA SI (American Urological Association Symptom Index), mean (SD)	6 months				
	Baseline		72 (22)	70 (23)	74 (21)	
	% baseline score		123 (52)	106 (34)	104 (42)	
Dahl 2009[126]	Not returned to baseline continence	12 months		37/78 (47)	37/72 (51)	12-month data collected by mail survey
	During last 4 weeks how often leaked urine?	12 months				
	Every day			14/78 (17.9)	11/73 (15.1)	
	About once/week			8/78 (10.3)	14/73 (19.2)	
	Less than once/week			24/78 (30.8)	18/73 (24.7)	
	Not at all			32/78 (41.0)	29/73 (39.7)	
	Best description of urinary control during last 4 weeks	12 months				
	No control whatsoever			0/78	0/73	
	Frequent dribbling			2/78 (2.6)	1/73 (1.4)	
	Occasional dribbling			30/78 (38.5)	37/73 (50.7)	
	Total control			46/78 (59.0)	35/73 (47.9)	
	How many pads/adult nappies daily during last 4 weeks?	12 months				
	3 or more			0/78	0/73	
	2			3/78 (3.8)	1/73 (1.4)	
	1			10/78 (12.8)	8/73 (11.0)	
	0			65/78 (83.3)	63/73 (86.3)	
Ficarra 2009[106]	Urinary incontinence (ICIQ-UI)	12 months	3/103 (2.9)		12/105 (11.4)	
	Time to urinary continence, mean	–	25 days (n=103)		75 days (n=105)	

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Ghavamian 2006[128]	Continence, defined as no leakage and no pad use					Continence data converted to incontinence
	Diurnal	3 months		30/70 (42.9)	31/70 (44.3)	
		6 months		21/70 (30.0)	20/70 (28.6)	
		12 months		7/70 (10.0)	8/65 (12.3)	
		18 months		7/70 (10.0)	5/63 (7.9)	
	Nocturnal	3 months		27/70 (38.6)	26/70 (37.1)	
		6 months		19/70 (27.1)	20/70 (28.6)	
		12 months		5/70 (7.1)	6/65 (9.2)	
		18 months		4/70 (5.7)	3/63 (4.8)	
Gosseine 2009[91]	I-PSS and ICS questionnaire scores	1 year				Study reports more than 92% questionnaire response rate
	Using at least one pad for protection		87% of those incontinent at 6 months (= 25% of respondents)	71% of those incontinent at 6 months (= 30% of respondents)		75% A and 70% B respondents reported continent at 6 months
	Using one or more pads for protection		19% of those incontinent at 6 months (= 25% of respondents)	17% of those incontinent at 6 months (= 30% of respondents)		
Greco 2010[129]	Minimal stress incontinence (one or two pads per day)	3 months		13/150 (8.7)	29/150 (19.3)	Data for absence of complete urinary continence converted from complete urinary continence data
	Moderate stress incontinence (two or four pads per day)	3 months		3/150 (2.0)	7/150 (4.7)	
	Absence of complete urinary continence	4 weeks		86/150 (57.3)	104/150 (69.3)	
		3 months		16/150 (10.7)	36/150 (24.0)	
		12 months		4/150 (2.7)	13/150 (8.7)	
Jacobsen 2007[130]	Incontinence (24-hour pad testing, total pad weight gain > 8 mg)	12 months		10/57 (17.5)	19/148 (12.8)	
	I-PSS [7-item (0, mildly to 35, severely symptomatic), subjectively administered urinary symptom questionnaire]	Baseline, mean (SD)		First half (*n* not reported): 7.9 (5.4); Second half (*n* not reported): 9.2 (6.7)	(*n* = 172) 7.3 (6.6)	
		12 months, mean (SD)		First half (*n* = 29): 5.9 (2.9); second half (*n* = 28): 5.7 (1.4)	(*n* = 148) 5.8 (5.0)	

continued

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]		Notes
Joseph 2005[93]	Continence verified by absence of leakage on Valsalva manoeuvre or coughing after catheter removal	Immediately	27/50 (54.0)	40/50 (80.0)			Converted to incontinence
		1 month	37/50 (74.0)	12/50 (24.0)			
		2 months	46/50 (92.0)	36/50 (72.0)			
		3 months	45/50 (90.0)	40/50 (80.0)			
Krambeck 2008[108]	One to two pads/day	12 months	17/244 (7.0)		23/476 (4.8)		
	Three pads/day		3/244 (1.2)		7/476 (1.5)		
Lama 2009[133]	Incontinence (no definition)	6 months		1/56 (1.8)	2/59 (3.4)		
		12 months		0/56	2/59 (3.4)		
Malcolm 2010[110]	Urinary function (UCLA-PCI), mean (SD)	Baseline	92 (13)		89 (18)		195 patients with function/bother score < 30 at baseline excluded from analysis
		3 months	71		73		
		6 months	69		80		
		12 months	74		79		
		18 months	74		82		
		24 months	76		84		
		30 months	75		82		
		36 months	78		83		
	Urinary bother (UCLA-PCI), mean (SD)	Baseline	93 (14)		92 (15)		
		3 months	65		68		
		6 months	77		77		
		12 months	81		84		
		18 months	81		85		
		24 months	83		87		
		30 months	85		88		
		36 months	86		88		
Namiki 2005[135]	Urinary function (UCLA-PCI), mean (SD)	Baseline		94.3 (14.6)	91.4 (18.1)		
		1 month		35.0 (18.8)	63.2 (26.7)		
		3 months		55.5 (29.5)	68.9 (25.3)		
		6 months		69.0 (27.5)	80.2 (21.8)		
		12 months		75.8 (19.2)	83.3 (20.4)		
	Urinary bother (UCLA-PCI), mean (SD)	Baseline		82.4 (25.6)	83.3 (27.1)		
		1 month		53.8 (29.6)	73.4 (26.6)		
		3 months		63.8 (33.5)	76.1 (28.0)		
		6 months		75.0 (28.9)	85.1 (24.4)		
		12 months		75.6 (24.2)	89.7 (20.5)		
Namiki 2006[136]					Retropubic	Perineal	
	Urinary function (UCLA-PCI), mean (SD)	Baseline		95.1 (14.6)	92.9 (18.1)	91.0 (14.6)	
		1 month		43.2 (18.8)	58.5 (26.7)	51.7 (18.8)	
		3 months		63.1 (29.5)	62.1 (25.3)	59.4 (29.5)	
		6 months		75.1 (27.5)	74.4 (21.8)	71.6 (27.5)	
		12 months		75.2 (19.2)	77.9 (20.4)	74.9 (19.2)	

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
	Urinary bother (UCLA-PCI), mean (SD)	Baseline		86.0 (25.6)	88.8 (27.1) 83.0 (25.6)	
		1 month		48.5 (29.6)	67.0 (26.6) 60.0 (29.6)	
		3 months		74.1 (33.5)	72.0 (28.0) 65.6 (33.5)	
		6 months		78.8 (28.9)	81.3 (24.4) 75.0 (28.9)	
		12 months		77.8 (24.2)	84.4 (20.5) 80.9 (24.2)	
Ou 2009[113]	Incontinence (need to wear a pad)	1 week	24/30 (80.0)		29/30 (96.7)	Converted from continence data
		12 months	0/30		1/30 (3.3)	
Poulakis 2007[137]	Incontinence (use of any number of pads)	6 months		Group I: 38/72 (52.8) Group II: 12/132 (9.1)	33/70 (47.1)	In paper reported as urinary continence (use of no pads)
Rocco 2009[114]	Incontinence [use pads (except safety pad)]	3 months	34/115 (29.6)		87/233 (37.3)	
		6 months	8/110 (7.3)		40/229 (17.5)	
		12 months	2/79 (2.5)		26/217 (12.0)	
Soderdahl 2005[142]	UCLA-PCI (score 0–100, with higher score indicating better function or less bother)					% baseline score (defined as a score of at least 80% of the pretreatment score)
	Urinary function, % baseline score	12 months		70.7 ($n=93$)	71.0 ($n=86$)	
	Urinary bother, % baseline score	12 months		83.8 ($n=93$)	86.4 ($n=86$)	Validated measure
Sundaram 2004[97]	Use pads (any number)	Mean: 3 months	3/10 (30.0)	2/10 (20.0)		Abstract Converted from continence data
Tewari 2003[116]	Not achieved continence (continence defined as using no pads or a liner for security reasons only)	Not reported	40/200 (20.0)		56/100 (56.0)	A third party telephone interview asked patients about pad use to manage urinary incontinence
Wagner 2007[146]	EPIC-UISS (score 1–100), mean (SD)	Baseline		95.6 (9.56)	88.2 (20.41)	
	% baseline score at 12 months, mean	12 months		64 ($n=55$)	73 ($n=39$)	Mean postoperative UISS score as a percentage of baseline preoperative function
	Pad use/day	Median: 12 months				
	0			43/67 (64.2)	31/66 (47.0)	
	1			12/67 (17.9)	14/66 (21.2)	
	2			8/67 (11.9)	10/66 (15.2)	
	≥3			4/67 (6)	11/66 (16.7)	

continued

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Erectile dysfunction						
Artibani 2003[123]	Sexual function not recovered	>6 months		52/57 (91.2)	36/40 (90.0)	Erectile function recovery defined as the ability to have intercourse spontaneously or sildenafil assisted
						5/57 (8.8) laparoscopic and 4/40 (10) open patients recovered sildenafil-assisted sexual function
Ball 2006[99]	Sexual function (UCLA-PCI), mean (SD)	6 months				Validated measure
	Baseline		65 (27)	56 (29)	59 (30)	
	% baseline score		43 (43)	25 (21)	33 (33)	
	Sexual bother (UCLA-PCI), mean (SD)	6 months				
	Baseline		69 (33)	60 (36)	64 (38)	
	% baseline score		32 (41)	38 (45)	27 (41)	
Dahl 2009[126]	Not returned to baseline state of erectile function	12 months		44/77 (57.1) (this group was encouraged earlier phosphodiesterase-5 inhibitor use)	50/73 (68.5)	Returning of baseline erectile function converted to non-recovery of baseline function
	During last 4 weeks usual quality of erections	12 months				
	None at all			21/77 (27.3)	18/73 (24.7)	
	Not firm enough for any activity			15/77 (19.5)	12/73 (16.4)	
	Firm enough for masturbation			16/77 (20.8)	26/73 (35.6)	
	Firm enough for intercourse			25/77 (32.5)	17/73 (23.3)	
Ficarra 2009[106]	Erectile function not recovered (in those having bilateral nerve sparing) (potency defined as a score of >17 on the IIEF-5)	12 months	12/64 (18.8)		21/41 (51.2)	Converted from recovery data

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Ghavamian 2006[128]	Erectile function (potency defined as a score of ≥ 3 on the IIEF-5, questions 2 and 3 – able to achieve and maintain erection satisfactory for intercourse more than half the time)					Converted from potency data
	Bilateral nerve sparing	3 months		32/40 (80.0)	25/30 (83.3)	
		6 months		18/40 (45.0)	17/30 (56.7)	
		12 months		11/40 (27.5)	12/29 (41.4)	
		18 months		8/39 (20.5)	8/29 (27.6)	
	Unilateral nerve sparing	3 months		8/10 (80.0)	11/12 (91.7)	
		6 months		8/10 (80.0)	9/12 (75.0)	
		12 months		7/10 (70.0)	7/11 (63.6)	
		18 months		4/9 (44.4)	6/11 (54.5)	
	All	3 months		40/50 (80.0)	36/42 (85.7)	
		6 months		26/50 (52.0)	26/42 (61.9)	
		12 months		18/50 (36.0)	19/40 (47.5)	
		18 months		12/48 (25.0)	14/40 (35.0)	
Greco 2010[129]	Potency, defined as patient's reported ability to achieve sexual intercourse with or without the use of phosphodiesterase-5 inhibitors	1 year		51/150 (34.0)	73/150 (48.7)	Converted from potency data
Joseph 2005[93]	Requires drug aid (sildenafil or tadalafil) (%)	3 months	46	36	Unclear if IIEF means are for those requiring drug aid only or also include those with spontaneous erections	% of patients interviewed at 3 months
	IIEF-5 score, mean (SD)		34 (11)	37 (15)		
Krambeck 2008[108]	Impotent – erections satisfactory for intercourse with or without the use of phosphodiesterase-5 inhibitors	12 months	61/203 (30.0)		155/417 (37.3)	
Lama 2009[133]	Erectile function not preserved (no definition)	12 months		41/56 (73.2)	33/59 (60.0)	Converted from erectile function preserved data

continued

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]	Notes
Malcolm 2010[110]	Sexual function (UCLA-PCI), mean (SD)	Baseline	73 (17)		74 (18)	
		3 months	28		24	
		6 months	33		37	
		12 months	40		43	
		18 months	42		48	
		24 months	45		46	
		30 months	41		50	
		36 months	46		48	
	Sexual bother (UCLA-PCI), mean (SD)	Baseline	84 (20)		86 (20)	
		3 months	41		27	
		6 months	42		28	
		12 months	47		40	
		18 months	51		46	
		24 months	48		52	
		30 months	52		54	
		36 months	45		58	
Namiki 2005[135]	Sexual function (UCLA-PCI), mean (SD)	Baseline		36.2 (23.3)	39.3 (24.7)	
		1 month		5.4 (8.0)	9.5 (15.6)	
		3 months		9.1 (9.5)	10.0 (11.6)	
		6 months		7.5 (8.5)	13.0 (13.9)	
		12 months		8.4 (12.6)	11.7 (15.2)	
	Sexual bother (UCLA-PCI), mean (SD)	Baseline		72.7 (21.4)	71.5 (27.4)	
		1 month		51.3 (34.9)	48.4 (34.1)	
		3 months		53.8 (32.3)	54.0 (34.9)	
		6 months		48.8 (33.6)	51.5 (36.4)	
		12 months		60.6 (34.8)	59.0 (33.2)	
Namiki 2006[136]					Retropubic / Perineal	
	Sexual function (UCLA-PCI), mean (SD)	Baseline		32.4 (23.3)	33.4 (24.7) / 38.0 (23.3)	
		1 month		4.0 (8.0)	7.5 (15.6) / 6.8 (8.0)	
		3 months		7.8 (9.5)	6.3 (11.6) / 7.1 (9.5)	
		6 months		9.7 (8.5)	7.2 (13.9) / 7.5 (8.5)	
		12 months		10.2 (12.6)	10.4 (15.2) / 8.8 (12.6)	
	Sexual bother (UCLA-PCI), mean (SD)	Baseline		68.5 (21.4)	68.9 (27.4) / 67.9 (21.4)	
		1 month		56.8 (34.9)	55.3 (34.1) / 49.0 (34.9)	
		3 months		63.7 (32.3)	56.2 (34.9) / 51.2 (32.3)	
		6 months		54.4 (33.6)	59.3 (36.4) / 55.1 (33.6)	
		12 months		62.2 (34.8)	58.2 (33.2) / 53.0 (34.8)	

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Ou 2009[113]	Impotent	12 months				Converted from potency data
	Patients had bilateral nerve sparing		0/11		0/1	
	Patients had unilateral nerve sparing		2/5 (40.0)		1/1 (100.0)	
	Unable to have sexual intercourse	12 months				
	Patients had bilateral nerve sparing		2/11 (18.2)		0/1	
	Patients had unilateral nerve sparing		4/5 (80.0)		1/1 (100.0)	
Rocco 2009[114]	Potency not recovered (unable to have complete sexual intercourse)	3 months	80/116 (69.0)		191/233 (82.0)	
		6 months	61/107 (57.0)		158/229 (69.0)	
		12 months	31/79 (39.2)		127/215 (59.1)	
Soderdahl 2005[142]	UCLA-PCI (score 0–100, with higher score indicating better function or less bother)					% baseline score (defined as a score of at least 75% of the pretreatment score) Validated measures
	Sexual function, % baseline score	12 months		35.9 (n=93)	46.0 (n=86)	
	Sexual bother, % baseline score	12 months		42.9 (n=93)	39.0 (n=86)	
Tewari 2003[116]	Time to return to erections (definition not reported) (days), mean	–	180		440	A third party telephone interviewer asked patients about preoperative sexual function, ability to obtain erection and use of sildenafil
Wagner 2007[146]	EPIC-SFSS (score 1–100), mean (SD)	Baseline		70.7 (14.75)	71.2 (16.36)	
	% baseline score at 12 months, mean	12 months		45 (n=37)	37 (n=25)	Mean postoperative UISS score as a % of baseline preoperative function
	Impotent (not had sexual intercourse during the last 4 weeks) in those with nerve sparing	12 months		22/37 (59.5)	14/25 (56.0)	Converted from potency data

continued

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Faecal incontinence						
Ball 2006[99]	Bowel function (UCLA-PCI), mean (SD)	6 months				
	Baseline		86 (14)	84 (18)	87 (15)	
	% baseline score		98 (24)	102 (25)	102 (26)	
	Bowel bother (UCLA-PCI), mean (SD)	6 months				
	Baseline		90 (19)	87 (25)	90 (20)	
	% baseline score		99 (30)	94 (27)	99 (26)	
Malcolm 2010[110]	Bowel function (UCLA-PCI), baseline: mean (SD), 3–36 months: mean % of baseline score	Baseline	88 (14)	87 (14)		
		3 months	101	98		
		6 months	102	102		
		12 months	103	102		
		18 months	103	103		
		24 months	101	104		
		30 months	102	102		
		36 months	102	101		
	Bowel bother (UCLA-PCI), baseline: mean (SD), 3–36 months: mean % of baseline score (PBS)	Baseline	94 (13)	92 (15)		
		3 months	98	93		
		6 months	100	102		
		12 months	100	99		
		18 months	100	100		
		24 months	97	102		
		30 months	99	96		
		36 months	94	99		
Namiki 2005[135]	Bowel function (UCLA-PCI), mean (SD)	Baseline		89.5 (13.9)	88.3 (15.1)	
		1 month		81.6 (18.1)	82.0 (20.1)	
		3 months		86.8 (20.1)	86.0 (18.3)	
		6 months		89.2(13.8)	91.0 (13.4)	
		12 months		89.0 (10.6)	90.2 (13.7)	
	Bowel bother (UCLA-PCI), mean (SD)	Baseline		91.5 (17.8)	91.0 (20.9)	
		1 month		86.0 (25.1)	86.1 (24.5)	
		3 months		87.5 (25.3)	91.5 (17.7)	
		6 months		93.5 (14.7)	94.3 (13.3)	
		12 months		86.5 (21.5)	93.0 (15.9)	

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]		Notes
Namiki 2006[136]					Retropubic	Perineal	
	Bowel function (UCLA-PCI), mean (SD)	Baseline		89.1 (13.9)	89.2 (15.1)	85.9 (13.9)	
		1 month		83.0 (18.1)	82.0 (20.1)	81.0 (18.1)	
		3 months		88.4 (20.1)	85.1 (18.3)	83.0 (20.1)	
		6 months		87.6 (13.8)	87.9 (13.4)	88.3 (13.8)	
		12 months		91.8 (10.6)	85.3 (13.7)	86.6 (10.6)	
	Bowel bother (UCLA-PCI), mean (SD)	Baseline		87.5 (17.8)	90.5 (20.9)	86.3 (17.8)	
		1 month		83.0 (25.1)	88.0 (24.5)	82.0 (25.1)	
		3 months		91.7 (25.3)	87.9 (17.7)	84.0 (25.3)	
		6 months		88.9 (14.7)	89.9 (13.3)	88.4 (14.7)	
		12 months		91.7 (21.5)	88.8 (15.9)	87.7 (21.5)	
Urinary continence							
Anastasiadis 2003[122]	Diurnal continence						% reported as continent
	No pad use (%)	6 months		59.2	43.3		
	No pad use (%)	1 year		76.1	66.7		
	Including pad use without leakage (%)	1 year		89	77.7		
	Nocturnal continence						
	No pad use (%)	1 year		87.1	66.7		
	Including pad use without leakage (%)	1 year		96	90		
Nadler 2010[112]	Continence defined as one or less precautionary pads/day	12 months	39/44 (88.6)		41/46 (89.1)		
Remzi 2005[139]	Early full continence (no pad)	1 month		Transperitoneal: 10/39 (25.6)	8/41 (19.5)		
				Extraperitoneal: 11/41 (26.8)			
		12 months		Transperitoneal: 33/39 (84.6)	33/41 (80.5)		
				Extraperitoneal: 36/41 (87.8)			

continued

TABLE 54 Summary of outcomes: dysfunction (*continued*)

Study	Measures	Timing	Robotic, *n/N* (%)[a]	Laparoscopic, *n/N* (%)[a]	Open, *n/N* (%)[a]	Notes
Potency						
Anastasiadis 2003[122]	Potency rate (%)	1 year		41	30	% reported potent
	Potency rate after preservation of one neurovascular bundle (%)	1 year		46	27	Potency defined as the ability to achieve and maintain an erection suitable for sexual intercourse
	Potency rate after preservation of both neurovascular bundles (%)	1 year		53	44	
	Potency rate patients < 60 years with bilateral neurovascular preservation (%)	1 year		81	72	
Joseph 2005[93]	% reporting spontaneous erections as assessed by interview	3 months	40	22		
Nadler 2010[112]	Potency	12 months	8/22 (36.4)		0/4	Analysis includes only patients potent at baseline, with bilateral nerve sparing and at least 12 months' follow-up (27/50 robot, 34/50 open)
		18 months	10/21 (47.6)		3/6 (50.0)	
		24 months	10/22 (45.5)		11/17 (64.7)	
						Potency defined as score > 17 on SHIM
Satisfied with the outcome of surgery						
Menon 2002[95]	Measure not reported	Robotics: mean 1.5 months	27/30 (90.0)	38/40 (95.0)		
		Laparoscopic: mean 6.5 months				

a Data expressed as *n/N* (%) unless indicated otherwise.

TABLE 55 Summary of outcomes: efficacy

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Positive margin						
Anastasiadis 2003[122]				61/230 (26.5)	20/70 (28.6)	
Artibani 2003[123]				21/71 (29.6)	12/50 (24.0)	
Barocas 2010[103]			281/1413 (19.9)		148/491 (30.1)	
Brown 2004[125]				10/59 (16.9)	12/60 (20.0)	
Dahl 2006[147]				43/286 (15.0)	124/714 (17.4)	
Doumerc 2010[105]	Total		45/212 (21.2)		84/502 (16.7)	
	PT2		17/212 (8.0)		33/502 (6.6)	
	PT3		28/212 (13.2)		51/502 (10.2)	
Drouin 2009[101]			12/71 (16.9)	16/85 (18.8)	15/83 (18.1)	
Ficarra 2009[106]			35/103 (34.0)		21/105 (20.0)	
Fornara 2004[127]				5/32 (15.6)	7/32 (21.9)	
Fracalanza 2008[107]			10/35 (28.6)		6/26 (23.1)	
Greco 2010[129]				12/150 (8.0)	17/150 (11.3)	PT2a/b/c
Guazzoni 2006[90]				16/60 (26.7)	13/60 (21.7)	RCT Positive surgical margin was considered as any ink on the specimen section regardless of pathological stage
Jacobsen 2007[130]				22/67 (32.8)	60/148 (40.5)	
Joseph 2007[94]			99/754 (13.1)	246/800 (30.8)		Abstract
Jurczok 2007[131]	Total			63/163 (38.7)	104/240 (43.3)	% for pathological stage only reported in paper
	T2 a/b/c			16/163 (9.8)	30/240 (12.5)	
	T3 a/b			47/163 (28.8)	74/240 (30.8)	
Kim 2007[132]				11/30 (36.7)	11/45 (24.4	
Krambeck 2008[108]			46/294 (15.6)		100/588 (17.0)	
Lama 2009[133]				16/56 (28.6)	21/59 (35.6)	
Loeb 2010[109]			22/152 (14.5)		25/137 (18.2)	
Martorana 2004[134]	Total			12/50 (24.0)	13/50 (26.0)	
	T2			6/50 (12.0)	5/50 (10.0)	
	T3			6/50 (12.0)	8/50 (16.0)	
Menon 2002[95]			7/40 (17.5)	10/40 (25.0)		

continued

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Nadler 2010[112]	Total		5/50 (10.0)		12/50 (24.0)	
	PT2		2/43 (4.7)		3/33 (9.1)	
	PT3		3/7 (42.9)		9/17 (52.9)	
Ou 2009[113]			15/30 (50.0)		6/30 (20.0)	
Poulakis 2007[137]				Group I: 15/72 (20.8) Group II: 14/132 (10.6)	16/70 (22.9)	Presence of tumour cells at the ink site of surgical specimen
Raventos Busquets 2007[138]				5.7%	16.5%	The sum of the malignant … and malignant margin (unclear in translated version; Spanish paper)
Remzi 2005[139]				Transperitoneal: 10/39 (25.6) Extraperitoneal: 8/41 (19.5)	8/41 (19.5)	
Rocco 2009[114]			26/120 (21.7)		60/240 (25.0)	
Rozet 2007[96]			26/133 (19.5)	21/133 (15.8)		
Salomon 2002[140]				32/155 (20.6)	30/151 (19.9)	
Schroeck 2008[115]			106/362 (29.3)		122/435 (28.0)	
Silva 2007[141]				22/90 (24.4)	37/89 (41.6)	
Soric 2004[143]				6/26 (23.1)	3/26 (11.5)	
Sundaram 2004[97]			2/10 (20.0)	2/10 (20.0)		Abstract
Terakawa 2008[144]				54/137 (39.4)	52/220 (23.6)	Presence of cancer at the inked margin of resection in the radical prostatectomy specimen
Tewari 2003[116]			18/200 (9.0)		23/100 (23.0)	
Touijer 2007[145]				Overall rate: 11.3%	Overall rate: 11%	Presence of cancer at the inked margin of resection in the radical prostatectomy specimen regardless of whether or not additional tissue was resected
	Incidence of positive surgical margins over time, OR per 100 patients (95% CI)			Overall rate: 0.72 (0.56 to 0.89), p=0.003 Organ-confined disease: 0.60 (0.40 to 0.90), p=0.01 Non-organ-confined disease: 0.26 (0.06 to 1.05), p=0.061	Overall rate: 1.06 (0.94 to 1.21), p=0.3 Organ-confined disease: 1.08 (0.80 to 1.46), p=0.6 Non-organ-confined disease: 1.39 (0.75 to 2.44), p=0.3	

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
	Risk of positive surgical margins, OR (95% CI)			1.156 (0.792 to 1.686)		Laparoscopic compared with open, adjusted for organ-confined probability ($p = 0.5$)
Trabulsi 2008[98]			3/50 (6.0)	35/190 (18.4)		Used a whole-mount step section technique. Positive if tumour appeared at the inked margin
Wagner 2007[146]				7/75 (9.3)	14/75 (18.7)	Extension of tumour to the inked surface of the resected specimen
White 2009[118]			11/50 (22.0)		18/50 (36.0)	Presence of tumour tissue on the inked surface of the specimen
Pathology stage						
Anastasiadis 2003[122]	T2a			165/230 (71.7)	46/70 (65.7)	
	T3a			38/230 (16.5)	12/70 (17.1)	
	T3b			27/230 (11.7)	12/70 (17.1)	
Artibani 2003[123]	T2			42/71 (59.2)	33/50 (66.0)	
	T3a			18/71 (25.4)	8/50 (16.0)	
	T3b			5/71 (7.0)	5/50 (10.0)	
	T4			4/71 (5.6)	2/50 (4.0)	
	N4			1/71 (1.4)	2/50 (4.0)	
Ball 2006[99]	T2		58/82 (70.7)	96/124 (77.4)	86/135 (63.7)	
	T3/4		23/82 (28.0)	26/124 (21.0)	46/135 (34.1)	
	Unknown		1/82 (1.2)	2/124 (1.6)	3/135 (2.2)	
Barocas 2010[103]	T0		7/1413 (0.5)		3/491 (0.6)	
	T2		1136/1413 (80.4)		342/491 (69.7)	
	T3		268/1413 (19.0)		144/491 (29.3)	
	T4		0/1413		2/491 (0.4)	
Bhayani 2003[124]	T0			0/33	1/24 (4.2)	
	T2			26/33 (78.8)	14/24 (58.3)	
	T3a			6/33 (18.2)	6/24 (25.0)	
	T3b			1/33 (3.0)	3/24 (12.5)	
Brown 2004[125]	T2a			14/59 (23.7)	13/60 (1.7)	
	T2b			34/59 (57.6)	39/60 (65.0)	
	T3a			8/59 (13.6)	4/60 (6.7)	
	T3b			2/59 (3.4)	3/60 (5.0)	
	T4			1/59 (1.7)	1/60 (1.7)	
Dahl 2006[147]						Pathological stage for positive margins
	T0			0/0	8/714 (1.1)	T0: 0/0 vs 0/8
	T2			246/286 (86.0)	583/714 (81.7)	T2: 32/246 (13.0) vs 77/583 (13.2)
	T3			40/286 (14.0)	123/714 (17.2)	T3: 11/40 (27.5) vs 47/123 (38.2)

continued

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Doumerc 2010[105]	T2a		18/212 (8.5)		37/502 (7.4)	
	T2b		12/212 (5.7)		20/502 (4.0)	
	T2c		116/212 (54.7)		268/502 (53.4)	
	T3a		55/212 (25.9)		129/502 (25.7)	
	T3b		11/212 (5.2)		48/502 (9.6)	
Drouin 2009[101]	T2a		3/71 (4.2)	6/85 (7.1)	5/83 (6.0)	
	T2b		10/71 (14.1)	6/85(7.1)	5/83 (6.0)	
	T2c		48/71 (67.6)	58/85 (68.2)	58/83 (69.9)	
	T3a		9/71 (12.7)	11/85 (12.9)	13/83 (15.7)	
	T3b		1/71 (1.4)	4/85 (4.7)	2/83 (2.4)	
Ficarra 2009[106]	T2		60/103 (58.3)		49/105 (46.7)	
	T3a		39/103 (37.9)		42/105 (40.0)	
	T3b		4/103 (3.9)		14/105 (13.3)	
Fornara 2004[127]	T2a			4/32 (12.5)	4/32 (12.5)	
	T2b			4/32 (12.5)	2/32 (6.3)	
	T2c			23/32 (71.9)	25/32 (78.1)	
	T3a			1/32 (3.1)	1/32 (3.1)	
Fracalanza 2008[107]	T2a		4/35 (11.4)		3/26 (11.5)	
	T2c		19/35 (54.3)		8/26 (30.8)	
	T3a		11/35 (31.4)		11/26 (42.3)	
	T3b		1/35 (2.9)		4/26 (15.4)	
Greco 2010[129]	T2a			120/150 (80.0)	118/150 (78.7)	Laparoscopic T2a reported as 129/150. Contacted author to clarify if this is a typo and should be 120 ($n=159$ otherwise)
	T2b			15/150 (10.0)	17/150 (11.3)	
	T2c			12/150 (8.0)	10/150 (6.7)	
	T3a/3b			3/150 (2.0)	5/150 (3.3)	
Guazzoni 2006[90]	T2			45/60 (75.0)	44/60 (73.3)	RCT
	T3a			12/60 (20.0)	14/60 (23.3)	
	T3b			3/60 (5.0)	2/60 (3.33)	
Jacobsen 2007[130]	T0			1/67 (1.5)	1/148 (0.7)	Numbers for open add to 144 but $n=148-4$ not reported
	T2a			7/67 (10.4)	16/148 (11.0)	
	T2b			1/67 (1.5)	4/148 (2.7)	
	T2c			39/67 (58.2)	78/148 (52.7)	
	T3a			6/67 (9.0)	30/148 (20.3)	
	T3b			3/67 (4.5)	15/148 (10.1)	
	T4			0/67	0/148	
Jurczok 2007[131]	T2a			26/162 (16.0)	45/240 (18.8)	Percentages only reported in paper. Laparoscopic percentages add up to 99%. No mention of withdrawals. Figures total 162 instead of total 163 patients in group
	T2b			44/162 (27.2)	53/240 (22.1)	
	T2c			38/162 (23.4)	60/240 (25.0)	
	T3a/b			54/162 (33.3)	82/240 (34.2)	
Kim 2007[132]	T2			26/30 (86.7)	36/45 (80.0)	Laparoscopic T2 reported as 16/30 (86.7%). Presumed 16 is an error and actual figure is 26/30
	T3			4/30 (13.3)	5/45 (11.1)	
	T4			0/30	4/45 (8.9)	

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]		Open, *n*/*N* (%)[a]	Notes
Martorana 2004[134]	T2			31/50 (62.0)		28/50 (56.0)	
	T3			19/50 (38.0)		22/50 (44.0)	
Menon 2002[95]	T2a		9/40 (22.5)	7/40 (17.5)			
	T2b		24/40 (60.0)	30/40 (75.0)			
	T3a		4/40 (10.0)	2/40 (5.0)			
	T3b		3/40 (7.5)	0/40			
	T4a		0/40	1/40 (2.5)			
Nadler 2010[112]	T2		43/50 (86.0)			33/50 (66.0)	
	T3		7/50 (14.0)			17/50 (34.0)	
Namiki 2006[136]	T2			53/64 (82.8)		200/283 (70.7)	
	T3			11/64 (17.2)		83/283 (29.0)	
Namiki 2005[135]	T2			30/45 (66.7)		103/121 (85.1)	
	T3			15/45 (33.3)		17/121 (14.0)	
	T4			0/45		1/121 (0.8)	
Poulakis 2007[137]				Group I:	Group II:		Groups I and II two age groups (data not combined)
	T2a			3/72 (4.2)	24/132 (18.2)	4/70 (5.7)	
	T2b			10/72 (13.9)	28/132 (21.2)	12/70 (17.1)	
	T2c			27/72 (37.5)	38/132 (28.8)	24/70 (34.3)	
	T3a			19/72 (26.4)	26/132 (19.7)	17/70 (24.3)	
	T3b			13/72 (18.1)	16/132 (12.1)	13/70 (18.6)	
Raventos Busquets 2007[138]	T2			80%		70.90%	Laparoscopic: *n* = 105; open: *n* = 75
	T3			20%		29.10%	
Remzi 2005[139]				Trans-peritoneal	Extra-peritoneal		
	T2			24/39 (61.5)	27/41 (65.9)	26/41 (63.4)	
	T3			14/39 (35.9)	14/41 (34.1)	14/41 (34.1)	
	T4			1/39 (2.6)	0	1/41 (2.4)	
Rocco 2009[114]	T2		88/120 (73.3)			150/240 (62.5)	
	T3		29/120 (24.2)			85/240 (35.4)	
	T4		3/120 (2.5)			5/240 (2.1)	
Rozet 2007[96]	T2a		16/133 (12.0)	11/133 (8.3)			
	T2b		2/133 (1.5)	6/133 (4.5)			
	T2c		92/133 (69.2)	86/133 (64.7)			
	T3a		16/133 (12.0)	22/133 (16.5)			
	T3b		7/133 (5.3)	8/133 (6.0)			
Salomon 2002[140]						Retropubic:	Figures presented in table 3 for perineal approach add to 100 instead of the 65 who received the procedure
	T2			126/155 (81.3)		66/86 (76.7)	
	T3a			20/155 (12.9)		13/86 (15.1)	
	T3b			9/155 (5.8)		7/86 (8.2)	

continued

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Silva 2007[141]	T2a			9/90 (10.0)	13/89 (14.6)	
	T2b			11/90 (12.2)	2/89 (2.2)	
	T2c			61/90 (67.8)	61/89 (68.5)	
	T3a			1/90 (1.1)	9/89 (10.1)	
	T3b			8/90 (8.9)	4/89 (4.5)	
Soderdahl 2005[142]	T0			1/93 (1.1)	1/86 (1.2)	
	T2			73/93 (78.5)	55/86 (64.0)	
	T3/4			19/93 (20.4)	30/86 (34.9)	
Soric 2004[143]	T1			9/26 (34.6)	6/26 (23.1)	
	T2			9/26 (34.6)	14/26 (53.8)	
	T3			6/26 (23.1)	5/26 (19.2)	
Terakawa 2008[144]	T2			106/137 (77.4)	139/220 (63)	
	T3			31/137 (22.6)	81/220 (36.8)	
Tewari 2003[116]	T2a		30/200 (15.0)		18/100 (18.0)	
	T2b		144/200 (72.0)		75/100 (75.0)	
	T3a		14/200 (7.0)		4/100 (4.0)	
	T3b		12/200 (6.0)		3/100 (3.0)	
Touijer 2007[145]	T0			3/485 (0.6)	8/692 (1.2)	
	T1			29/485 (6.0)	25/692 (3.6)	
	T2a			65/485 (13.4)	89/692 (12.9)	
	T2b			261/485 (53.8)	355/692 (51.3)	
	T3a			105/485 (21.6)	170/692 (24.6)	
	T3b			17/485 (3.5)	35/692 (5.1)	
	T4			5/485 (1.0)	10/692 (1.4)	
Trabulsi 2008[98]	T0		0/50	1/190 (0.5)		
	T2a		12/50 (24.0)	40/190 (21.1)		
	T2b		0/50	2/190 (1.1)		
	T2c		31/50 (62.0)	119/190 (62.6)		
	T3a		5/50 (10.0)	12/190 (6.3)		
	T3b		2/50 (4.0)	6/190 (3.2)		
	T4		0/50	10/190 (5.3)		
Truesdale 2010[117]	T2		71/99 (71.7)		136/217 (62.7)	% do not match those reported in paper
	T3		23/99 (23.2)		70/217 (32.3)	
	T4		4/99 (4.0)		7/217 (3.2)	
Wagner 2007[146]	T0			1/75 (1.3)	1/75 (1.3)	
	T2			67/75 (89.3)	52/75 (69.5)	
	T3			7/75 (9.3)	21/75 (28.0)	
	T4			0/75	1/75 (1.3)	
White 2009[118]	T2a		12/50 (24.0)		12/50 (24.0)	
	T2c		35/50 (70.0)		35/50 (70.0)	
	T3a		3/50 (6.0)		3/50 (6.0)	

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Pathological Gleason score						
Anastasiadis 2003[122]				6.7, 1.1 (4–10)	6.9, 0.9 (5–10)	Mean, SD (range)
Artibani 2003[123]				6.4 (1.3)	6.3 (0.9)	Mean (SD)
Barocas 2010[103]	≤ 6		723/1413 (51.2)		221/491 (45.0)	
	7		588/1413 (41.6)		213/491 (43.4)	
	8–10		94/1413 (6.7)		54/491 (11.0)	
Dahl 2006[147]	≤ 6		45/212 (21.2)		76/502 (15.2)	**Biopsy Gleason score for positive margins**: 0: 0/0, 0/8; 5–6: 20/192 (10.4), 60/452 (13.3); 7: 17/78 (21.8), 48/199 (24.1); 8–9: 6/16 (7.5), 16/55 (29.1)
	7		149/212 (70.3)		357/502 (71)	
	8–10		18/212 (8.5)		69/502 (13.7)	
Doumerc 2010[105]	≤ 6		45/212 (21.2)		76/502 (15.2)	
	7		149/212 (70.3)		357/502 (71)	
	8–10		18/212 (8.5)		69/502 (13.7)	
Fornara 2004[127]				6.4	5.7	Median
Jacobsen 2007[130]				First half = 6.7 (0.61), Second half = 6.6 (0.74)	6.6 (0.9)	Mean (SD)
Joseph 2007[94]			6.5 (4–10)	6.9 (6–10)		Abstract Mean (range)
Jurczok 2007[131]				6.4	5.7	Median
Kim 2007[132]				6.6 (0.8)	6.6 (0.7)	Mean (SD)
Krambeck 2008[108]	≤ 6		192/294 (65.3)		391/588 (66.5)	
	7		87/294 (29.6)		167/588 (28.4)	
	8–10		14/294 (4.8)		30/588 (5.1)	
Martorana 2004[134]				6.10 (0.91)	6.16 (0.71)	Median (SD)
Menon 2002[95]			6.8 (0.82)	6.8 (0.82)		Mean (SD)
Namiki 2005[135]	6			19/45 (42)	48/121 (39.7)	
	7			26/45 (58)	73/121 (60.3)	
Namiki 2006[136]	≤ 6			20/64 (31.3)	65/283 (23.0)	
	≥ 7			44/64 (68.8)	218/283 (77.0)	
Ou 2009[113]			7.2 (1.1)		6.7 (1.6)	Mean (SD)

continued

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Poulakis 2007[137]				Group I: 7 (5–9) Group II: 6 (5–9)	7 (5–9)	Median (range). Groups I and II two age groups (data not combined)
Remzi 2005[139]				Transperitoneal: 5.1 (2.0) Extraperitoneal: 5.5 (1.9)	4.7 (2.2)	Mean (SD)
Rocco 2009[114]			7 (4–9)		7 (3–9)	Median (range)
Rozet 2007[96]			6.5 (5–9)	6.5 (5–9)		Mean (range)
Salomon 2002[140]				6.6 (4–10)	Retropubic: 6.2 (3–10) Perineal: 6.1 (4–9)	Median (range)
Schroeck 2008[115]	≤6		168/362 (46.4)		177/435 (40.7)	
	7		176/362 (48.6)		199/435 (45.7)	
	8–10		18/362 (4.9)		59/435 (13.6)	
Silva 2007[141]				7	7	Median
Soric 2004[143]				6.25 (4–9)	5.7 (4–7)	Median (range)
Tewari 2003[116]	≤6		87/200 (43.5)		42/100 (42.0)	
	7		80/200 (40.0)		38/100 (38.0)	
	8–10		21/200 (10.5)		20/100 (20.0)	
Touijer 2007[145]	≤6			184/485 (38.0)	280/692 (40.5)	
	7			270/485 (55.7)	349/692 (50.4)	
	8–10			25/485 (5.2)	56/692 (8.1)	
	Missing			6/485 (1.2)	7/692 (1.0)	
Trabulsi 2008[98]	≤6		33/50 (66.0)	109/190 (57.4)		
	7		15/50 (30.0)	67/190 (35.3)		
	≥8		2/50 (4.0)	8/190 (4.2)		
Truesdale[117]	≤6		14/99 14.1)		26/217 (12.0)	
	7		71/99 (71.7)		135/217 (62.2)	
	8–10		14/99 (14.1)		56/217 (25.8)	
White 2009[118]	≤6		25/50 (50.0)		35/50 (70.0)	
	7		24/50 (48.0)		15/50 (30.0)	
	8–10		1/50 (2.0)		0/50	
PSA recurrence						
Definition						
Artibani 2003[123]		A: mean 10 (range 4–16) months B: mean 10 (range 4–18) months		12/63 (19.0)	5/44 (11.4)	PSA > 0.3 ng/ml

TABLE 55 Summary of outcomes: efficacy (*continued*)

Study	Subgroup	Timing	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]	Notes
Barocas 2010[103]		3 years postoperatively	181/425 (42.6)		155/257 (60.3)	PSA > 0.2 ng/ml on one or more assays, or when a patient received postoperative hormone therapy, radiation or chemotherapy in the face of an increasing PSA
Drouin 2009[101]		Mean 49.7 (range 18–103) months	7/71 (9.9)	10/85 (11.8)	12/83 (14.5)	A single measure of PSA > 0.2 ng/ml
Krambeck 2008[108]		Median 1.3 years	14/248 (5.6)		32/492 (6.5)	PSA progression (no definition)
Lama 2009[133]		6 months		6/56 (10.7)	6/59 (10.2)	Biochemical relapse (no definition)
		1 year		6/56 (10.7)	7/59 (11.9)	
		2 years		6/56 (10.7)	9/59 (15.2)	
		3 years		11/56 (19.6)	12/59 (20.3)	
Loeb 2010[109]		Not reported				14/266 men with follow-up data had PSA > 0.2 ng/ml
Menon 2002[95]				38/40 (95.0)	39/40 (97.5)	Undetectable postoperative PSA
Nadler 2010[112]		During 27.1 months of follow-up	4/50 (8.0)		3/50 (6.0)	During 27.1 months of follow-up 92% and 94% reported undetectable PSA defined as PSA ≤ 0.1 ng/ml
Ou 2009[113]		15 months	6/30 (20.0)		5/30 (16.7)	Two consecutive postoperative PSA > 0.2 ng/ml
Poulakis 2007[137]		6 months		Group I: 10/72 (13.9) Group II: 7/132 (5.3)	11/70 (15.7)	PSA ≥ 0.1 ng/ml. Groups I and II two age groups (data not combined)
Salomon 2002[140]		3-year actuarial PSA recurrence-free rate		86.2%	Retropubic: 89.3% Perineal: 89.2%	
Schroeck 2008[115]		A: mean 1.09 years B: mean 1.37 years	29/362 (8.0)		54/435 (12.4)	Adjusted hazard ratio for risk of PSA recurrence and *p*-values reported in paper
Tewari 2003[116]		A: mean 236 days B: mean 556 days	16/200 (8.0)		15/100 (15.0)	> 0.2 ng/ml (converted from undetectable PSA% data)
Local recurrence						
Krambeck 2009[108]		Median 1.3 years	3/248 (1.2)		5/492 (1.0)	
Metastatic recurrence						
Krambeck 2009[108]		Median 1.3 years	1/248 (0.4)		0/492	Reported as 'systematic progression'

a Data presented as *n*/*N* (%) unless indicated otherwise.

TABLE 56 Summary of outcomes: further treatment

Study	Treatment/outcome	Timing/duration of follow-up	Robotic, *n*/*N* (%)[a]	Laparoscopic, *n*/*N* (%)[a]	Open, *n*/*N* (%)[a]
Further cancer treatment					
Dahl 2009[126]	Radiation	12 months		3/104	0/102
	Androgen deprivation			1/104	2/102
	Both radiation and androgen deprivation			1/104	0/102
				Subtotal: 5/104 (4.8)	Subtotal: 2/102 (2.0)
Treatment of urinary incontinence					
Carlsson 2010[104]		30 days–15 months	7/1253 (0.6)		11/485 (2.3)
Treatment of erectile dysfunction					
No studies reported data on this outcome					
Treatment of faecal incontinence					
No studies reported data on this outcome					
Death, specify reasons					
Carlsson 2010[104]		< 30 days postoperatively	0/1253		1/485 (0.2)
Doumerc 2010[105]	Death from cerebral vascular accident		0/212		1/502 (0.2)
Drouin 2009[101]	Pulmonary embolism	5 years	0/71	0/85	1/83 (1.2)
Hu 2006[92]		Not reported	0/322	0/358	
Krambeck 2008[108]	Death from prostate cancer	Median 1.3 years	0/248		0/492
	Death from any cause		4/248 (1.6)		4/492 (0.8)
Menon 2002[95]		Robotic: mean 3 (SD 1.3) months	0/40	0/40	
		Laparoscopic: mean 8.5 (SD 3.2) months			
Poulakis 2007[137]				Group I: 0/72	0/70
				Group II: 0/132	
Rozet 2007[96]		Not reported	0/133	0/133	
Salomon 2002[140]	Pulmonary embolism	First day post operation		1/155 (0.6)	0/151
Tewari 2003[116]		A: mean 236 days	0/200		0/100
		B: mean 556 days	0/200		0/100

TABLE 57 Summary of outcomes: quality of life

Study	Measures	Timing	Robotic	Laparoscopic	Open	Notes, e.g. validated measure or not
Guazzoni 2006 [90]	Postoperative pain, mean (SD)	Recovery room		1.88 (1.31)	1.92 (1.08)	RCT
		3 hours		1.92 (1.46)	2.75 (1.99)	Pain assessed with the use of a validated 10-point VAS for pain (0 = no pain, 10 = worst possible pain)
		Day 1		1.7 (1.45)	2.65 (1.44)	
		Day 2		1.61 (0.9)	1.96 (1.2)	
		Day 3		1.03 (0.82)	1.53 (1.13)	
	Pain at discharge			Not reported	2/60 (3.3)	
Jacobsen 2007[130]	I-PSS quality-of-life question (patient asked how he feels about tolerating his current level of urinary symptoms for the rest of his life: 0, mildly to 6, terrible), mean (SD)	Baseline		First half: 1.9 (1.8) (*n* not reported); Second half: 1.4 (1.2) (*n* not reported)	1.6 (1.6) (*n* = 172)	
		1 year		First half: 1.9 (1.4) (*n* = 29); Second half: 1.9 (1.2) (*n* = 28)	1.5 (1.4) (*n* = 148)	
Miller 2007[111]	SF-12 v.2 Physical and Mental Health Survey Acute Form					Validated tool, scale not reported
	Mental component score, mean (SD)	Preoperatively	49.8 (6.2)	45.7 (9.8)		
		6 weeks	57.4 (4.3)	58.0 (4.7)		
	Physical component score, mean (SD)	Preoperatively	57.6 (2.4)	56.9 (6.0)		
		6 weeks	56.4 (1.7)	52.8 (4.7)		
Namiki 2005[135]	SF-36					
	Physical function, mean (SD)	Baseline		88.9 (11.8)	88.9 (11.4)	
		1 month		84.0 (15.8)	85.5 (13.4)	
		3 months		88.7 (11.5)	88.7 (9.2)	
		6 months		89.2 (11.1)	87.4 (12.8)	
		12 months		87.8 (12.9)	89.5 (11.0)	
	Role limitation, physical, mean (SD)	Baseline		77.1 (27.2)	83.3 (23.3)	
		1 month		67.1 (29.9)	73.2 (29.7)	
		3 months		75.2 (25.3)	79.1 (23.6)	
		6 months		85.0 (18.7)	83.2 (23.4)	
		12 months		82.4 (25.0)	86.2 (22.0)	
	Bodily pain, mean (SD)	Baseline		82.0 (21.2)	84.6 (18.7)	
		1 month		74.5 (22.6)	71.2 (20.9)	
		3 months		82.3 (19.5)	80.9 (19.8)	
		6 months		82.7 (21.9)	86.0 (16.8)	
		12 months		84.2 (17.9)	85.9 (17.1)	

continued

TABLE 57 Summary of outcomes: quality of life (*continued*)

Study	Measures	Timing	Robotic	Laparoscopic	Open		Notes, e.g. validated measure or not
	General health perception, mean (SD)	Baseline		60.3 (17.3)	60.9 (14.4)		
		1 month		54.9 (16.6)	57.3 (12.2)		
		3 months		61.3 (14.9)	61.6 (16.1)		
		6 months		59.8 (13.3)	64.0 (15.2)		
		12 months		61.0 (19.0)	64.5 (16.4)		
	Mental health, mean (SD)	Baseline		71.5 (16.4)	69.1 (20.9)		
		1 month		63.5 (13.2)	68.7 (17.8)		
		3 months		70.9 (18.7)	73.8 (20.4)		
		6 months		74.6 (16.1)	75.9 (21.8)		
		12 months		75.1 (18.6)	77.8 (18.6)		
	Role limitation, emotional, mean (SD)	Baseline		78.2 (26.4)	80.5 (22.9)		
		1 month		66.7 (27.9)	72.2 (26.9)		
		3 months		76.1 (27.0)	77.9 (24.0)		
		6 months		82.3 (21.6)	84.3 (20.4)		
		12 months		83.1 (22.3)	86.6 (22.3)		
	Social function, emotional, mean (SD)	Baseline		77.3 (22.3)	80.9 (23.1)		
		1 month		60.6 (28.1)	76.6 (25.2)		
		3 months		74.7 (22.7)	81.5 (22.3)		
		6 months		79.2 (25.2)	85.6 (19.6)		
		12 months		84.3 (19.6)	88.3 (19.9)		
	Vitality, mean (SD)	Baseline		68.0 (17.0)	68.7 (19.3)		
		1 month		61.5 (17.6)	63.3 (16.2)		
		3 months		67.0 (18.3)	71.3 (22.4)		
		6 months		72.3 (13.8)	71.5 (17.4)		
		12 months		70.7 (14.6)	72.4 (19.0)		
Namiki 2006[136]	SF-36				Retropubic	Perineal	
	Physical function, mean (SD)	Baseline		90.5 (10.6)	86.9 (11.8)	86.6 (14.0)	
		1 month		89.6 (8.3)	83.8 (16.8)	84.3 (12.6)	
		3 months		91.2 (8.5)	85.7 (15.6)	84.2 (13.7)	
		6 months		90.5 (9.3)	88.2 (16.7)	82.6 (12.9)	
		12 months		89.1 (9.0)	87.0 (13.4)	86.0 (14.0)	
	Role limitation, physical, mean (SD)	Baseline		83.4 (16.1)	83.1 (22.7)	80.8 (24.3)	
		1 month		67.7 (25.3)	61.8 (25.0)	66.1 (23.2)	
		3 months		77.4 (22.6)	74.9 (23.6)	72.7 (31.4)	
		6 months		83.9(19.6)	80.6 (21.8)	80.1 (26.2)	
		12 months		82.3 (24.4)	83.2 (20.3)	75.4 (27.1)	
	Bodily pain, mean (SD)	Baseline		87.9 (16.5)	85.2 (20.1)	80.7 (22.5)	
		1 month		66.1 (22.3)	66.1 (23.0)	74.5 (23.2)	
		3 months		87.4 (15.2)	77.2 (20.7)	77.0 (25.9)	
		6 months		88.8 (16.6)	84.1 (19.1)	82.3 (24.9)	
		12 months		88.9 (21.8)	86.6 (18.1)	75.8 (25.2)	
	General health perception, mean (SD)	Baseline		64.9 (14.7)	57.4 (16.3)	62.3 (16.3)	
		1 month		50.4 (14.5)	58.9 (16.5)	61.3 (15.9)	
		3 months		63.8 (16.4)	58.9 (16.2)	56.6 (17.1)	
		6 months		63.6 (14.6)	61.4 (16.3)	60.4 (18.2)	
		12 months		56.3 (14.5)	61.1 (17.0)	57.3 (20.2)	

TABLE 57 Summary of outcomes: quality of life (*continued*)

Study	Measures	Timing	Robotic	Laparoscopic	Open		Notes, e.g. validated measure or not
	Mental health, mean (SD)	Baseline		68.9 (16.7)	68.9 (16.7)	72.3 (20.9)	
		1 month		58.6 (20.3)	58.6 (20.3)	71.5 (25.4)	
		3 months		75.7 (15.4)	75.7 (15.4)	66.1 (20.0)	
		6 months		75.7 (15.2)	75.7 (15.2)	74.8 (18.1)	
		12 months		71.7 (17.2)	71.7 (17.2)	72.5 (20.0)	
	Role limitation, emotional, mean (SD)	Baseline		86.7 (16.9)	81.9 (22.6)	78.4 (25.5)	
		1 month		70.6 (20.8)	65.4 (28.9)	66.7 (26.3)	

TABLE 58 Summary of outcomes: learning curve

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Al-Shaiji 2010[121]						2/5 attending urologists		70		
Anastasiadis 2003[122]								230		
Artibani 2003[123]						1	> 60	71		
Ball 2006[99]	2		82 in total		Completed robotic training and proctoring	2		124 in total		
Barocas 2010[103]	4		1413							
Bhayani 2003[124]						2		36		
Bolenz 2009[102] (secondary to Bolenz 2010[100])	NR	NR	264			NR	NR	220		
Bolenz 2010[100]	2		262		A learning curve was included in robort-assisted laparoscopic prostatectomy patients, but between the 50 patients initially operated and the most recently treated 50 patients there was no significant difference in median operative time and median length of hospital stay	1		211		

Open

No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
3/5 attending urologists		70			Safety (blood loss, operating time, hospital stay)	
		70			Safety (catheterisation, surgical complications) Efficacy (margins, pT stage, pathological Gleason score) Dysfunction (urinary continence)	Laparoscopic and robotic radical prostatectomy performed by different surgeons with a high level of experience in their preferred technique
1	Experienced	50			Safety (hospital stay, catheterisation, surgical complications) Efficacy (margin, pT stage, pathological Gleason score, PSA recurrence) Dysfunction (urinary incontinence, erectile)	
3		135 in total		All fellowship-trained oncological surgeons	Efficacy (pT stage) Dysfunction (urinary incontinence, erectile)	
4		491			Efficacy (margins, pT stage, pathological Gleason score, PSA recurrence	
2		24			Safety (open conversion, operating time, hospital stay, surgical complications, catheterisation, blood loss) Efficacy (pT stage)	Same two fellowship-trained surgeons in their first year of practice with comparable experience and training
NR	NR	162			Safety (operating time, hospital stay)	
3		156		Performed by experienced surgeons after their learning curve in robotic and laporascopic radical prostataectomy procedures	Safety (blood transfusion)	

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Brown 2004[125]						NR	0	60	Operating time (minutes), mean: 1–10: 456; 11–20: 402; 21–30: 384; 31–60: 306	
Carlsson 2010[104]	6		I: 451; II: 444; III: 181; IV: 112; V: 35; VI: 30							
Chan 2008[119]	2		660 in total	Operating time (minutes): 63–483	I: performed both; II: robotics only 'experienced'					
Dahl 2009[126]						1/3		104		
Dahl 2006[147] (secondary to Dahl 2009[126])	1					1		286		
Doumerc 2010[105]	1		212							
Drouin 2009[101]	1					3				

Open						
No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
NR	NR	60			Safety (operating time, hospital stay, readmission, surgical complications) Efficacy (margins, pT stage) Learning curve (operating time)	Procedures performed by or under the direction of two staff surgeons (different surgeons for each procedure)
9 (6 also performed robot)	I: >250; II: >250; III: <7; IV: <7; V: >100; VI: >250	485 in total			Safety (surgical complications)	
3		340 in total	Operating time (minutes): 82–245	III and IV: open only 'experienced'	Safety (open conversion, operating time, hospital stay) Learning curve	
1/3		102			Safety (surgical complications) Dysfunction (urinary incontinence, erectile) Further treatment	1/3 experienced surgeons
1/5		714		Open surgery performed by five experienced urologists in the same department	Efficacy (margins, pT stage, pathological Gleason score)	
1	>2000	502			Safety (surgical complications, operating time, hospital stay, catheterisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score) Dysfunction and learning curve data in graph form only	Surgeries were performed by one experienced surgeon. Surgeon had performed >2000 RRPs cases Learning curve was based on the number of cases needed to achieve competency in each of the following areas: console time, pathological outcome (over all pT2 and pT3 positive surgical margin rates) and early continence, i.e. 6 weeks Learning curve analysed by positive surgical margin rates and the EPIC score (%) at 6 weeks
3					Safety (surgical complications, open conversion, operating time, catheterisation, blood loss) Efficacy (margins, pT stage, PSA recurrence) Death	

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Ficarra 2009[106]	2	>50/ surgeon	103 in total							
Fornara 2004[127]								32		
Fracalanza 2008[107]	1	>50	35 in total	Time (minutes), mean (SD): 195.6 (45)						
Ghavamian 2006[128]						1	60	70		First 60 cases not included in the comparison
Gosseine 2009[91]	1		122							
Greco 2010[129]						2	At least 60 nerve-sparing and 150 laparo-scopic radical prostatec-tomies	150		
Guazzoni 2006[90] (RCT)						1	>150	60		

Open						
No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
4	>400/ surgeon	105 in total			Safety (surgical complications, operating time, hospital stay, catherisation, blood loss) Efficacy (margins, pT stage) Dysfunction (urinary incontinence, erectile)	
		32			Safety (surgical complications, operating time, hospital stay, catheterisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score)	German
3	>200	26 in total	Time (minutes), mean (SD): 127.2 (31.7)		Safety (surgical complications, operating time, hospital stay, blood loss, surgical incision, time to mobilisation, oral feeding) Efficacy (margins, pT stage) Learning curve	'experienced'
1	>300				Safety (open conversion, surgical complications, operating time, hospital stay, blood loss) Dysfunction (urinary incontinence, erectile)	Same surgeon for both procedures with >7 years practice at a major metropolitan academic university hospital
1		125			Safety (surgical complications, operating time, hospital stay, catheterisation, blood loss) Dysfunction (urinary incontinence)	Performed by the same surgeon at the beginning of his experience (French)
2	At least 60 nerve-sparing and 150 open prostatec-tomies				Safety (open conversion, surgical complications, operating time, catheterisation, blood loss) Efficacy (margins, pT stage) Dysfunction (urinary incontinence, erectile)	All surgical procedures performed by two surgeons
1	Performed radical retropubic prostatec-tomies for 15 years prior to study	60			Safety (open conversion, surgical complications, operating time, discharge time, catheterisation, blood loss, mobilisation, oral feeding) Efficacy (margins, pT stage) Quality of life (pain)	Single surgeon ('senior urologist') not under learning curve, started general laparoscopic experience 12 years before the study and in particular laparoscopic radical prostatectomies in 1990

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Hu 2006[92]	3		I: 126; II: 144; III: 52	Time (minutes), median (range): 186 (114–528)		Same 3		I: 167; II: 124; III: 65		Time (minutes), median (range): 246 (150–768)
Jacobsen 2007[130]						10	0	67 in total		
Joseph 2005[93] (linked to Joseph 2007[94])	NR	150	50 (cases 151–200)			NR	28	50 (cases 29–78)		Laparoscopic radical prostatectomy-experienced surgeons with assistants generally untrained in laparoscopic radical prostatectomy. Laparoscopic series completed first. University of Rochester Medical Centre
Joseph 2007[94]	NR	NR	754		University of Rochester Medical Centre	NR	NR	800		Henry Mondor Hospital
Jurczok 2007[131]						3		163		
Kim 2007[132]								30		
Kordan 2010[120] (secondary to Barocas 2010[103])	2/4	NR	830							

Open						
No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
					Equipment failure (presume this is not learning curve dependent)	
					Safety (surgical complications, operating time, blood loss)	
					Learning curve?? (operating time)	
					Death (none)	
Same 10		172 in total			Efficacy (margins, pT stage, pathological Gleason score)	
					Dysfunction (urinary incontinence)	
					Quality of life	
					Dysfunction (urinary incontinence, erectile, potency)	
					Efficacy (margins, pathological Gleason score)	Abstract
3		240			Safety (open conversion, surgical complications, operating time, hospital stay, catheterisation, blood loss)	Performed by three experienced surgeons with no difference between the operative results of each
					Efficacy (margins, pT stage, pathological Gleason score)	
	45				Safety (surgical complications, operating time, hospital stay, catheterisation)	Korean
					Efficacy (margins, pT stage, pathological Gleason score)	
3/4	NR	414			Safety (blood transfusion, blood loss)	One surgeon performed both robotic radical prostatectomy and robot-assisted laparoscopic prostatectomy

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Krambeck 2009[108]	3		294	Time (minutes), median (25th–75th percentile): early: *n* = 94, 295 (248–357); middle: *n* = 100, 235 (201–268); late: *n* = 100, 211 (186–236)						
Lama 2009[133]						1	0	56	Time (minutes), mean (SD): 202.5 (52.1)	Laparoscopic radical prostatectomy performed by a urologist trained in laparoscopy whose learning curve was completed for open prostatectomy
Loeb 2010[109]	1		152							
Malcolm 2010[110]	1		447		Robotic: performed by one of three fellowship-trained endourology or oncology surgeons					
Martorana 2004[134]						1	0	50	Operating time (minutes), mean: patients 1–25: 399; patients 26–50: 316; patients 35–50: 265	
Menon 2002[95] (linked to Tewari 2003[116])	3	0	I and III: 4; II and III: 10; III: 36 Total: 50	Time (minutes), mean (SD): 274 (94.3) Time first year (minutes): 490.89		4	I and II: 600; III: 0 (1000 open cases)	I: 27; II: 19; IV: 2 Total: 48	Time (minutes), mean, (SD); 258 (80.3) Time first year (minutes): 228.08	III: assisted; I and II: experience in laparoscopic prostatectomy

Open

No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
17		588	Time (minutes), median (25th–75th percentile): early: *n* = 188, 190 (158–245); middle: *n* = 200, 206 (162–268); late: *n* = 200, 228 (169–288)		Safety (surgical complications, operating time, hospital stay) Efficacy (margins, pathological Gleason score, PSA recurrence, local recurrence, metastatic recurrence) Dysfunction (urinary incontinence, erectile) Death Learning curve (operating time)	
NR	NR	59			Safety (surgical complications, operating time, hospital stay, catheterisation) Efficacy (margins, PSA recurrence) Dysfunction (urinary incontinence, erectile) Learning curve (operating time)	RRP completed learning curve
1	> 1000 open	137			Efficacy (margins, PSA recurrence)	Single surgeon
1		135		Open: performed by one of four fellowship-trained urological oncologists	Dysfunction (urinary function, sexual function)	
1		50	Operating time (minutes), mean: patients 1–50: 159		Safety (open conversion, surgical complications, operating time, hospital stay, catheterisation) Efficacy (margins, pT stage, pathological Gleason score) Learning curve (operating time) Equipment failure Safety (surgical complications, operating time, discharge, blood loss) Patient satisfaction Efficacy (margins, pT stage, pathological Gleason score, PSA recurrence) Death (none) Learning curve (operating time)	For both procedures, surgery was performed by the same first surgeon with experience in open but not laparoscopic surgery

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Miller 2007[111]	NR	NR	42							
Nadler 2010[112]	1		50							
Namiki 2005[135]						2	>50	45		
Namiki 2006[136]						2	>100	65 in total		
Ou 2009[113]	1	0	30	Time (minutes), mean (SD): 205 (103)						
Poulakis 2007[137]	NR	NR	72			NR	NR	132		
Raventos Busquets 2007[138]								105 in total	Time (minutes), mean (SD): 172.3 (43.7)	56% were conducted by surgeons experienced in laparoscopic surgery

Open

No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
NR	NR	120			Safety (blood loss) Quality of life	
1	>460 open and 24 laparo-scopic				Safety (surgical complications, operating time, hospital stay, blood loss) Efficacy (margins, pT stage, PSA recurrence) Dysfunction (urinary continence, potency)	Single-experience laparoscopic urologist. Before performing robotic surgery the surgeon attended a 2-day training course
5	>50	121			Efficacy (pT stage, pathological Gleason score) Dysfunction (urinary function, sexual function) Quality of life (SF-36)	Staff urologist level UCLA-PCI figures available in graph form for baseline, 1 month, 3 months, 6 months and 12 months for urinary function, urinary bother, sexual function, sexual bother
Retro-pubic: 5; perineal: 2	Perineal: >50	Retro-pubic: 218; perineal: 66		Considerable experience with retropubic surgery	Efficacy (pathological Gleason score) Dysfunction (urinary function, sexual function) Quality of life (SF-36)	
Same one		30	Time (minutes), mean (SD): 213 (37)		Safety (open conversion, surgical complications, operating time, hospital stay, catherisation, blood loss) Efficacy (margins, pathological Gleason score, PSA recurrence) Dysfunction (incontinence, erectile) Learning curve (operating time)	
NR	NR	70			Safety (surgical complications, operating time, hospital stay, catherisation, blood loss, mobilisation, oral feeding) Efficacy (margins, pT stage, pathological Gleason score, PSA recurrence) Dysfunction (urinary incontinence) Death (none)	
			Time (minutes), mean (SD): 145.1 (32.9)	51% of cases were conducted by surgeons experienced in open surgery	Safety (operating time, hospital stay) Efficacy (margins, pT stage) Learning curve (operating time)	Spanish

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Remzi 2005[139]						1	>300 major laparo-scopic surgeries	80 in total		Experienced. Initial learning curve overcome
Rocco 2009[114]	3									
Rozet 2007[96]	4		133	Time (minutes), mean (range): 166 (90–300)		4		133	Time (minutes), mean (range): 160 (90–270)	
Salomon 2002[140]						NR	NR	155		
Schroeck 2008[115]	1/4	NR	362							
Silva 2007[141]						1		90		'experienced single surgeon under a learning curve'
Soderdahl 2005[142]						2		116 in total		Both fellowship trained
Soric 2004[143]						NR	NR	26		

Open						
No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
NR		41 in total			Safety (open conversion, operating time, hospital stay, surgical complications, catheterisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score) Dysfunction (urinary continence) Quality of life (postoperative pain)	
Same three					Safety (operating time, hospital stay, catherisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score) Dysfunction (urinary incontinence, potency) Safety (open conversion, surgical complications, operating time, hospital stay, catherisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score) Death (none)	
NR	NR	151			Safety (blood transfusion, operating time, hospital stay, catheterisation, surgical complications) Efficacy (margins, pT stage, pathological Gleason score, PSA recurrence)	
1/6	NR	435			Safety (blood loss) Efficacy (margins, pathological Gleason score, PSA recurrence)	Two surgeons performed both robotic radical prostatectomy and robot-assisted laparoscopic prostatectomy
1		89		'Resident physicians under a teacher's supervision at University'	Efficacy (margins, pT stage, pathological Gleason score)	
3		186 in total		All fellowship trained	Efficacy (pT stage) Dysfunction (urinary function, sexual function)	
NR	NR	26			Safety (open conversion, surgical complications, operating time, hospital stay, catheterisation) Efficacy (margins, pT stage, pathological Gleason score)	Croatian

continued

TABLE 58 Summary of outcomes: learning curve (*continued*)

	Robotic					Laparoscopic				
Study	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information
Sundaram 2004[97]	1	0	10	Time (minutes), mean (range): 290 (210–340)		Same one	>40	10	Time (minutes), mean (range): 394 (240–280)	
Terakawa 2008[144]						5		I: 54; II: 42; III: 31; IV: 7; V: 3		Paper stated that surgeons were well experienced in 'laparaoscopy surgery'
Tewari 2003[116]	1		200							
Touijer 2007[145]	2		I: 398; II: 87							
Trabulsi 2008[98]		0	50	Positive margins: 3/50 (6%)			147	50		
Truesdale 2010[117]	1		99		Cases limited to a single high-volume surgeon					
Wagner 2007[146]						1	0	75	Time (minutes), mean (SD): 282 (53)	
White 2009[118]	1	2	50							

NR, not reported.

Open						
No. surgeons	No. procedures conducted before this study	No. procedures conducted during this study	Learning curve outcome	Other information	Reported outcomes/measures	Other information
					Safety (operating time, hospital stay, surgical complications, blood loss) Efficacy (margins) Dysfunction (urinary incontinence)	Abstract
NR		220 in total		Less experienced, residents in training	Efficacy (margins, pT stage)	
8	Combined experience of >1400	100			Safety (open conversion, surgical complications, hospital stay, catheterisation, blood loss) Efficacy (margins, pT stage, pathological Gleason score, PSA recurrence) Dysfunction (urinary incontinence, erectile) Quality of life (pain) Death (none)	
2		III: 422; IV: 270			Efficacy (margins, pT stage, pathological Gleason score)	
			Positive margins: 10/50 (20%)		Safety (open conversion, blood loss) Efficacy (margins, pT stage, pathological Gleason score)	
4		217		Cases limited to those performed at a single institution by four high-volume surgeons	Safety (operating time, blood loss) Efficacy (pT stage, pathological Gleason score)	
Same one	0	75	Time (minutes), mean (SD): 162 (39)		Safety (operating time, surgical complications, blood loss) Efficacy (margins, pT stage) Dysfunction (urinary incontinence, erectile)	Just out of training
Same one		50			Safety (open conversion) Efficacy (margins, pT stage, pathological Gleason score)	

Appendix 10

Classification of reported adverse effects using the Clavien–Dindo classification of surgical complications[68]

TABLE 59 Classification of reported adverse effects: Clavien I

Study	Reported adverse effect(s)
Artibani 2003[123]	Acute urinary retention, fever, wound infection
Bhayani 2003[124]	Dislodged catheter requiring replacement, inadvertent cystotomy
Brown 2004[125]	Anastomotic leak, rectus haematoma, ulnar neuropathy, wound infection
Carlsson 2010[104]	Wound infection, infection, anastomotic leak
Dahl 2009[126]	Anastomotic leak, chronic abdomen pain, genital femoral nerve irritation, seroma, urinary retention, vasovagal syncope, wound infection
Doumerc 2010[105]	Anastomotic leak
Drouin 2009[101]	Anastomotic leak, urinary retention, urinary infection
Fornara 2004[127]	Wound infection
Fracalanza 2008[107]	Fever
Ghavamian 2006[128]	Anastomotic leak, clot retention, urinary infection
Guazzoni 2006[90]	Urinary retention, anastomotic leak, fever
Hu 2006[92]	Urinary retention, urinary leak, clot retention
Joseph 2007[94]	Urinary leakage, urinary retention
Jurczok 2007[131]	Wound infection
Kim 2007[132]	Subcutaneous emphysema, anastomotic leak
Krambeck 2009[108]	Urinary retention, urinary infection, drug reaction
Lama 2009[133]	Urinary leakage, urinary retention, seroma
Martorana 2004[134]	Anastomotic leak
Nadler 2010[112]	Anastomotic leak
Ou 2009[113]	Anastomotic leak
Poulakis 2007[137]	Urinary infection
Remzi 2005[139]	Anastomotic leak
Rozet 2007[96]	Anastomotic leak, wound abscess?, urinary infection, retention, infected pelvic haematoma
Salomon 2002[140]	Anastomotic leak, wound infection
Sundaram 2004[97]	Anastomotic leak, urinary retention
Tewari 2003[116]	Obturator neuropathy

TABLE 60 Classification of reported adverse effects: Clavien II

Study ID	Reported adverse effect(s)
Al-Shaji 2010[121]	Blood transfusion
Anastasiadis 2003[122]	Blood transfusion
Artibani 2003[123]	Blood transfusion, cardiovascular complications, ileus, pelvic haematoma
Bhayani 2003[124]	Calf myositis, obturator nerve palsy
Bolenz 2010[100]	Blood transfusion
Brown 2004[125]	Blood transfusion, deep-vein thrombosis, ileus
Carlsson 2010[104]	Blood transfusion
Dahl 2009[126]	Bladder neck contracture
Doumerc 2010[105]	Pelvic haematoma, blood transfusion, blood loss
Drouin 2009[101]	Blood transfusion, postoperative bleeding
Ficarra 2009[106]	Postoperative bleeding, ileus, cardiovascular complications, blood loss, blood transfusion
Fornara 2004[127]	Blood transfusion
Fracalanza 2008[107]	Blood transfusion
Ghavamian 2006[128]	Blood transfusion, deep-vein thrombosis, ileus, neuropraxia
Gosseine 2009[91]	Blood transfusion
Greco 2010[129]	Blood transfusion
Guazzoni 2006[90]	Blood transfusion, lymphorrhea
Hu 2006[92]	Nerve damage/injury, intra-abdominal drain retraction, ileus, blood loss, blood transfusion
Joseph 2007[94]	Blood transfusion
Jurczok 2007[131]	Blood transfusion
Kim 2007[132]	Blood transfusion
Kordan 2010[120]	Blood transfusion
Krambeck 2009[108]	Blood transfusion, deep-vein thrombosis, haemorrhage/haematoma, ileus, lymphoedema
Lama 2009[133]	Perioperative hypercapnia, deep-vein thrombosis, blood loss, blood transfusion
Martorana 2004[134]	Blood transfusion, ileus
Menon 2002[95]	Ileus, blood transfusion
Nadler 2010[112]	Ileus, deep-vein thrombosis, blood transfusion
Ou 2009[113]	Blood transfusion, lymph leakage
Poulakis 2007[137]	Haemorrhage/haematoma, gastrointestinal symptoms, fever >39°C, delirium, blood loss, blood transfusion
Remzi 2005[139]	Ileus, haemorrhage/haematoma
Rozet 2007[96]	Postoperative bleeding, cardiovascular complications
Salomon 2002[140]	Blood transfusion, deep-vein thrombosis, ileus, lymphorrhea, pelvic haematoma, postoperative neuropathy
Soric 2004[143]	Blood transfusion, nerve damage/injury
Tewari 2003[116]	Blood transfusion, deep-vein thrombosis, ileus

TABLE 61 Classification of reported adverse effects: Clavien IIIa

Study	Reported adverse effect(s)
Dahl 2009[126]	Lymphocele
Drouin 2009[101]	Lymphocele
Fornara 2004[127]	Lymphocele
Ghavamian 2006[128]	Lymphocele
Hu 2006[92]	Lymphocele
Jurczok 2007[131]	Lymphocele
Krambeck 2009[108]	Abdominal abscess, lymphocele
Martorana 2004[134]	Lymphocele
Poulakis 2007[137]	Lymphocele, prolonged urinary leakage
Soric 2004[143]	Ureter wound
Tewari 2003[116]	Lymphocele

TABLE 62 Classification of reported adverse effects: Clavien IIIb

Study	Reported adverse effect(s)
Artibani 2003[123]	Rectal injury/lesion
Bhayani 2003[124]	Bladder neck contracture, epigastric artery/vessel injury, hydroureteronephrosis, postoperative hydrocele
Brown 2004[125]	Bladder neck contracture, ureteral injury
Carlsson 2010[104]	Ureteral injury, surgical reintervention, small bowel injury, rectal lesion/injury, bladder neck contracture
Dahl 2009[126]	Hematoma leading to contracture, hematuria, meatal stricture
Doumerc 2010[105]	Bowel injury
Drouin 2009[101]	Rectal injury/lesion
Ficarra 2009[106]	Wound dehiscence, surgical re-exploration, rectal lesion/injury, colon lesion
Fornara 2004[127]	Rectal injury/lesion
Ghavamian 2006[128]	Bladder injury, bladder neck contracture, inferior epigastric injury
Greco 2010[129]	Rectal injury/lesion
Guazzoni 2006[90]	Rectal injury/lesion
Hu 2006[92]	Rectal injury/lesion, bladder neck contracture
Jurczok 2007[131]	Rectal injury/lesion, revision
Kim 2007[132]	Rectal injury/lesion, epigastric artery/vessel injury
Krambeck 2009[108]	Bladder neck contracture, ureteric obstruction
Lama 2009[133]	Rectal injury/lesion, bladder neck stenosis
Martorana 2004[134]	Bladder injury, epigastric artery/vessel injury
Menon 2002[95]	Hernia, ureter entrapment
Nadler 2010[112]	Hernia, bladder neck contracture
Ou 2009[113]	Bladder injury, rectal injury, anastomotic stricture
Poulakis 2007[137]	Dehiscence/rupture of wound, bladder neck contracture
Remzi 2005[139]	Rectal injury/lesion, anastomotic stricture
Salomon 2002[140]	Rectal injury/lesion, ureteral injury
Soric 2004[143]	Bladder neck sclerosis, blood vessel damage, ureteral injury
Tewari 2003[116]	Rectal injury/lesion, surgical re-exploration, wound dehiscence, wound hernia
Wagner 2007[146]	Bladder neck contracture

TABLE 63 Classification of reported adverse effects: Clavien IVa

Study	Reported adverse effect(s)
Carlsson 2010[104]	Pulmonary embolism, myocardial infarction
Dahl 2009[126]	Pulmonary embolism
Ficarra 2009[106]	Re-exploration due to bleeding
Hu 2006[92]	Pulmonary embolism, myocardial infarction, cerebral vascular accident, acute tubular necrosis
Krambeck 2009[108]	Pulmonary embolism, renal failure, myocardial infarction, stroke
Lama 2009[133]	Embolic stroke
Poulakis 2007[137]	Cardiovascular including arrhythmias and myocardial infarction, respiratory insufficiency
Rozet 2007[96]	Pulmonary embolism, renal insufficiency
Salomon 2002[140]	Pulmonary embolism
Tewari 2003[116]	Myocardial infarction

TABLE 64 Classification of reported adverse effects: Clavien V

Study	Reported adverse effect(s)
Carlsson 2010[104]	Fatal cardiac arrest
Dahl 2009[126]	Fatal cardiac arrest
Doumerc 2010[105]	Death due to cerebral vascular accident
Salomon 2002[140]	Death due to pulmonary embolism

No studies reported adverse effects classed as Clavien IVb or d.

TABLE 65 Individual study event rates: Clavien I

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		16/71 (22.5)	3/50 (6.0)
Bhayani 2003[124]		2/33 (6.1)	0/24 (0)
Brown 2004[125]		11/60 (18.3)	4/60 (6.7)
Carlsson 2010[104]	37/1253 (3.0)		83/485 (17.1)
Dahl 2009[126]		9/104 (8.7)	0/102 (0)
Doumerc 2010[105]	1/212 (0.5)		0/502 (0)
Drouin 2009[101]	2/71 (2.8)	0/85 (0)	
Fornara 2004[127]		0/32 (0)	2/32 (6.3)
Fracalanza 2008[107]	2/35 (5.7)		4/26 (15.4)
Ghavamian 2006[128]		3/70 (4.3)	5/70 (7.1)
Guazzoni 2006[90]		10/60 (16.7)	24/60 (40.0)
Hu 2006[92]	38/322 (11.8)	69/358 (19.3)	
Joseph 2007[94]	24/754 (3.2)	160/800 (20.0)	
Jurczok 2007[131]		5/163 (3.1)	8/240 (3.3)
Kim 2007[132]		9/30 (30.0)	0/45 (0)
Krambeck 2009[108]	13/294 (4.4)		20/588 (3.4)
Lama 2009[133]		2/56 (3.6)	7/59 (11.9)
Martorana 2004[134]		1/50 (2%)	2/50 (4%)
Nadler 2010[112]	2/50 (4.0)		2/50 (4.0)
Ou 2009[113]	0/30 (0)		2/30 (6.7)
Poulakis 2007[137]		1/204 (0.5)	1/70 (1.4)
Remzi 2005[139]		8/80 (10.0)	6/41 (14.6)
Rozet 2007[96]	12/133 (9.0)	7/133 (5.3)	
Salomon 2002[140]		6/155 (3.9)	14/151 (9.3)
Sundaram 2004[97]	1/10 (10.0)	1/10 (10.0)	
Tewari 2003[116]	0/200 (0)		2/200 (1.0)

TABLE 66 Individual study event rates: Clavien II

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Al-Shaji 2010[121]	3/70 (4.3)		42/70 (60.0)
Anastasiadis 2003[122]		6/230 (2.6)	6/70 (8.6)
Artibani 2003[123]		5/71 (7.0)	0/50 (0)
Bhayani 2003[124]		2/33 (6.1)	0/24 (0)
Bolenz 2010[100]	12/262 (4.6)	4/211 (1.9)	32/156 (20.5)
Brown 2004[125]		3/60 (5.0)	36/60 (60.0)
Carlsson 2010[104]	58/1253 (4.6)		116/485 (23.9)
Dahl 2009[126]		2/104 (1.9)	0/104 (0)
Doumerc 2010[105]	4/212 (1.9)		11/502 (2.2)
Drouin 2009[101]	8/71 (11.3)	5/85 (5.9)	
Ficarra 2009[106]	10/103 (9.7)		25/105 (23.8)
Fornara 2004[127]		2/32 (6.3)	6/32 (18.8)
Fracalanza 2008[107]	7/35 (20.0)		12/26 (46.2)
Ghavamian 2006[128]		9/70 (12.9)	24/70 (34.3)
Gosseine 2009[91]	4/122 (3.3)	8/125 (6.4)	
Greco 2010[129]		3/150 (2.0)	9/150 (6.0)
Guazzoni 2006[90]		12/60 (20.0)	37/60 (61.7)
Hu 2006[92]	24/322 (7.5)	33/358 (9.2)	
Joseph 2007[94]	10/754 (1.3)	35/800 (4.4)	
Jurczok 2007[131]		5/163 (3.1)	22/240 (9.2)
Kim 2007[132]		7/30 (23.3)	10/45 (22.2)
Kordan 2010[120]	7/830 (0.8)		14/414 (3.4)
Krambeck 2009[108]	31/294 (10.5)		104/588 (17.7)
Lama 2009[133]		8/56 (14.3)	28/59 (47.5)
Martorana 2004[134]		3/50 (6.0)	4/50 (8.0)
Menon 2002[95]	1/40 (2.5)	2/40 (5.0)	
Nadler 2010[112]	12/50 (24.0)		46/50 (92.0)
Ou 2009[113]	6/30 (20.0)		18/30 (60.0)
Poulakis 2007[137]		17/204 (8.3)	32/70 (45.7)
Remzi 2005[139]		2/80 (2.5)	3/41 (7.3)
Rozet 2007[96]	21/133 (15.8)	7/133 (5.3)	
Salomon 2002[140]		45/151 (29.8)	12/155 (7.7)
Soric 2004[143]		1/26 (3.9)	0/26 (0)
Tewari 2003[116]	4/200 (2.0)		75/100 (75.0)

TABLE 67 Individual study event rates: Clavien IIIa

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Dahl 2009[126]		4/104 (3.8)	0/102 (0)
Drouin 2009[101]	0/71 (0)	0/85 (0)	1/83 (1.2)
Fornara 2004[127]		0/32 (0)	1/32 (3.1)
Ghavamian 2006[128]		2/70 (2.9)	2/70 (2.9)
Hu 2006[92]	3/322 (0.9)	3/358 (0.8)	
Jurczok 2007[131]		5/163 (3.1)	7/240 (2.9)
Krambeck 2009[108]	1/294 (0.3)		5/588 (0.9)
Martorana 2004[134]		0/50 (0)	2/50 (4.0)
Poulakis 2007[137]		5/204 (2.5)	5/70 (7.1)
Soric 2004[143]		2/26 (7.7)	0/26 (0)
Tewari 2003[116]	0/200 (0)		2/100 (2.0)

TABLE 68 Individual study event rates: Clavien IIIb

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Artibani 2003[123]		2/71 (2.8)	0/50 (0)
Bhayani 2003[124]		3/33 (9.1)	6/24 (25.0)
Brown 2004[125]		2/60 (3.3)	2/60 (3.3)
Carlsson 2010[104]	31/1253 (2.5)		44/485 (9.1)
Dahl 2009[126]		7/104 (6.7)	1/102 (1.0)
Doumerc 2010[105]	1/212 (0.5)		0/502 (0)
Drouin 2009[101]	0/71 (0)	1/85 (1.2)	1/83 (1.2)
Ficarra 2009[106]	5/103 (4.9)		7/105 (6.7)
Fornara 2004[127]		1/32 (3.1)	0/32 (0)
Ghavamian 2006[128]		3/70 (4.3)	3/70 (4.3)
Greco 2010[129]		2/150 (1.3)	1/150 (0.7)
Guazzoni 2006[90]		1/60 (1.7)	0/60 (0)
Hu 2006[92]	3/322 (0.9)	26/358 (7.3)	
Jurczok 2007[131]	5/163 (3.1)	10/240 (4.2)	
Kim 2007[132]		2/30 (6.7)	0/45 (0)
Krambeck 2009[108]	3/294 (1.0)		24/588 (4.1)
Lama 2009[133]		5/56 (8.9)	2/59 (3.4)
Martorana 2004[134]		2/50 (4.0)	0/50 (0)
Menon 2002[95]	0/40 (0)	2/40 (5.0)	
Nadler 2010[112]	2/50 (4.0)	8/50 (16.0)	
Ou 2009[113]	3/30 (10.0)	1/30 (3.3)	
Poulakis 2007[137]		2/204 (1.0)	13/70 (18.6)
Remzi 2005[139]		4/80 (5.0)	5/41 (12.2)
Salomon 2002[140]		4/155 (2.6)	3/151 (2.0)
Soric 2004[143]		3/26 (11.5)	0/26 (0)
Tewari 2003[116]	2/200 (1.0)		1/100 (1.0)
Wagner 2007[146]		2/75 (2.7)	12/75 (16.0)

TABLE 69 Individual study event rates: Clavien IVa

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Carlsson 2010[104]	3/1253 (0.2)		7/485 (1.4)
Dahl 2009[126]		1/104 (1)	0/102 (0)
Ficarra 2009[106]	4/103 (3.9)		7/105 (6.7)
Hu 2006[92]	0/322 (0)	1/358 (0.3)	
Krambeck 2009[108]	5/294 (1.7)	12/588 (2.0)	
Lama 2009[133]		0/56 (0)	1/59 (1.7)
Poulakis 2007[137]		4/204 (2.0)	5/70 (7.1)
Rozet 2007[96]	2/133 (1.5)	1/133 (0.8)	
Salomon 2002[140]		0/155 (0)	1/151 (0.7)
Tewari 2003[116]	1/200 (0.5)		5/100 (5.0)

TABLE 70 Individual study event rates: Clavien IVb

Study	Robotic, *n*/*N* (%)	Laparoscopic, *n*/*N* (%)	Open, *n*/*N* (%)
Carlsson 2010[104]	0/1253 (0)		1/485 (0.2)
Dahl 2009[126]		0/140 (0)	1/102 (1.0)
Doumerc 2010[105]	0/212 (0)		1/502 (0.2)
Salomon 2002[140]		1/155 (0.7)	0/151 (0)

Not possible to meta-analyse Clavien V adverse events.

Appendix 11

Results of the systematic review of economic evaluations

- 802 titles and abstracts screened
- 23 selected for full-text assessment.

Reasons for exclusion

Not a primary study (n = 1)

1. Patel HRH. Robotic and laparoscopic surgery: cost and training. *Surg Oncol* 2009;**18**:242–6.

Clinical stage unclear (unsure if a relevant patient group is being considered) (n = 5)

1. Burgess SV. Cost analysis of radical retropubic, perineal, and robotic prostatectomy. *J Endourol* 2006;**20**:827–30.
2. Hohw L, Ehlers L, Borre M, Pedersen KV. Cost-effectiveness study of robot-assisted laparoscopic versus open retropubic radical prostatectomy. *Eur Urol Suppl* 2010;**9**:505.
3. O'Malley SP. Review of a decision by the Medical Services Advisory Committee based on health technology assessment of an emerging technology: the case for remotely assisted radical prostatectomy. *Int J Technol Assess Health Care* 2007;**23**:286–91.
4. Scales J, Jones PJ. Local cost structures and the economics of robot assisted radical prostatectomy. *J Urol* 2005;**174**:2323–9.
5. Taylor J. *Individualized predictions of disease progression following radiation therapy for prostate cancer.* University of Michigan Department of Biostatistics Working Paper Series no. 1024. Berkeley, CA: Berkeley Electronic Press;2004.

Not laparoscopic or robot surgery (n = 8)

1. Bayoumi AM, Brown AD, Garber AM. Cost-effectiveness of androgen suppression therapies in advanced prostate cancer. *J Natl Cancer Inst* 2000;**92**:1731–9.
2. Konski A, Sherman E, Krahn M, Bremner K, Beck JR, Watkins-Bruner D, *et al.* Economic analysis of a phase III clinical trial evaluating the addition of total androgen suppression to radiation versus radiation alone for locally advanced prostate cancer (Radiation Therapy Oncology Group protocol 86-10). *Int J Radiat Oncol Biol Physics* 2005;**63**:788–94.
3. Konski A, Watkins-Bruner D, Brereton H, Feigenberg S, Hanks G. Long-term hormone therapy and radiation is cost-effective for patients with locally advanced prostate carcinoma. *Cancer* 2006;**106**:51–7.
4. Lazzaro C, Bartoletti R, Guazzoni G, Orestano F, Pappagallo GL, Prezioso D, *et al.* Economic evaluation of different hormonal therapies for prostate cancer: final results from the Quality of Life Antiandrogen Blockade Italian Observational Study (QuABIOS). *Arch Ital Urol Androl* 2007;**79**:104–7.

5. Neymark N, Adriaenssen I, Gorlia T, Caleo S, Bolla M. Estimating survival gain for economic evaluations with survival time as principal endpoint: a cost-effectiveness analysis of adding early hormonal therapy to radiotherapy in patients with locally advanced prostate cancer. *Health Econ* 2002;**11**:233–48.
6. Perez CA, Michalski J, Ballard S, Drzymala R, Kobeissi BJ, Lockett MA, *et al.* Cost benefit of emerging technology in localized carcinoma of the prostate. *Int J Radiat Oncol Biol Physics* 1997;**39**:875–83.
7. Ramsey S, Veenstra D, Clarke L, Gandhi S, Hirsch M, Penson D. Is combined androgen blockade with bicalutamide cost-effective compared with combined androgen blockade with flutamide. *Urology* 2005;**66**:835–9.
8. Samant RS, Dunscombe PB, Roberts GH. A cost-outcome analysis of long-term adjuvant goserelin in addition to radiotherapy for locally advanced prostate cancer. *Semin Urol Oncol* 2003;**21**:171–7.

Not cost-effectiveness analysis (form of cost comparison only) (n = 9)

1. Al-Shaiji TF, Kanaroglou N, Thom A, Prowse C, Comondore V, Orovan W, *et al.* A cost-analysis comparison of laparoscopic radical prostatectomy versus open radical prostatectomy: the McMaster Institute of Urology experience. *Can Urol Assoc J* 2010;**4**:237–41 (included in effectiveness review).
2. Anderson JK. Cost comparison of laparoscopic versus radical retropubic prostatectomy. *Urology* 2005;**66**:557–60.
3. Bolenz C. Cost comparison of robotic, laparoscopic, and open radical prostatectomy for prostate cancer. *Eur Urol* 2010;**57**:453–8.
4. Gregori A, Galli S, Goumas I, Scieri F, Stener S, Gaboardi F. A cost comparison of laparoscopic versus open radical cystoprostatectomy and orthotopic ileal neobladder at a single institution. *Arch Ital Urol Androl* 2007;**79**:127–9.
5. Link RE, Su LM, Bhayani SB, Pavlovich CP. Making ends meet: a cost comparison of laparoscopic and open radical retropubic prostatectomy. *J Urol* 2004;**172**:269–74.
6. Lotan Y. The new economics of radical prostatectomy: cost comparison of open, laparoscopic and robot assisted techniques. *J Urol* 2004;**172**:1431–5.
7. Mouraviev V. Financial comparative analysis of minimally invasive surgery to open surgery for localized prostate cancer: a single-institution experience. *Urology* 2007;**69**:311–14.
8. Satoh T. Cost comparison of curative therapies for localized prostate cancer in Japan: a single-institution experience. *Japn J Radiol* 2009;**27**:348–54.
9. Steinberg PL, Merguerian PA, Bihrle W III, Heaney JA, Seigne JD. A da Vinci robot system can make sense for a mature laparoscopic prostatectomy program. *J Soc Laparoendosc Surg* 2008;**12**:9–12.

Appendix 12

Costs of robotic equipment

TABLE 71 Illustrative payment plans for robotic system

Surgical system procurement	List price (£)	4 years, arrears (£)	5 years, advance (£)	5 years, arrears (£)	6 years, advance (£)	6 years, arrears (£)	7 years, advance (£)	Annual service contract (£)
Plan 1: da Vinci Si HD Dual Console	2,100,000.00	487,200.00	386,400.00	417,900.00	338,100.00	365,400.00	310,800.00	165,000.00
Plan 2: da Vinci Si HD Single Console	1,600,000.00	371,000.00	294,400.00	318,400.00	259,200.00	278,400.00	236,800.00	140,000.00
Plan 3: da Vinci S HD	1,375,000.00	348,000.00	276,000.00	298,500.00	243,000.00	261,000.00	222,000.00	140,000.00
Plan 4: da Vinci S HD reconditioned (four arm)	1,250,000.00	324,800.00	257,600.00	278,600.00	226,800.00	243,600.00	207,200.00	140,000.00
Plan 5: da Vinci S EZ (three arm)	1,150,000.00	273,760.00	NS	234,820.00	191,160.00	205,320.00	174,640.00	120,000.00

NS, not supplied.

TABLE 72 Illustrative costs per procedure under alternative payment plans and under different assumptions about the number of times the equipment would be used per year

Total system cost (including service contract) (£)	Number of procedures	Service life	Cost per procedure (£)	Cost of surgical equipment (£)	Cost of consumables (£)	Total cost per procedure (£)
Procurement cost based on purchase plan 1						
3,090,000.00	200	7	2207.14	66.10	1194.11	3467.35
3,090,000.00	150	7	2942.86	88.14	1194.11	4225.11
3,090,000.00	100	7	4414.29	132.21	1194.11	5740.61
3,090,000.00	50	7	8828.57	264.42	1194.11	10,287.10
Procurement cost based on purchase plan 2						
2,440,000.00	200	7	1742.86	66.10	1194.11	3003.07
2,440,000.00	150	7	2323.81	88.14	1194.11	3606.06
2,440,000.00	100	7	3485.71	132.21	1194.11	4812.03
2,440,000.00	50	7	6971.43	264.42	1194.11	8429.96
Procurement cost based on purchase plan 3						
2,215,000.00	200	7	1582.14	66.10	1194.11	2842.35
2,215,000.00	150	7	2109.52	88.14	1194.11	3391.77
2,215,000.00	100	7	3164.29	132.21	1194.11	4490.61
2,215,000.00	50	7	6328.57	264.42	1194.11	7787.10

continued

TABLE 72 Illustrative costs per procedure under alternative payment plans and under different assumptions about the number of times the equipment would be used per year (*continued*)

Total system cost (including service contract) (£)	Number of procedures	Service life	Cost per procedure (£)	Cost of surgical equipment (£)	Cost of consumables (£)	Total cost per procedure (£)
Procurement cost based on purchase plan 4						
2,090,000.00	200	7	1492.86	66.10	1194.11	2753.07
2,090,000.00	150	7	1990.48	88.14	1194.11	3272.73
2,090,000.00	100	7	2985.71	132.21	1194.11	4312.03
2,090,000.00	50	7	5971.43	264.42	1194.11	7429.96
Procurement cost based on purchase plan 5						
1,870,000.00	200	7	1335.71	66.10	1194.11	2595.92
1,870,000.00	150	7	1780.95	88.14	1194.11	3063.20
1,870,000.00	100	7	2671.43	132.21	1194.11	3997.45
1,870,000.00	50	7	5342.86	264.41	1194.11	6801.38

Payment plan 1 represents the cost of a state-of-the-art five-arm machine; payment plan 5 represents the cost of a basic three-arm machine.

TABLE 73 Details of illustrative costs of upgrading a robotic system

Surgical system upgrade	List price (£)	4 years, arrears (£)	5 years, advance (£)	5 years, arrears (£)	6 years, advance (£)	6 years, arrears (£)	7 years, advance (£)
da Vinci S HD to da Vinci Si HD	600,000.00	139,020.00	110,400.00	119,400.00	97,200.00	104,400.00	88,800.00
da Vinci Si HD Single Console to da Vinci Si HD Dual Console	500,000.00	116,000.00	92,000.00	99,500.00	81,000.00	87,000.00	74,000.00
da Vinci S EZ 3 Arm to 4 Arm	220,000.00	51,040.00	40,480.00	43,780.00	35,640.00	38,280.00	32,560.00

TABLE 74 Cost of the robotic system

Surgical equipment	Number of units	Unit cost (capital) (£)	Operative service life	Number of procedures	Cost per procedure (£)	Total cost per procedure (£)
200 cases per annum						
Olympus EndoEYE® O DEG Telescope (Olympus Ltd, Japan)	1	13,961.00	5	200	13.96	66.10
Valleylab® Diathermy Generator (Tyco Healthcare Inc., USA)	1	13,000.00	7	200	9.29	
Olympus® Stack Unit (Insufflator) (Olympus Ltd, Japan)	1	60,000.00	7	200	42.86	
150 cases per annum						
Olympus EndoEYE O DEG Telescope	1	13,961.00	5	150	18.61	88.14
Valleylab Diathermy Generator	1	13,000.00	7	150	12.38	
Olympus Stack Unit (Insufflator)	1	60,000.00	7	150	57.14	
100 cases per annum						
Olympus EndoEYE O DEG Telescope	1	13,961.00	5	100	27.92	132.21
Valleylab Diathermy Generator	1	13,000.00	7	100	18.57	
Olympus Stack Unit (Insufflator)	1	60,000.00	7	100	85.71	
50 cases per annum						
Olympus EndoEYE O DEG Telescope	1	13,961.00	5	50	55.84	264.42
Valleylab Diathermy Generator	1	13,000.00	7	50	37.14	
Olympus Stack Unit (Insufflator)	1	60,000.00	7	50	171.43	

TABLE 75 Cost of reusable surgical equipment (robotic)

Consumables description (reusable)	Number of units	Unit cost (£)	Number of procedures	Total cost per procedure (£)
Hot Shears	1	248.35	10	24.84
Large Needle Driver	2	195.80	10	39.16
Maryland Bipolar Forceps	1	240.90	10	24.09
Pro-grasp® Forceps (Intuitive Surgical, CA, USA)	1	195.80	10	19.58
Total				107.67

TABLE 76 Cost of consumable surgical equipment (robotic)

Consumables description (disposable)	Number of units	Unit cost (£)	Number used per procedure	Total cost per procedure (£)
Anti-fog	1	3.00	1	3.00
Camera arm drape	1	26.40	1	26.40
Camera drape	1	22.28	1	22.28
Catheter tip syringe	1	0.27	1	0.27
Drain	1	8.30	1	8.30
Drape set	1	8.20	1	8.20
Hourly Uri-metre	1	3.60	1	3.60
Insufflation tubing	1	2.70	1	2.70
Major swab pack	1	9.63	1	9.63
Ports blunt	1	40.00	1	40.00
Ports sharp	1	62.00	1	62.00
Silastic catheter	1	9.75	1	9.75
Spigot	1	0.08	1	0.08
Stryker suction	1	34.50	1	34.50
Suction irrigation	1	22.00	1	22.00
Surgical blades × 2	2	0.11	2	0.22
Tip cover accessory	1	18.15	1	18.15
Urinary catheter bag	1	0.45	1	0.45
Hypodermic needles × 2	2	0.05	2	0.10
S-shaped retractors × 2[a]	2	1.96	2	3.92
Instrument arm drape	3	40.15	3	120.45
Ligamax® Endoclips 5 mm (Ethicon Inc., USA) (1–6 used, price each)	3	108.66	3	325.98
Memopouch bags	3	31.60	3	94.80
Seals	3	13.42	3	40.26
Velcro fastening strips × 3	3	1.20	3	3.60
Syringes × 4	4	0.20	4	0.80
Sutures × 9	9	25.00	9	225.00
				1086.44
Total				1194.11

Appendix 13

Costs of laparoscopic equipment

TABLE 77 Cost of laparoscopic system

Surgical equipment	Number of units	Unit cost (capital) (£)	Operative service life (years)	Numbers of procedures	Cost per procedure (£)
Olympus EndoEYE O DEG Telescope	1	13,961.00	5	200	13.96
Ethicon® Needle Holders´2 (Ethicon Inc., USA)	2	689.33	2	200	3.45
Laparoscopic instruments and storage case	1	8400.00	2	200	21.00
Valleylab Diathermy Generator	1	13,000.00	7	200	9.29
Harmonic® Scalpel generator and Handpiece (Ethicon Inc., USA)	1	5499.00	7	200	3.93
Olympus Stack Unit	1	60,000.00	7	200	42.86
Total					94.49

TABLE 78 Cost of other surgical equipment (laparoscopic)

Consumables description	Number of units	Unit cost (£)	Number used per procedure	Cost per procedure (£)
Anti-fog	1	3.00	1	3.00
Catheter tip syringe	1	0.27	1	0.27
Drain	1	8.30	1	8.30
Drape set	1	8.20	1	8.20
Harmonic shears	1	405.00	1	405.00
Hourly Uri-metre	1	3.60	1	3.60
Hypodermic needles × 2	2	0.05	2	0.10
Insufflation tubing	1	2.70	1	2.70
Laparoscopic instrument pouch	2	6.50	2	13.00
Ligamax Endoclips 5 mm (1–6 used, price each)	3	108.66	3	325.98
Major swab pack	1	9.63	1	9.63
Memopouch bags	3	31.60	3	94.80
Ports blunt	1	40.00	1	40.00
Ports sharp	1	62.00	1	62.00
S-shaped retractors × 2[a]	2	1.96	2	3.92
Seals	3	11.00	3	33.00
Shears	1	61.50	1	61.50
Silastic catheter	1	9.75	1	9.75
Spigot	1	0.08	1	0.08
Stryker Suction	1	34.50	1	34.50
Suction irrigation	1	22.00	1	22.00

continued

TABLE 78 Cost of other surgical equipment (laparoscopic) (*continued*)

Consumables description	Number of units	Unit cost (£)	Number used per procedure	Cost per procedure (£)
Surgical blades × 2	2	0.11	1	0.11
Sutures × 9	9	25.00	9	225.00
Syringes × 4	4	0.20	4	0.80
Urinary catheter bag	1	0.45	1	0.45
Velcro fastening strips × 3	3	1.20	3	3.60
Total				1371.29

Appendix 14

Estimates of numbers of survivors and mean duration of survival

TABLE 79 Estimates of numbers of survivors and mean duration of survival for each treatment and each analysis presented in *Chapter 6*

Analysis	Outcome	Robotic	Laparoscopic
Base case (10 years)	Survivors	3950/5000	3922/5000
	Life-years	9.033	8.98
Base case (lifetime)	Survivors	0/5000	0/5000
	Life-years	21.810	20.26
Relative difference in positive margin rate was 0.61	Survivors	3932/5000	3922/5000
	Life-years	9.108	8.975
Relative difference in positive margin rate was 0.88	Survivors	3874/5000	3922/5000
	Life-years	8.978	8.975
Difference in biochemical recurrence was 0.89	Survivors	3976/5000	3922/5000
	Life-years	9.05	8.98
Biochemical recurrence rates twice those of base case and difference was 0.89	Survivors	3913/5000	3822/5000
	Life-years	9.001	8.600

All sensitivity analyses run over a time horizon of 10 years. All cohorts included 5000 men.

Appendix 15

Density charts describing the distribution of total costs and quality-adjusted life-years for the cohort of modelled men for each analysis presented

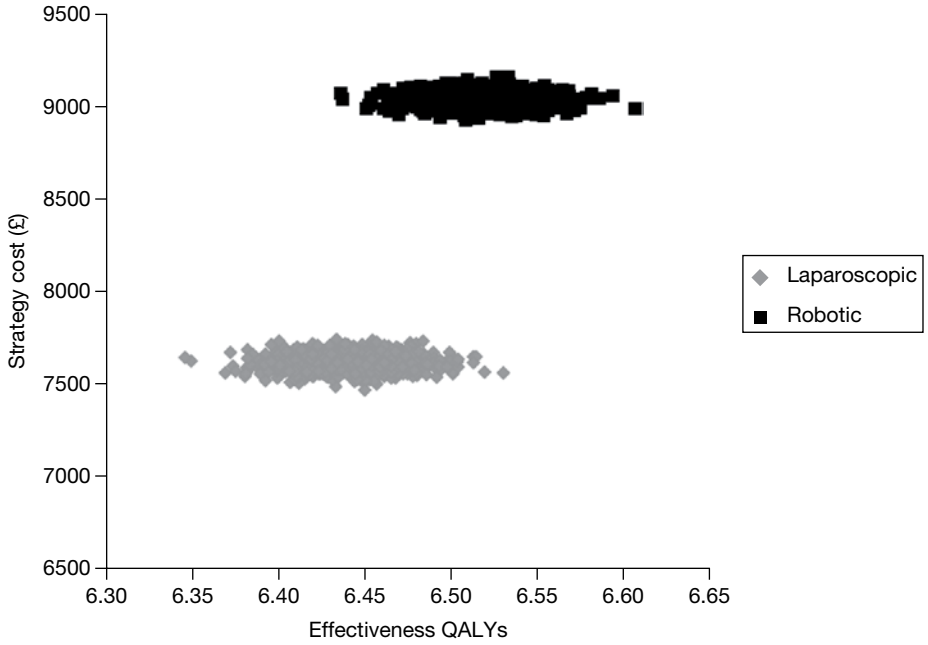

FIGURE 27 Distribution of costs and QALYs for each intervention in the base case, 10-year time horizon (200 procedures).

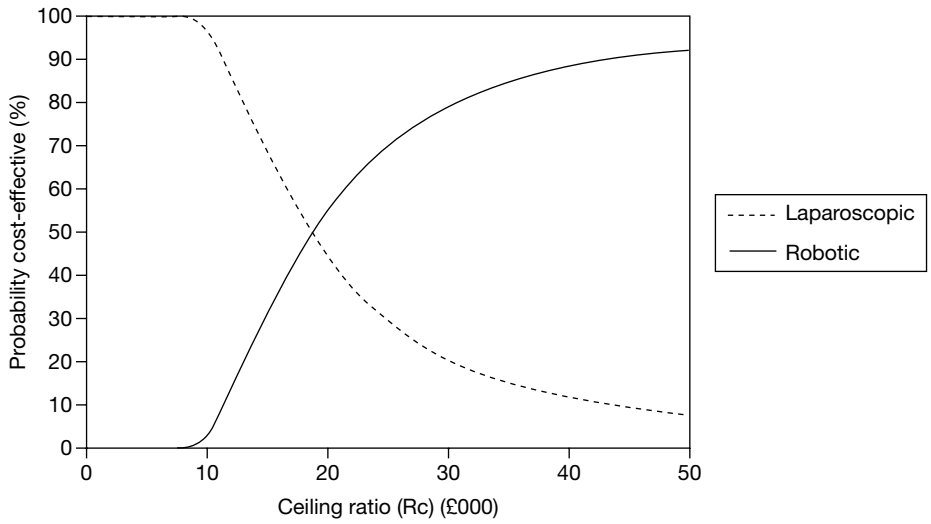

FIGURE 28 Cost-effectiveness acceptability curve for each intervention in the base case, 10-year time horizon (200 procedures).

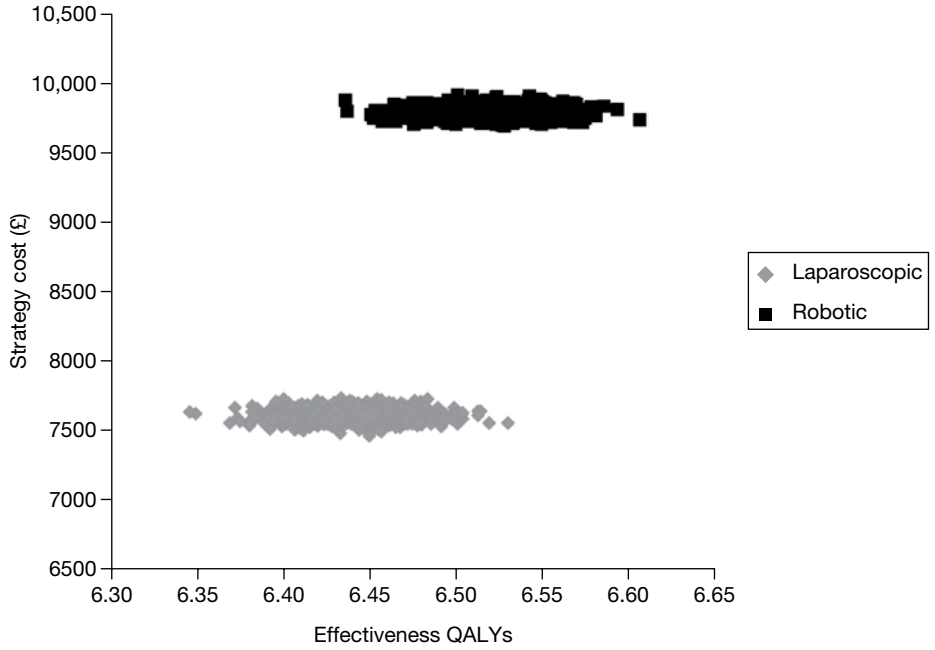

FIGURE 29 Distribution of costs and QALYs for each intervention in the base case, 10-year time horizon (150 procedures).

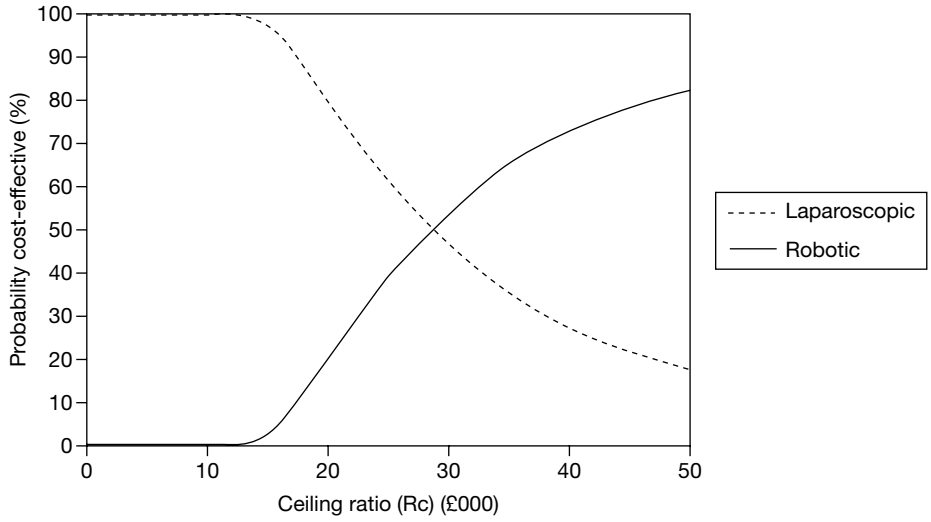

FIGURE 30 Cost-effectiveness acceptability curve for each intervention in the base case, 10-year time horizon (150 procedures).

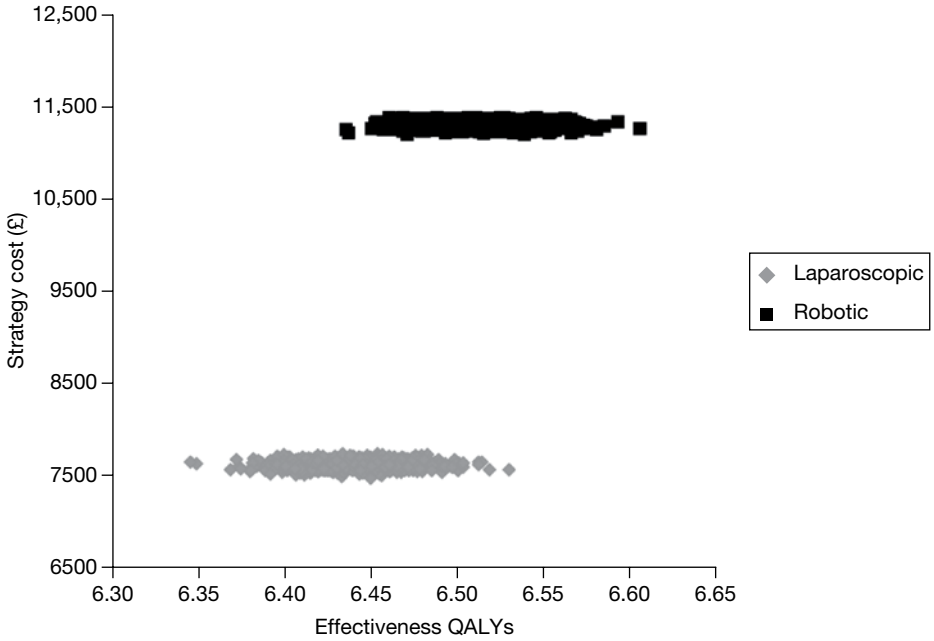

FIGURE 31 Distribution of costs and QALYs for each intervention in the base case, 10-year time horizon (100 procedures).

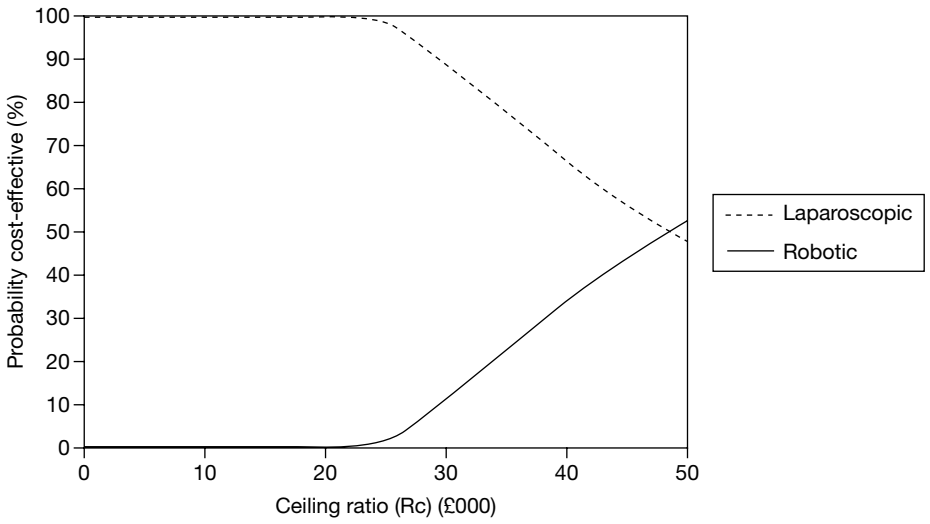

FIGURE 32 Cost-effectiveness acceptability curve for each intervention in the base case, 10-year time horizon (100 procedures).

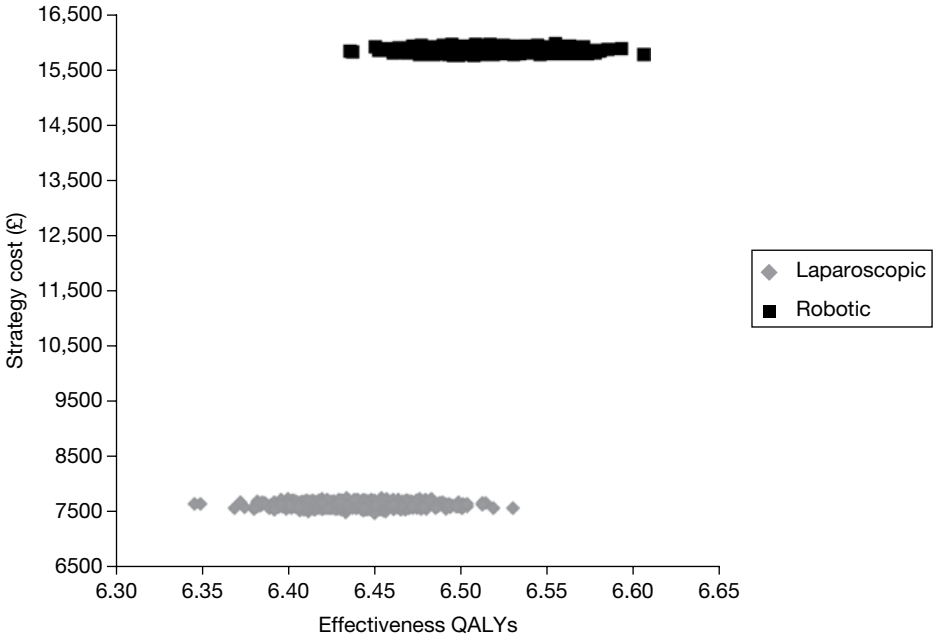

FIGURE 33 Distribution of costs and QALYs for each intervention in the base case, 10-year time horizon (50 procedures).

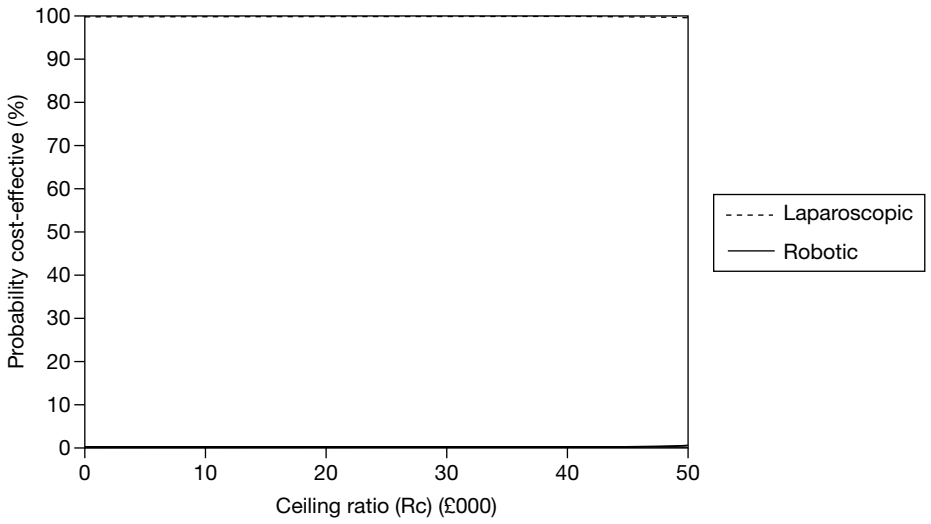

FIGURE 34 Cost-effectiveness acceptability curve for each intervention in the base case, 10-year time horizon (50 procedures).

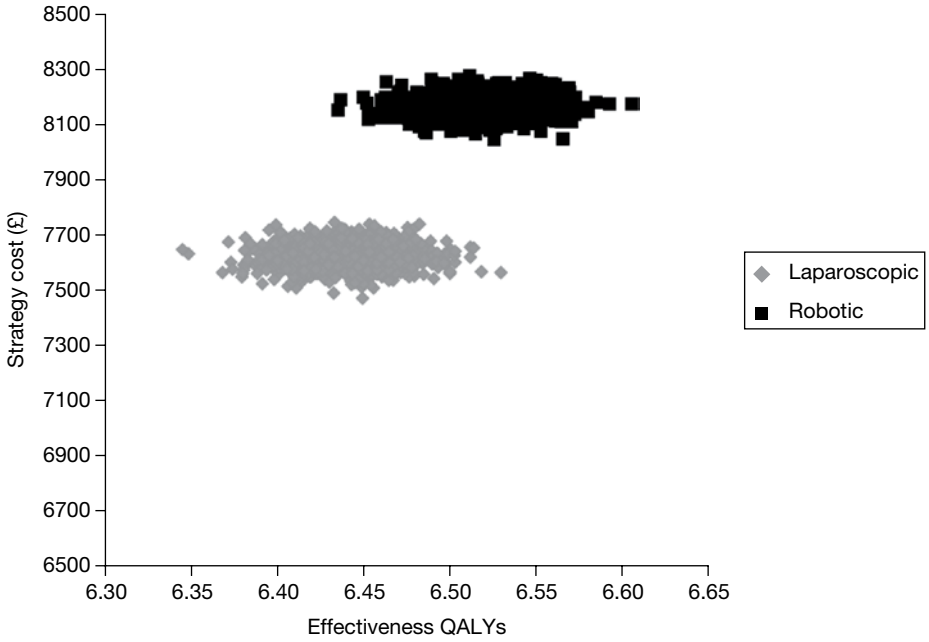

FIGURE 35 Distribution of costs and QALYs for each intervention in the base case, 10-year time horizon (200 procedures using the least expensive procurement plan for the robotic system).

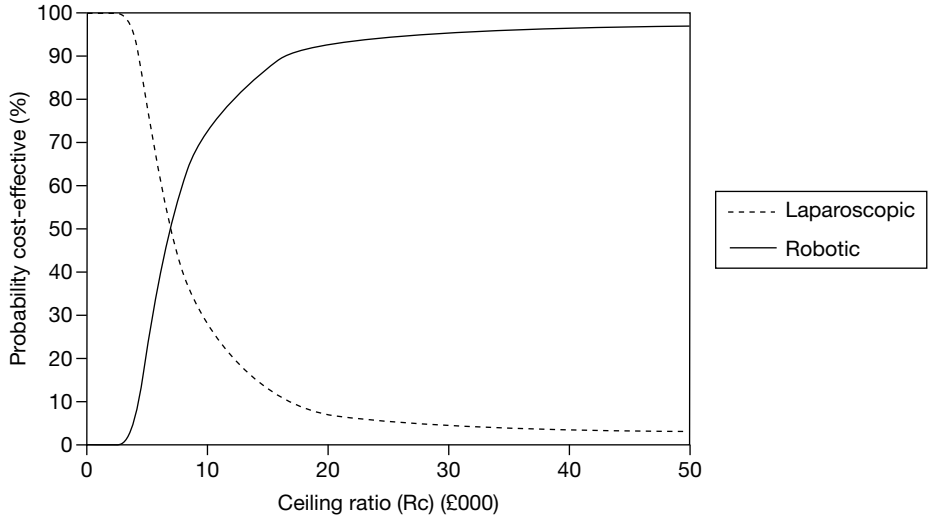

FIGURE 36 Cost-effectiveness acceptability curve for each intervention in the base case, 10-year time horizon (200 procedures using the least expensive procurement plan for the robotic system).

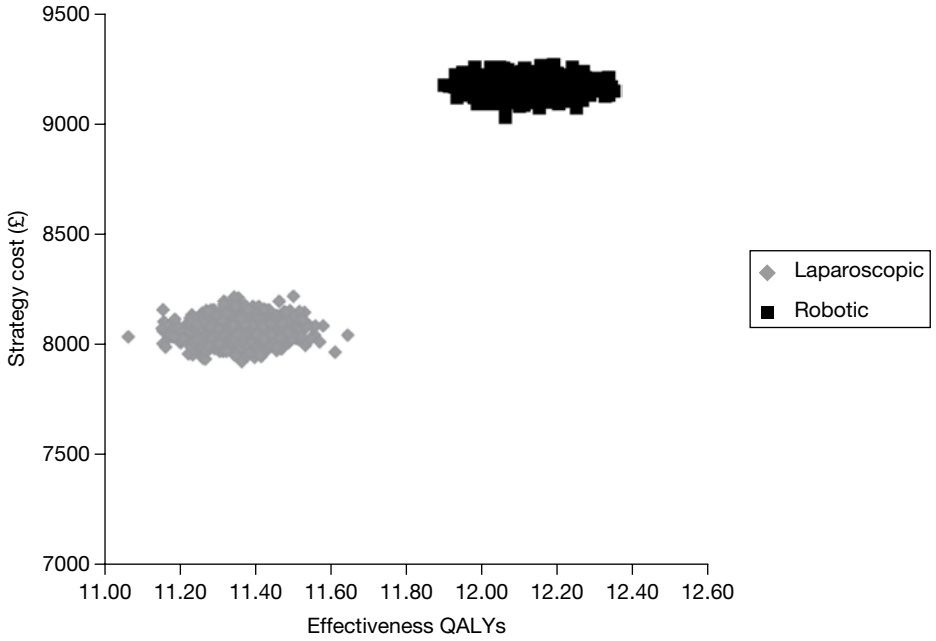

FIGURE 37 Distribution of costs and QALYs for each intervention in the base case, 70-year time horizon (200 procedures).

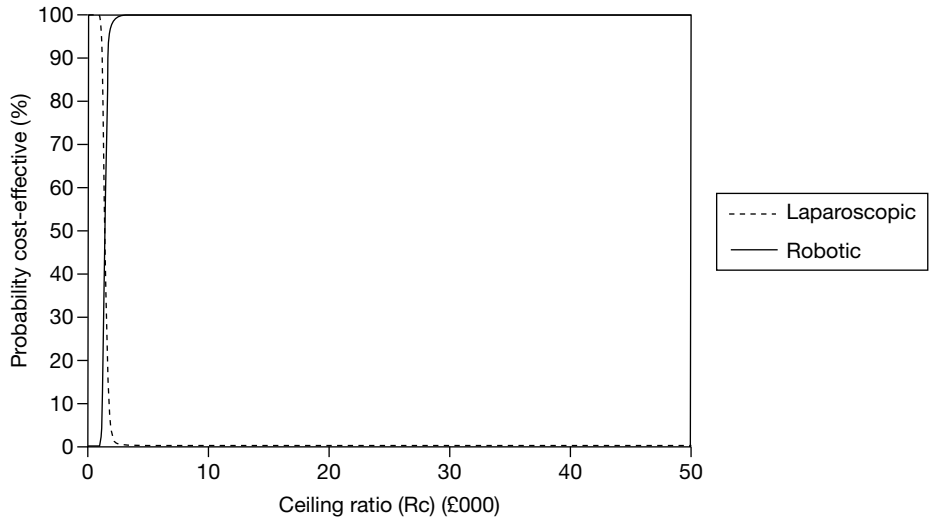

FIGURE 38 Cost-effectiveness acceptability curve for each intervention in the base case, 70-year time horizon (200 procedures).

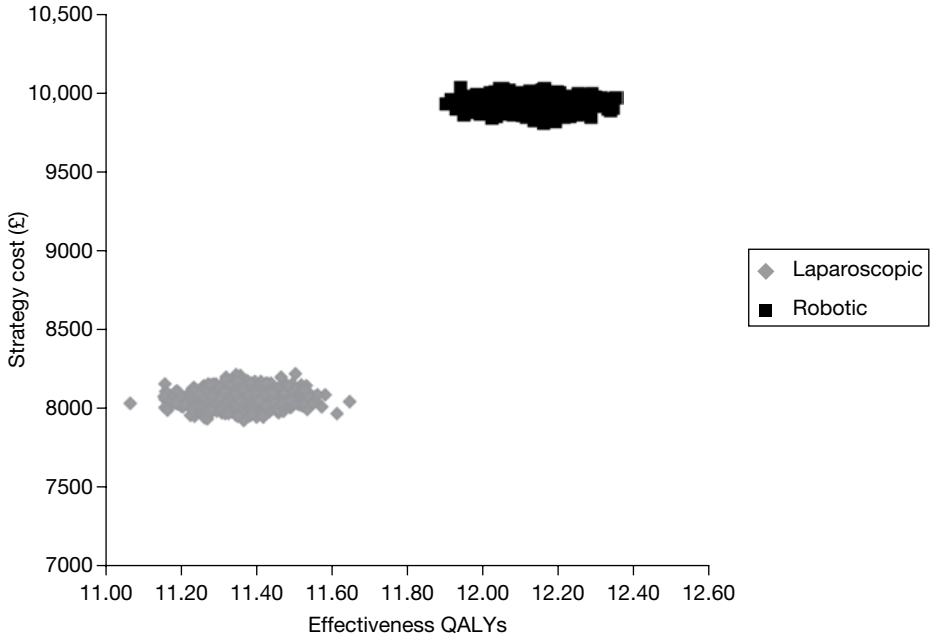

FIGURE 39 Distribution of costs and QALYs for each intervention in the base case, 70-year time horizon (150 procedures).

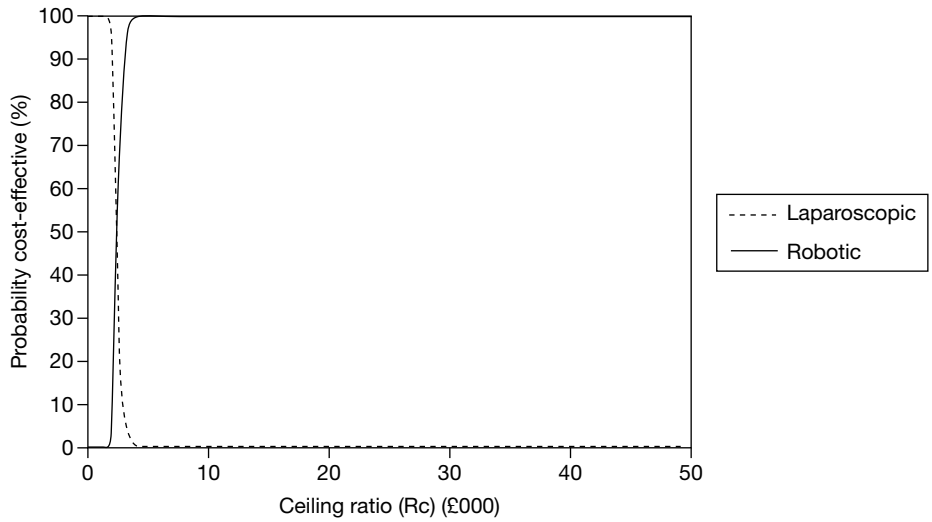

FIGURE 40 Cost-effectiveness acceptability curve for each intervention in the base case, 70-year time horizon (150 procedures).

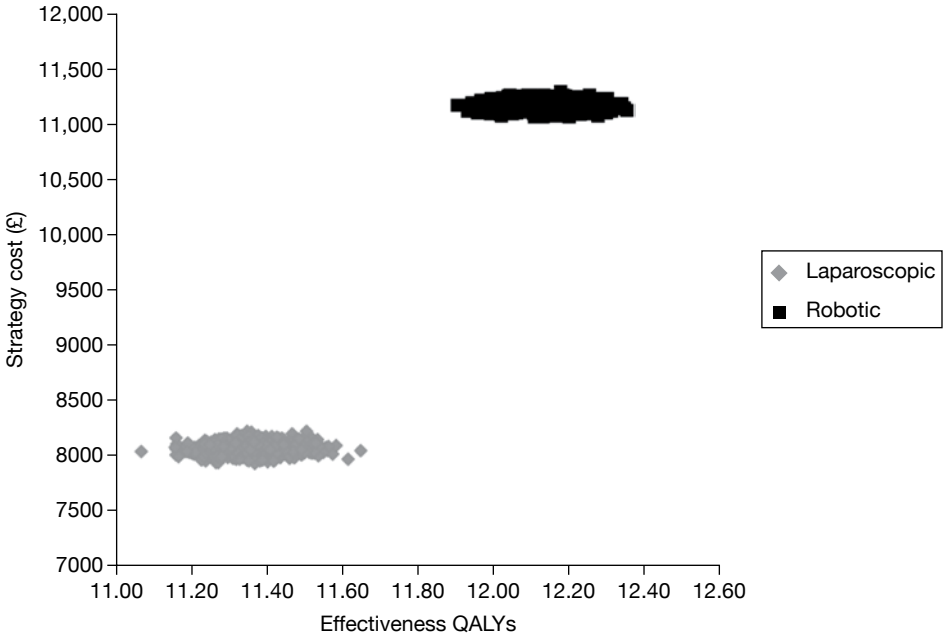

FIGURE 41 Distribution of costs and QALYs for each intervention in the base case, 70-year time horizon (100 procedures).

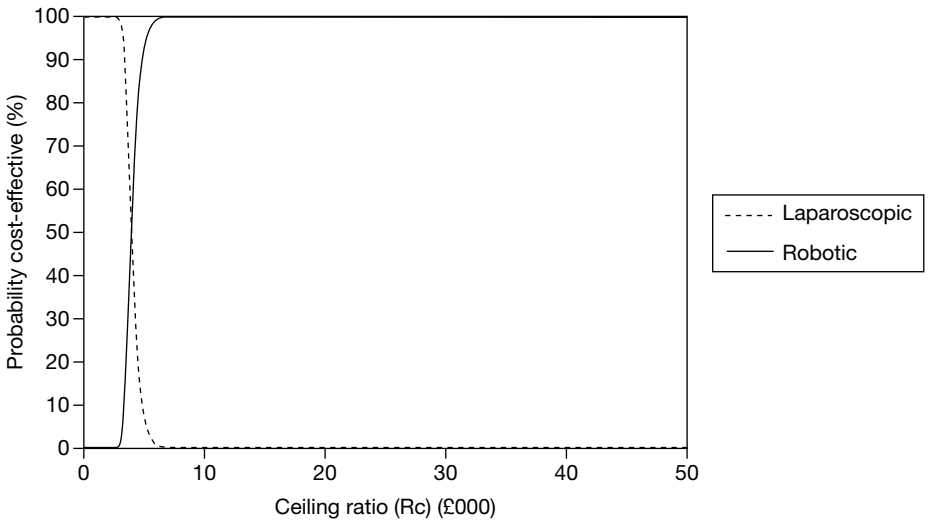

FIGURE 42 Cost-effectiveness acceptability curve for each intervention in the base case, 70-year time horizon (100 procedures).

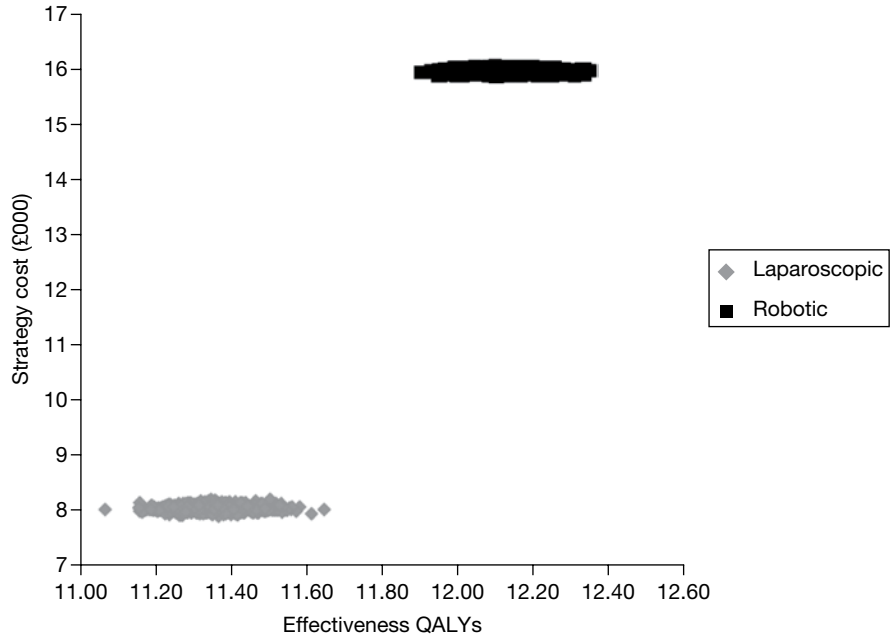

FIGURE 43 Distribution of costs and QALYs for each intervention in the base case, 70-year time horizon (50 procedures).

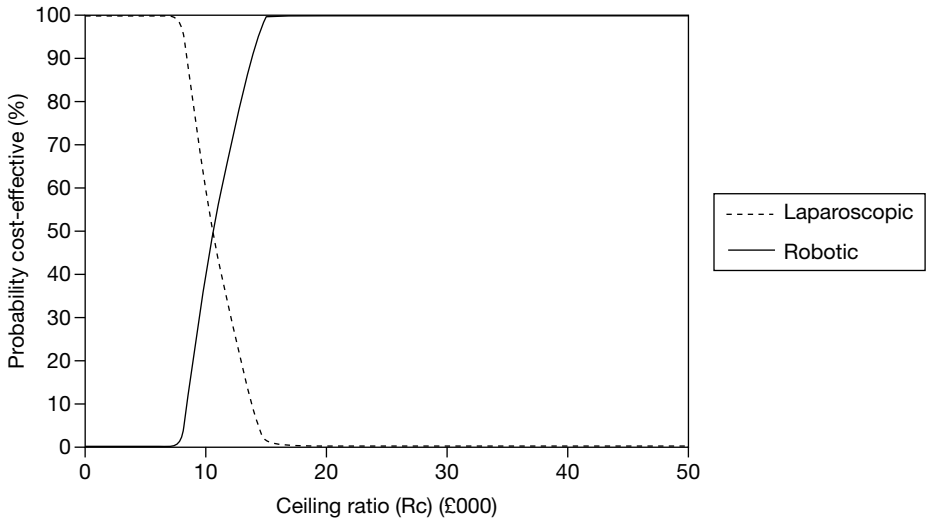

FIGURE 44 Cost-effectiveness acceptability curve for each intervention in the base case, 70-year time horizon (50 procedures).

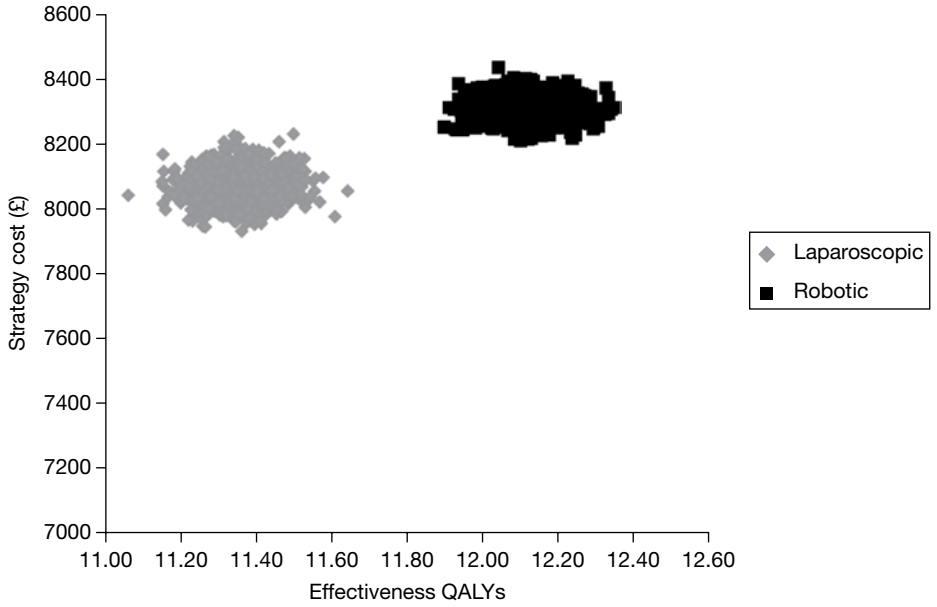

FIGURE 45 Distribution of costs and QALYs for each intervention in the base case, 70-year time horizon (200 procedures using the least expensive procurement plan for the robotic system).

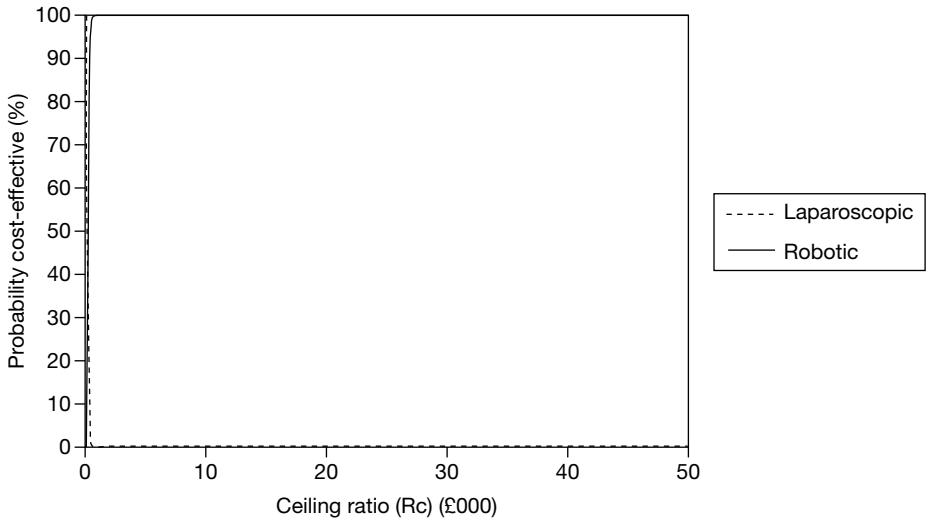

FIGURE 46 Cost-effectiveness acceptability curve for each intervention in the base case, 70-year time horizon (200 procedures using the least expensive procurement plan for the robotic system).

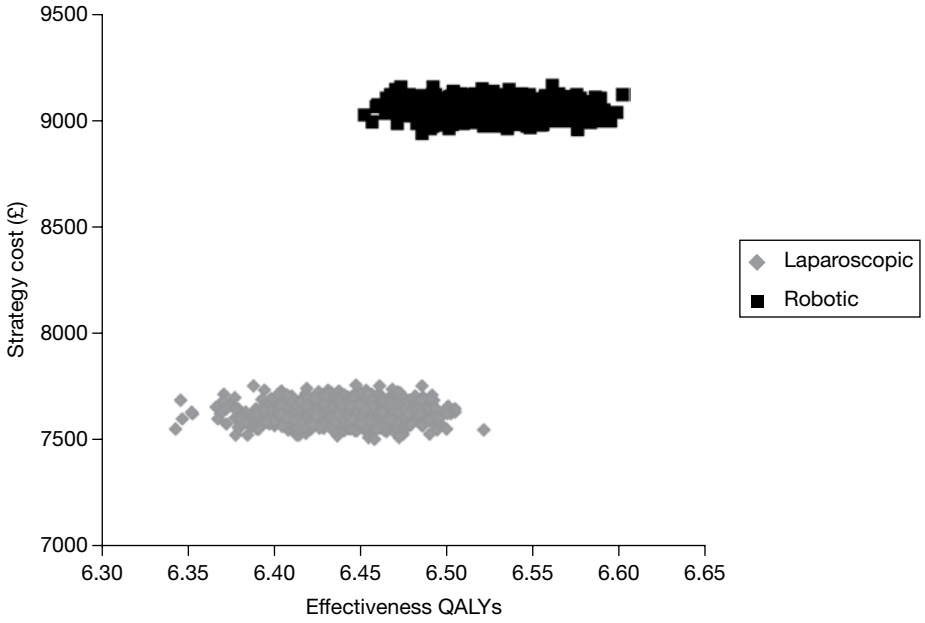

FIGURE 47 Distribution of costs and QALYs for each intervention following sensitivity analysis at the higher rate of biochemical recurrence (200 procedures).

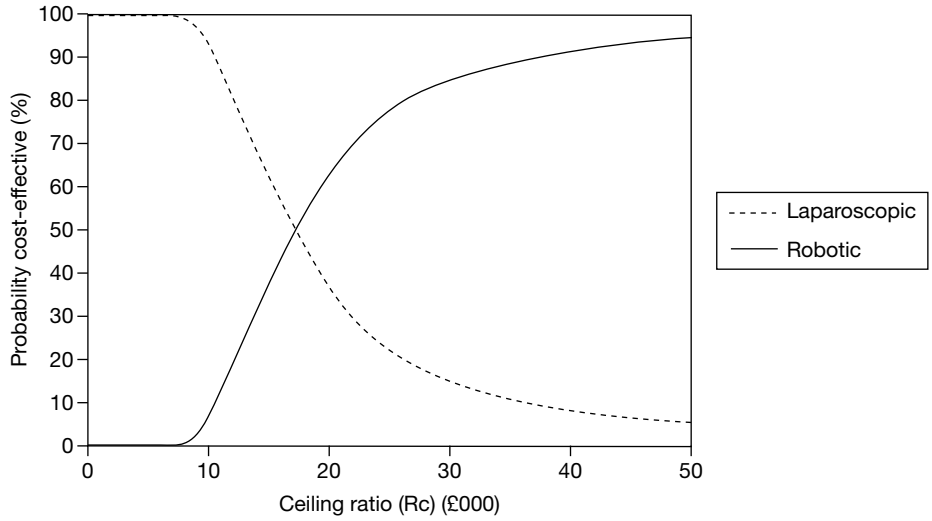

FIGURE 48 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis at the higher rate of biochemical recurrence (200 procedures).

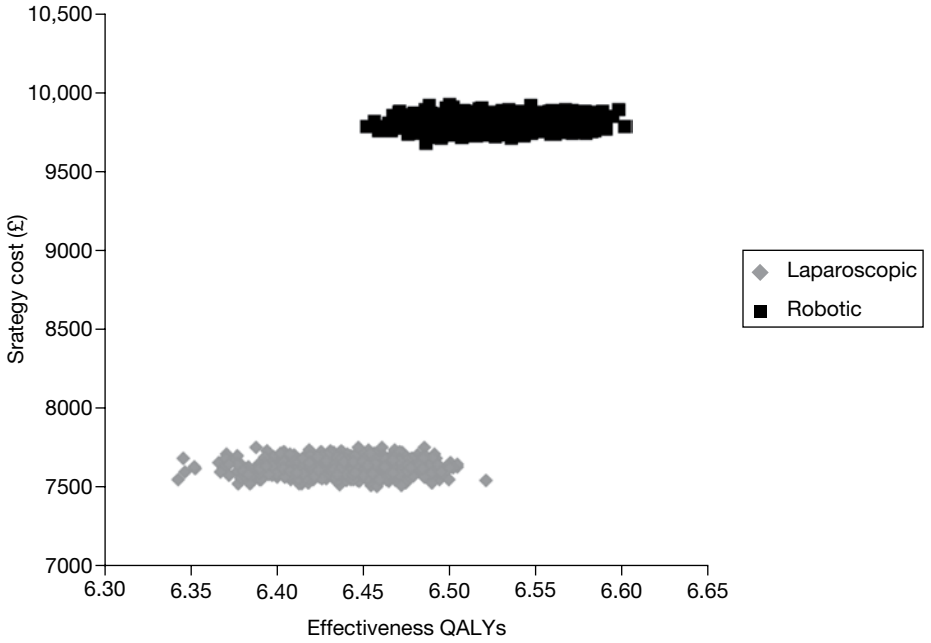

FIGURE 49 Distribution of costs and QALYs for each intervention following sensitivity analysis at the higher rate of biochemical recurrence (150 procedures).

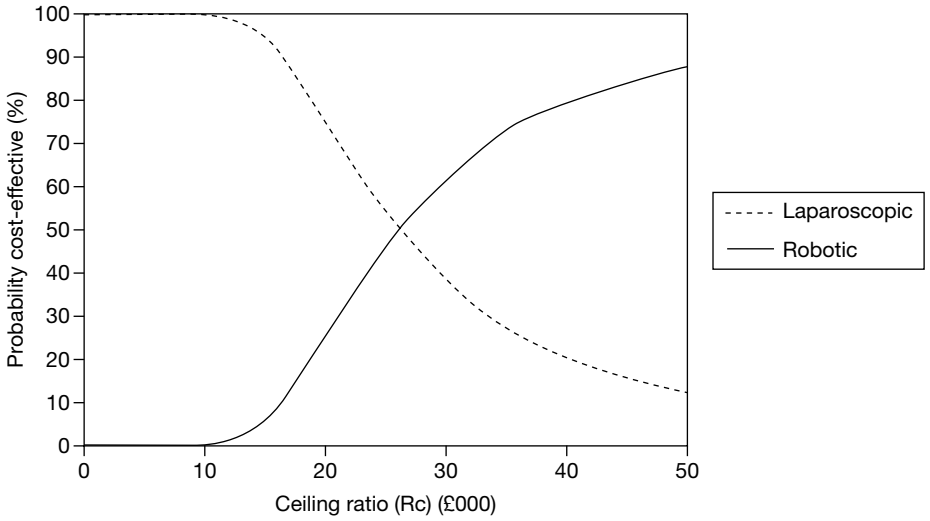

FIGURE 50 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis at the higher rate of biochemical recurrence (150 procedures).

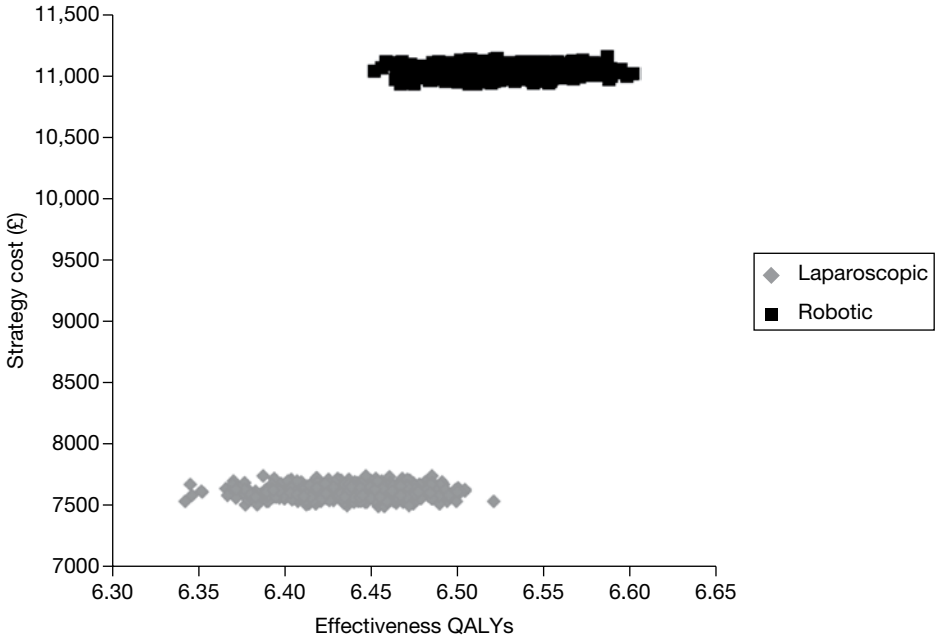

FIGURE 51 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (100 procedures).

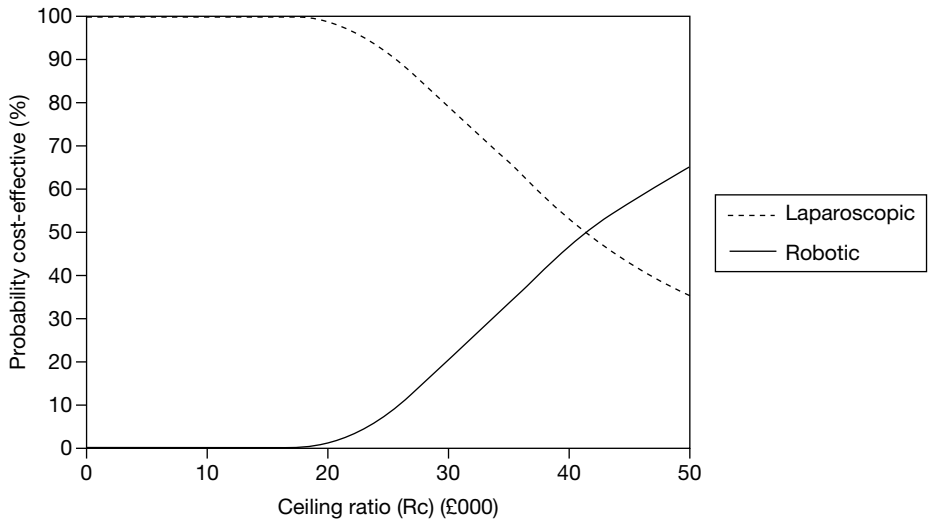

FIGURE 52 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (100 procedures).

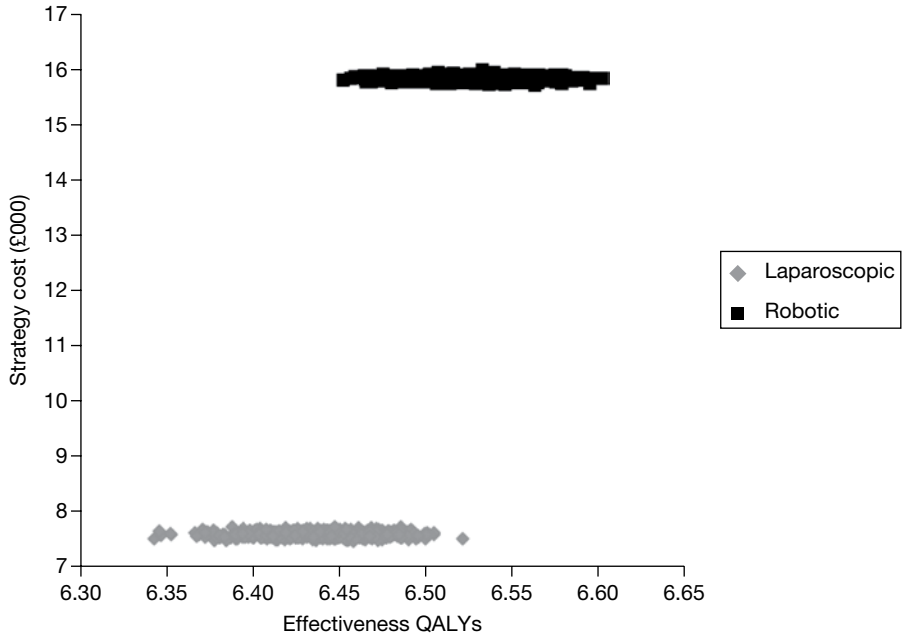

FIGURE 53 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (50 procedures).

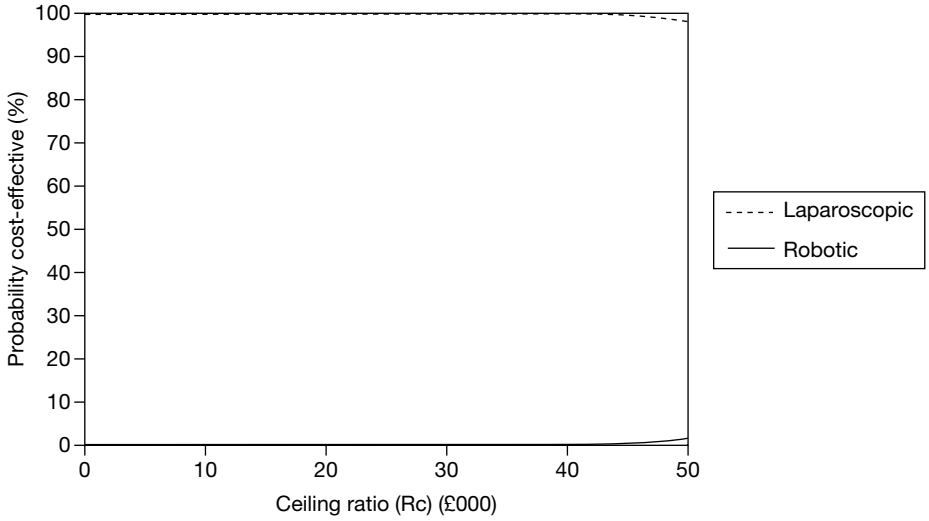

FIGURE 54 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (50 procedures).

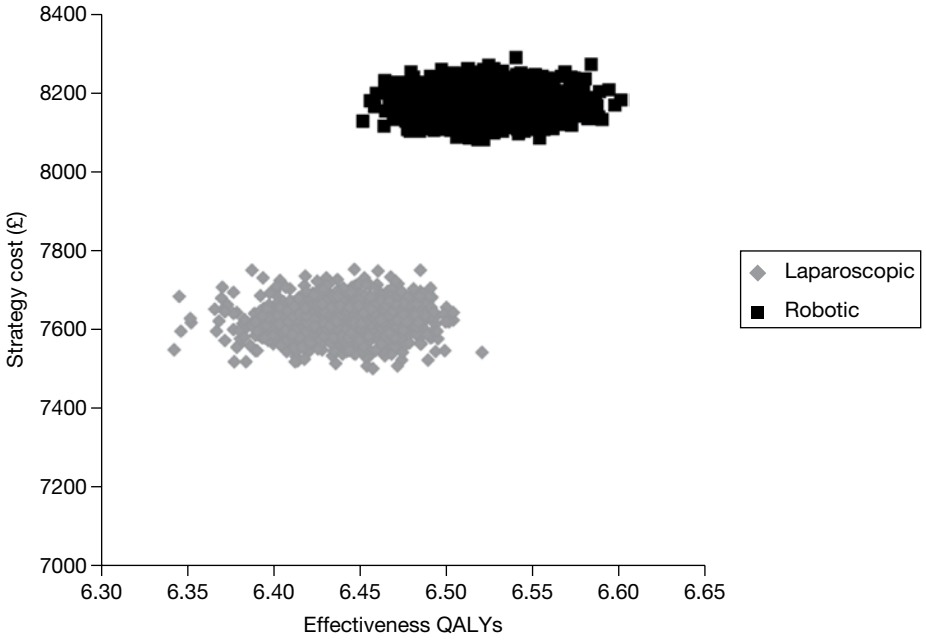

FIGURE 55 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (200 procedures using the least expensive procurement plan for the robotic system).

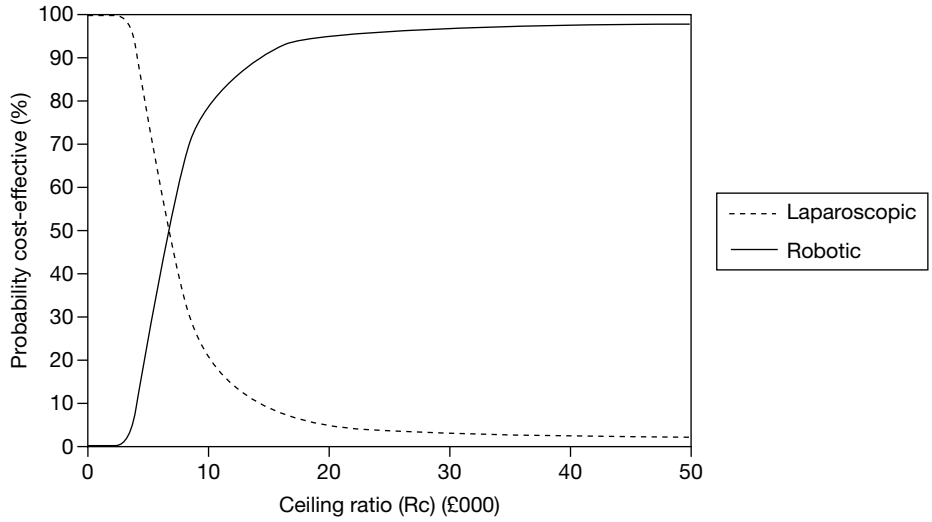

FIGURE 56 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years at the higher rate of biochemical recurrence (200 procedures using the least expensive procurement plan for the robotic system).

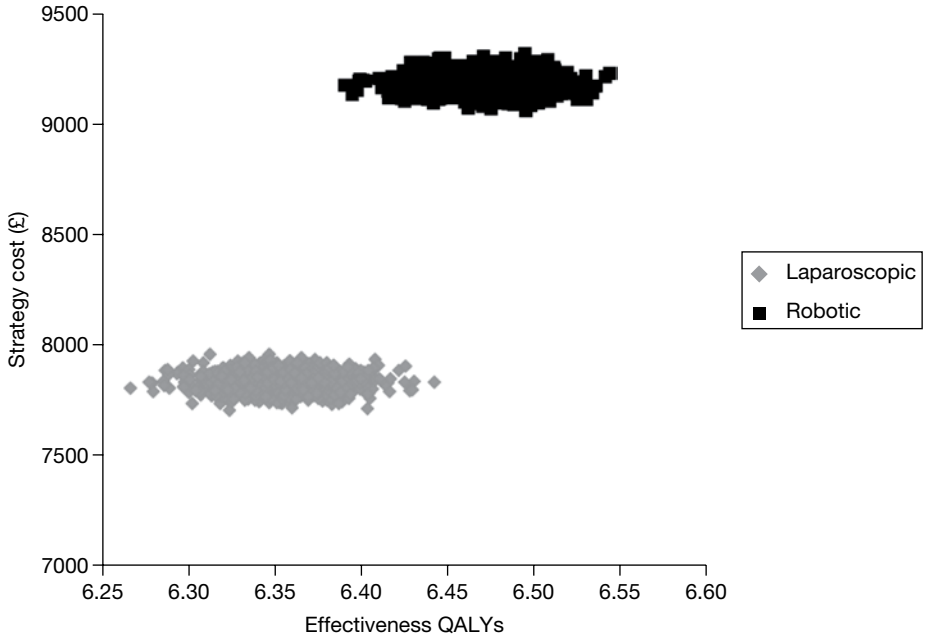

FIGURE 57 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the lower rate of biochemical recurrence (200 procedures).

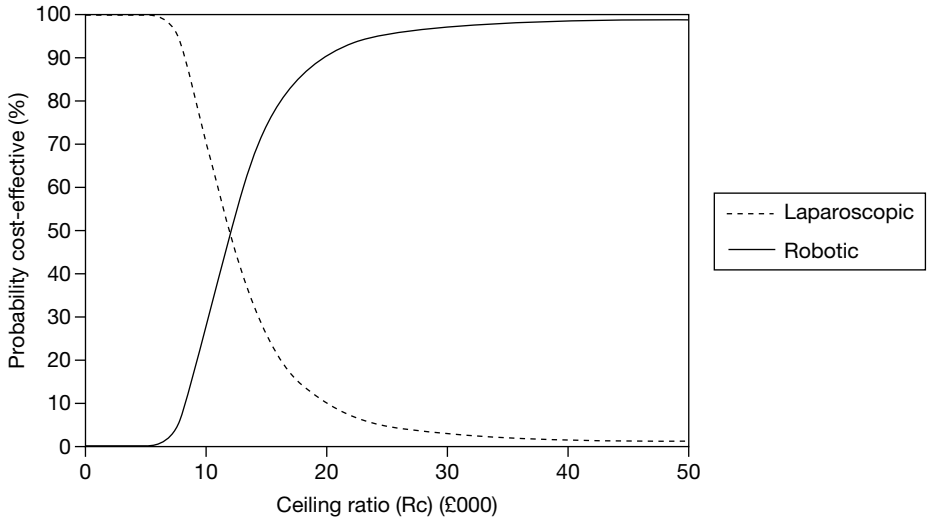

FIGURE 58 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years with rates of biochemical recurrence doubled (200 procedures).

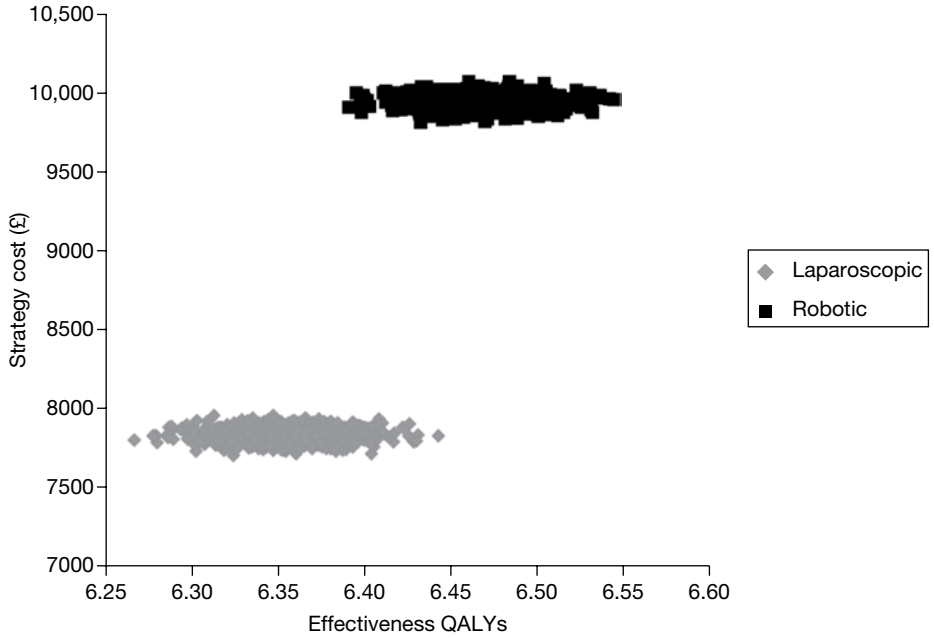

FIGURE 59 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the lower rate of biochemical recurrence (150 procedures).

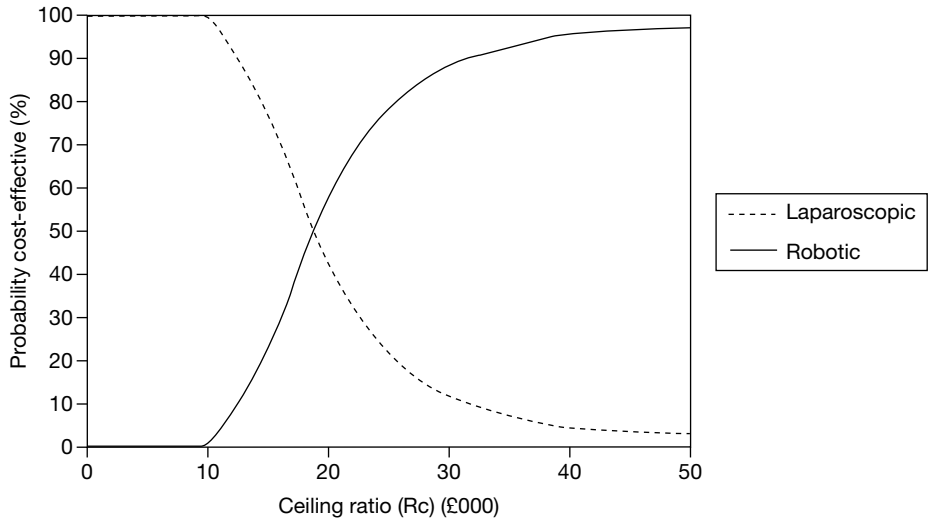

FIGURE 60 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years with rates of biochemical recurrence doubled (150 procedures).

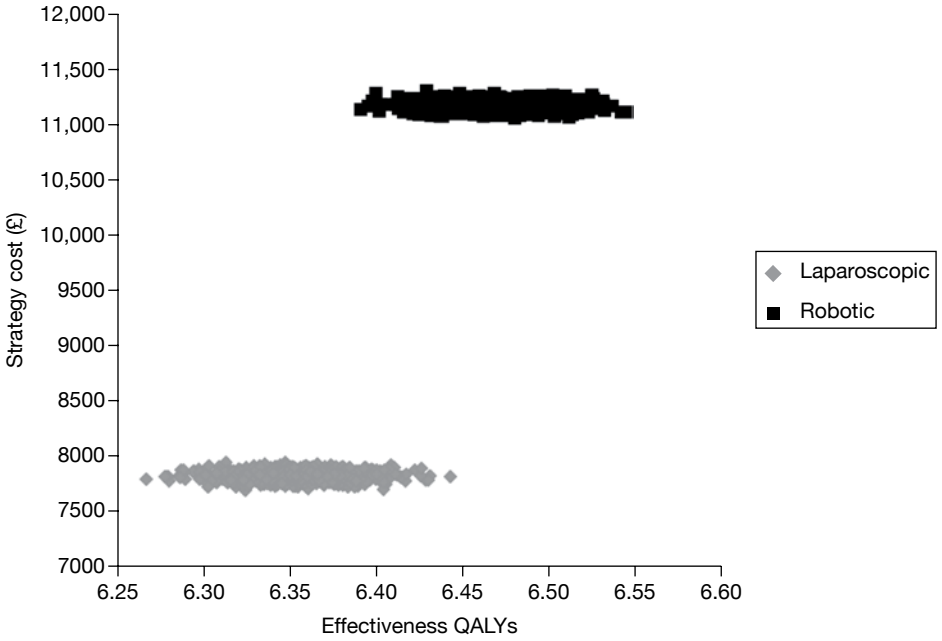

FIGURE 61 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the lower rate of biochemical recurrence (100 procedures).

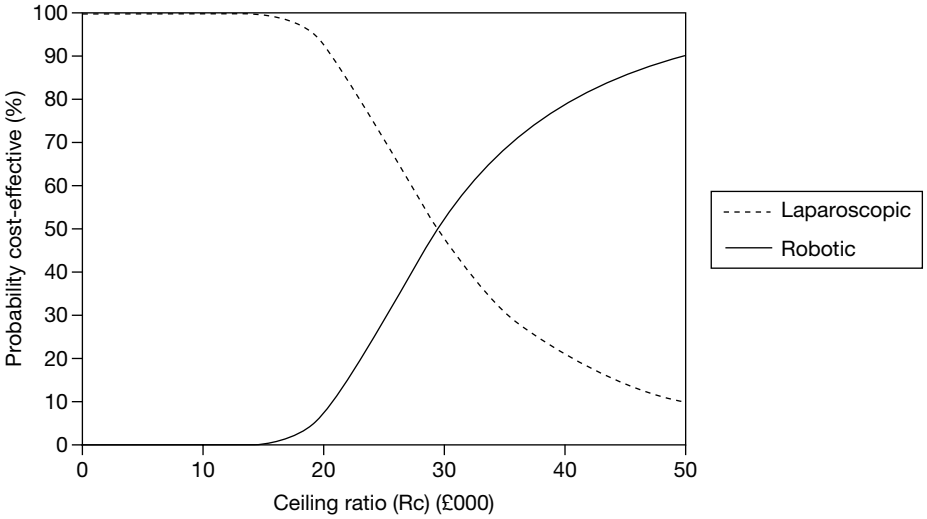

FIGURE 62 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years with rates of biochemical recurrence doubled (100 procedures).

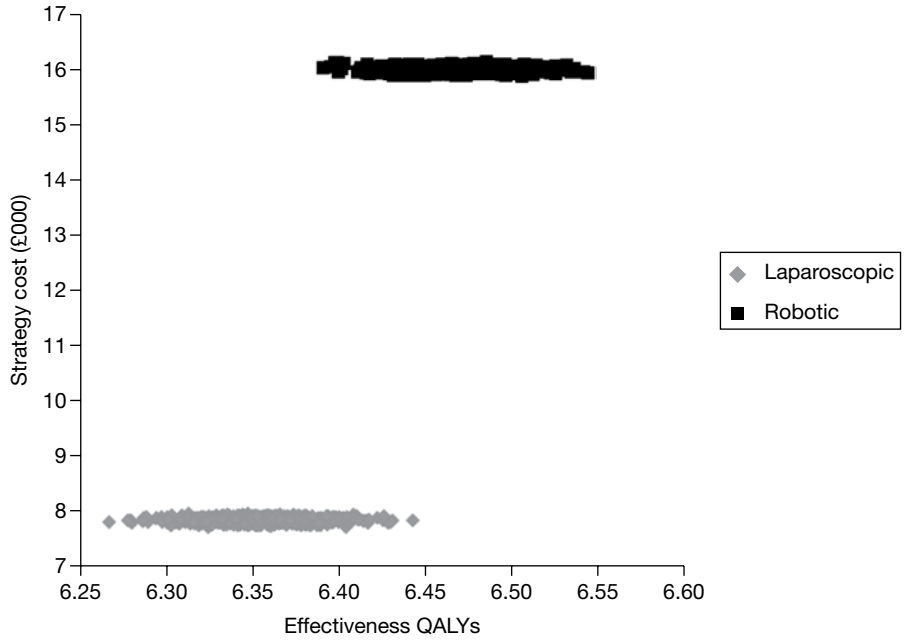

FIGURE 63 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the lower rate of biochemical recurrence (50 procedures).

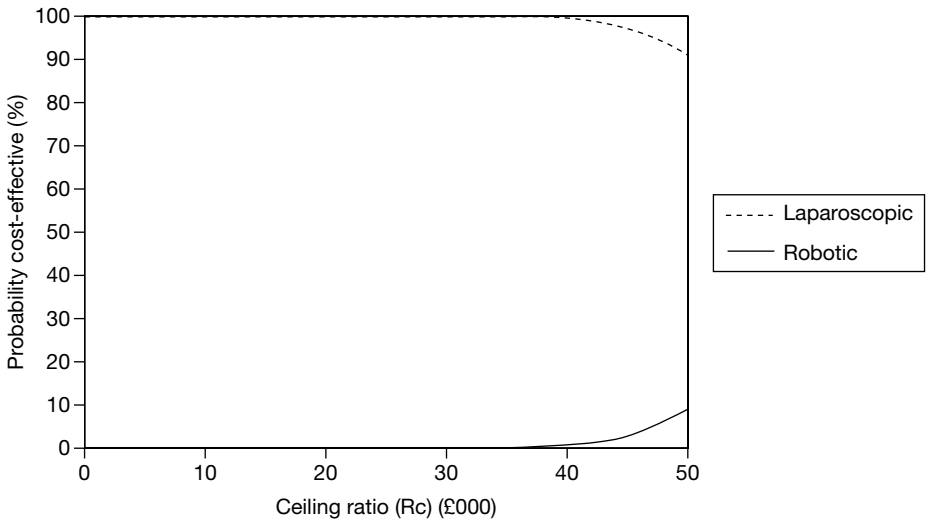

FIGURE 64 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years with rates of biochemical recurrence doubled (50 procedures).

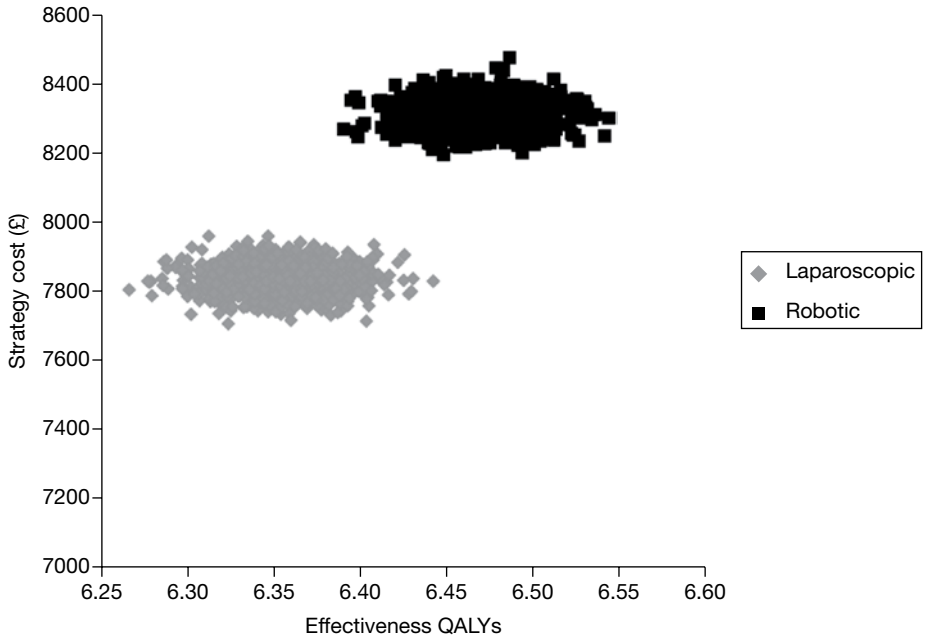

FIGURE 65 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years at the lower rate of biochemical recurrence (200 procedures using the least expensive procurement plan for the robotic system).

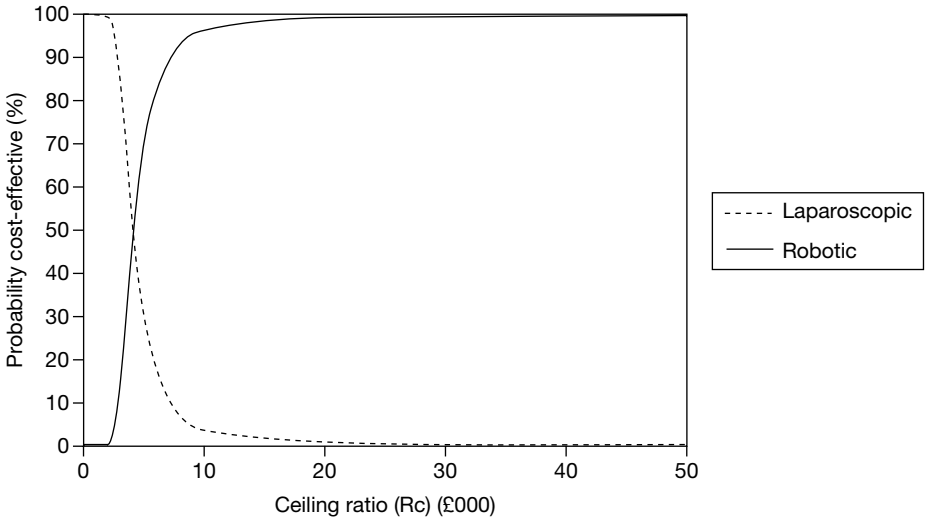

FIGURE 66 Cost-effectiveness acceptability curve of each intervention following sensitivity analysis over 10 years with rates of biochemical recurrence doubled (200 procedures using the least expensive procurement plan for the robotic system).

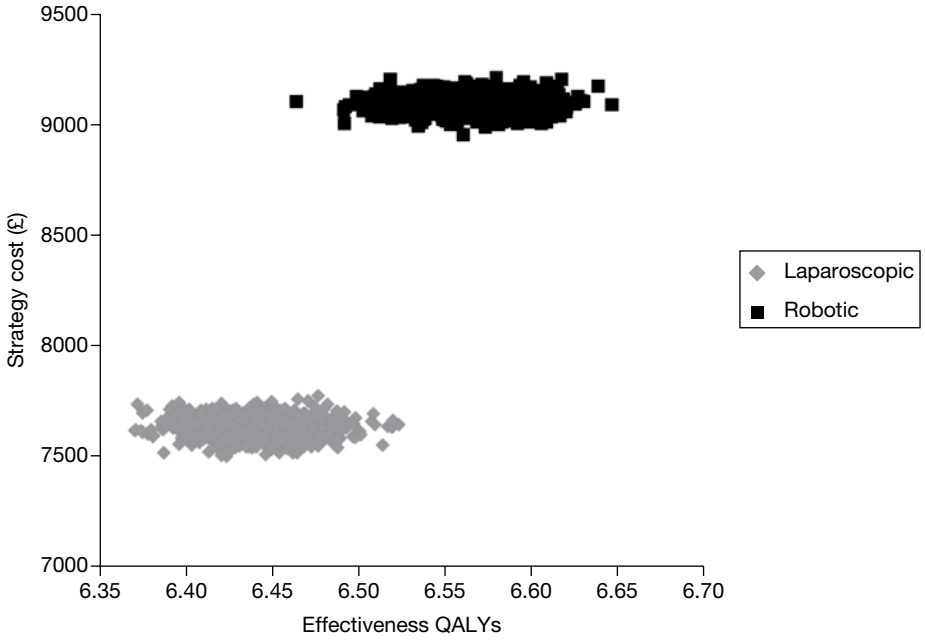

FIGURE 67 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (200 procedures).

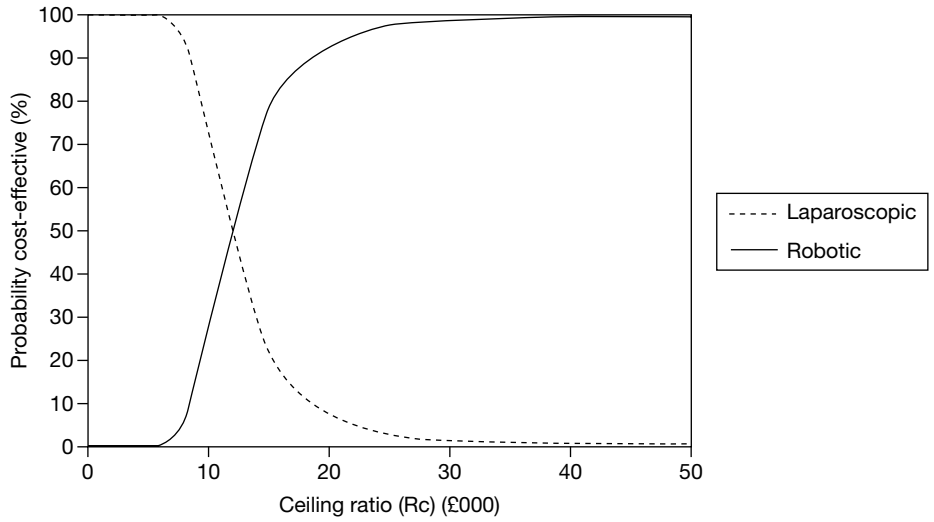

FIGURE 68 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (200 procedures).

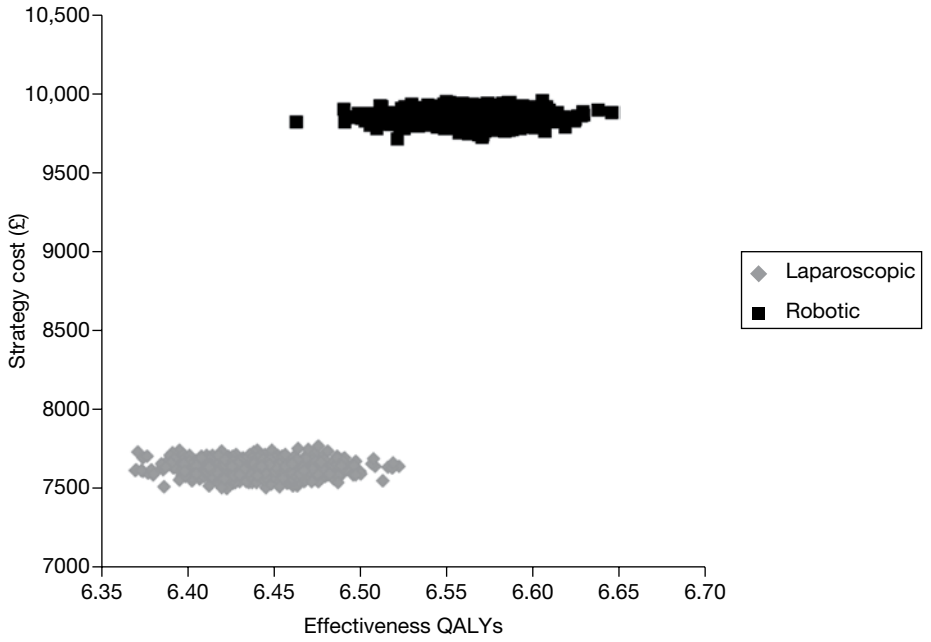

FIGURE 69 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (150 procedures).

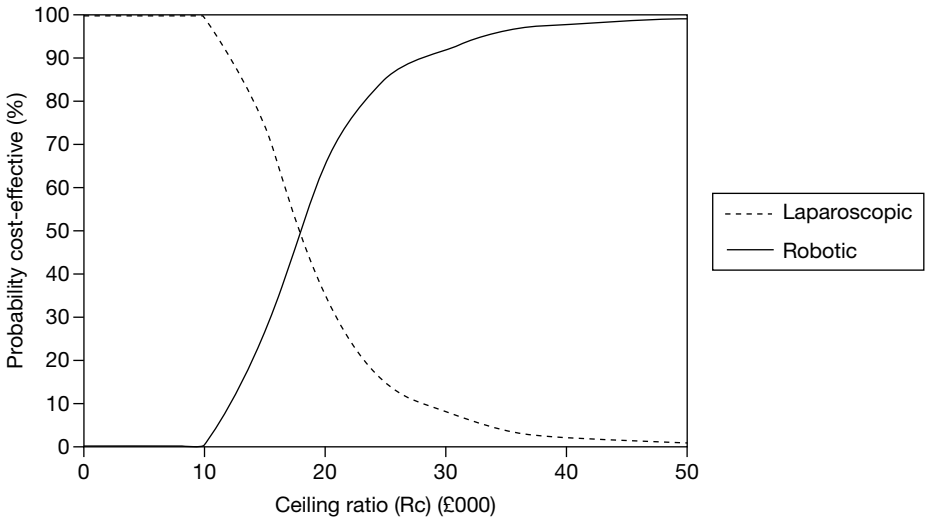

FIGURE 70 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (150 procedures).

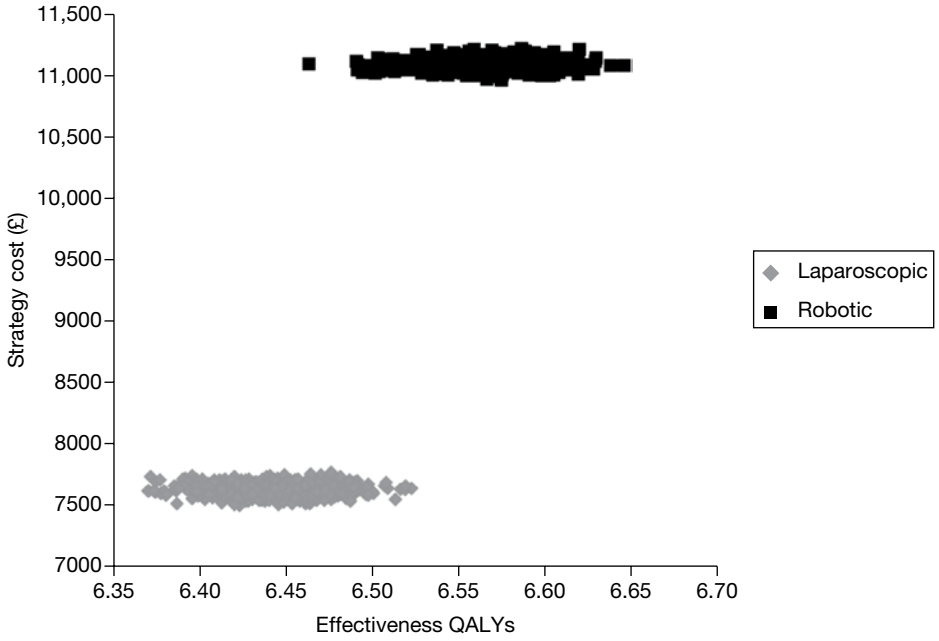

FIGURE 71 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (100 procedures).

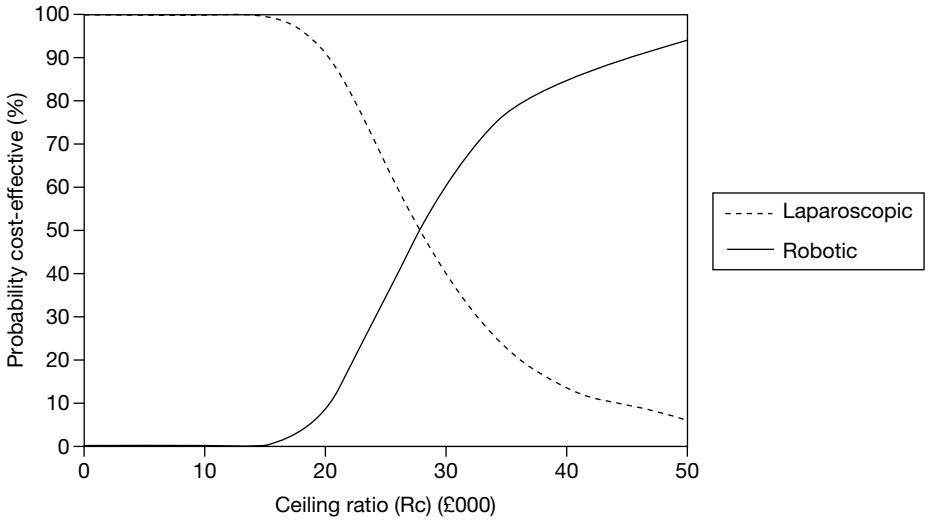

FIGURE 72 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (100 procedures).

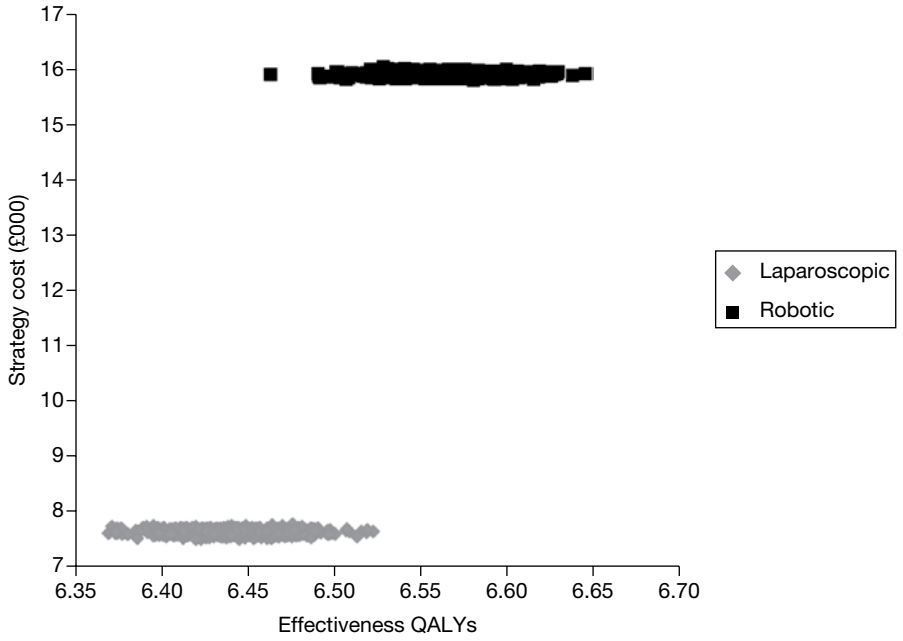

FIGURE 73 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (50 procedures).

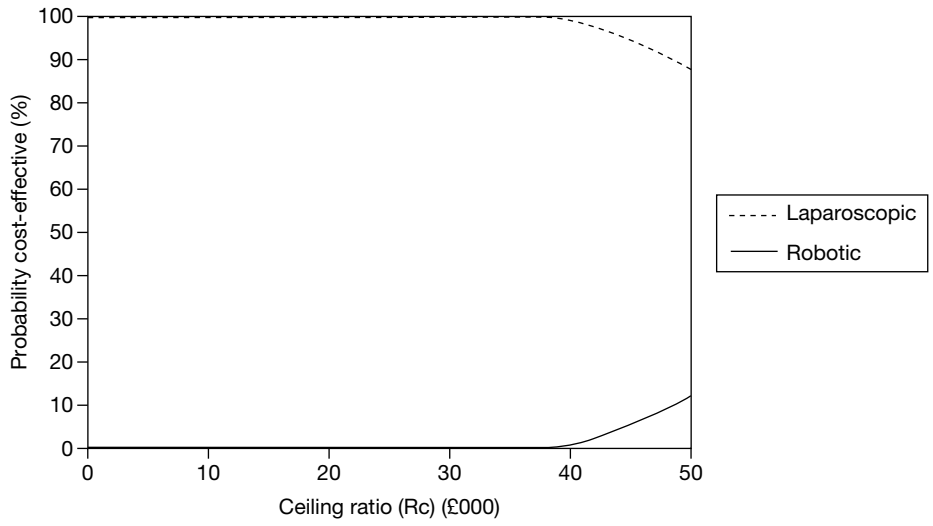

FIGURE 74 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (50 procedures).

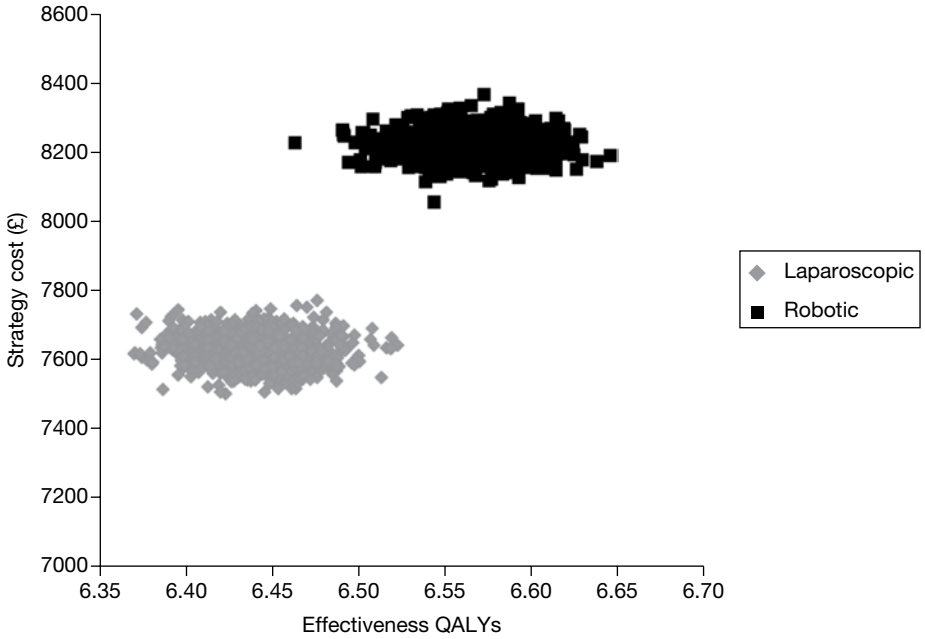

FIGURE 75 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (200 procedures using the least expensive procurement plan for the robotic system).

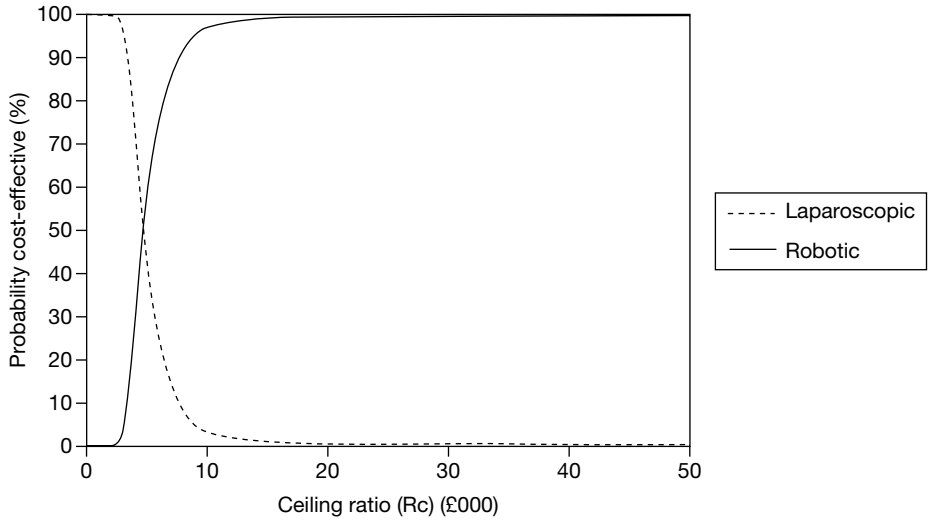

FIGURE 76 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.506 (200 procedures using the least expensive procurement plan for the robotic system).

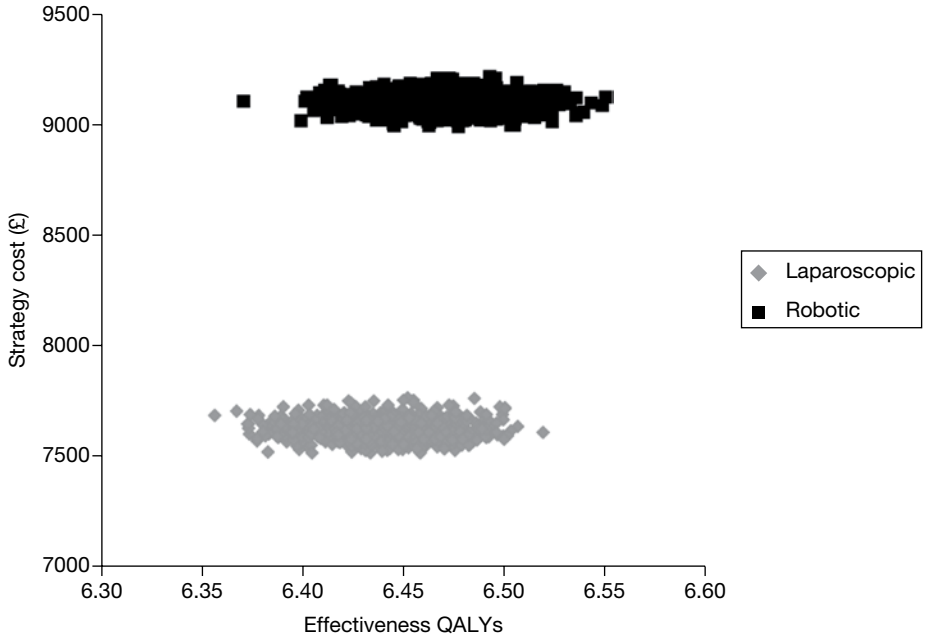

FIGURE 77 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (200 procedures).

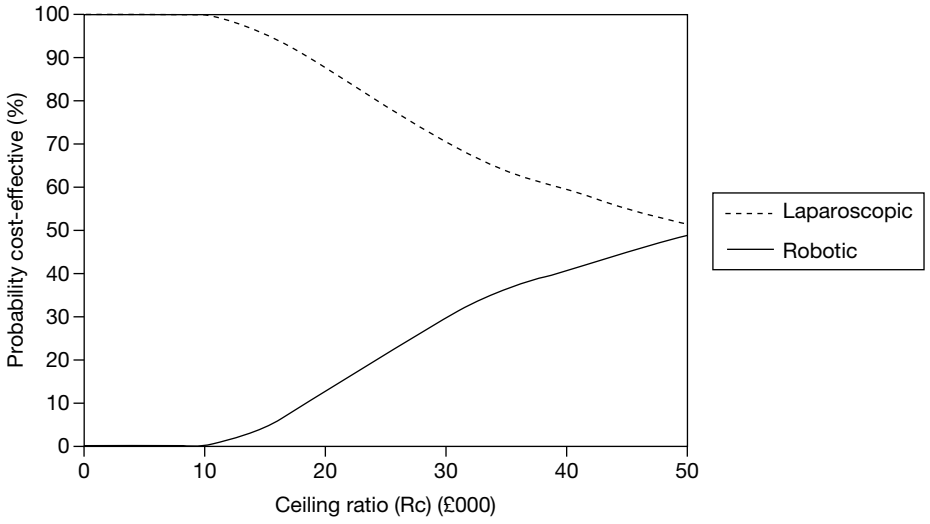

FIGURE 78 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (200 procedures).

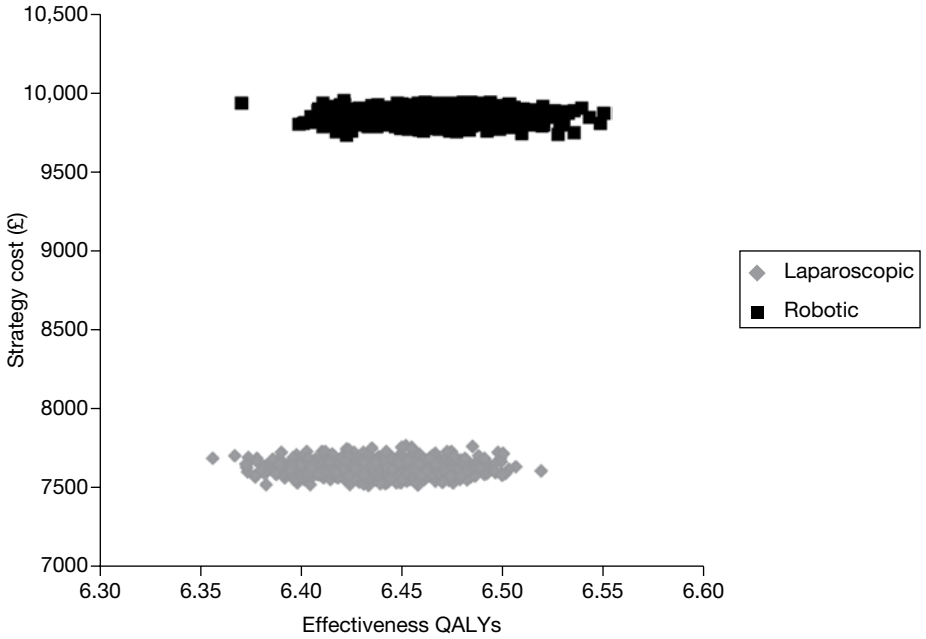

FIGURE 79 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (150 procedures).

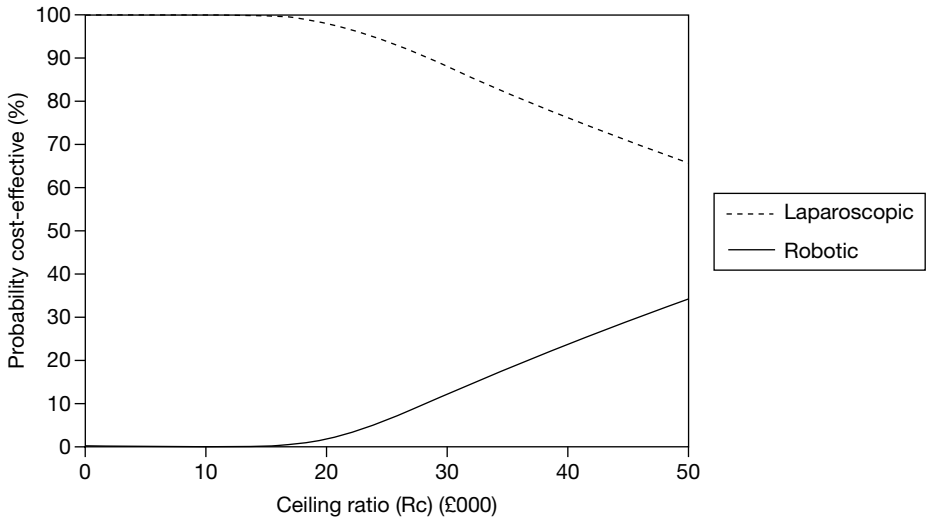

FIGURE 80 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (150 procedures).

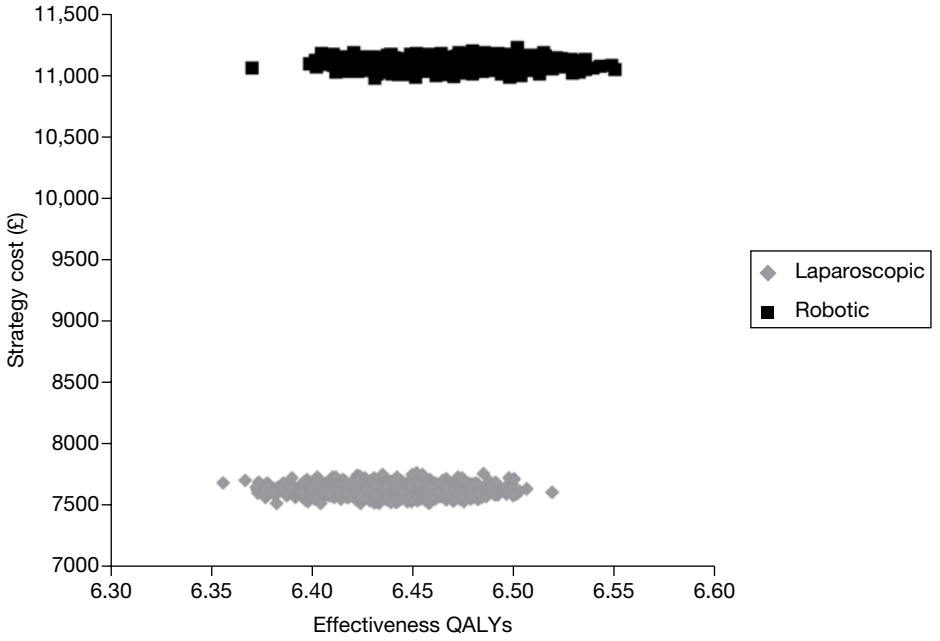

FIGURE 81 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (100 procedures).

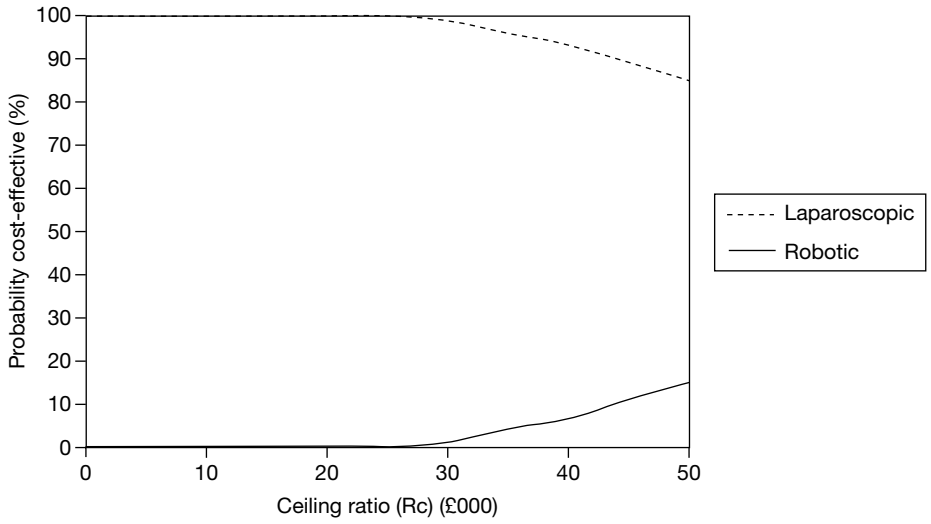

FIGURE 82 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (100 procedures).

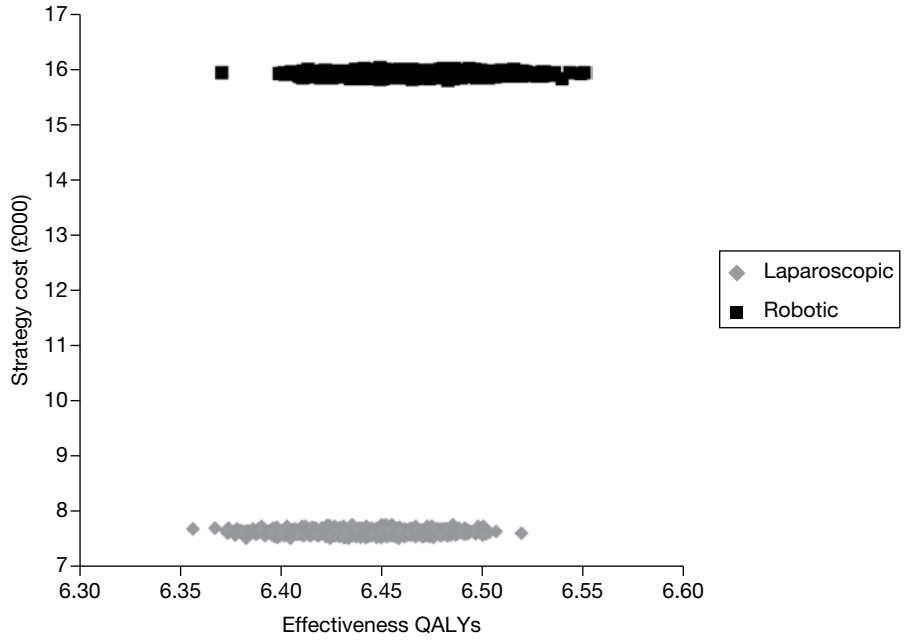

FIGURE 83 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (50 procedures).

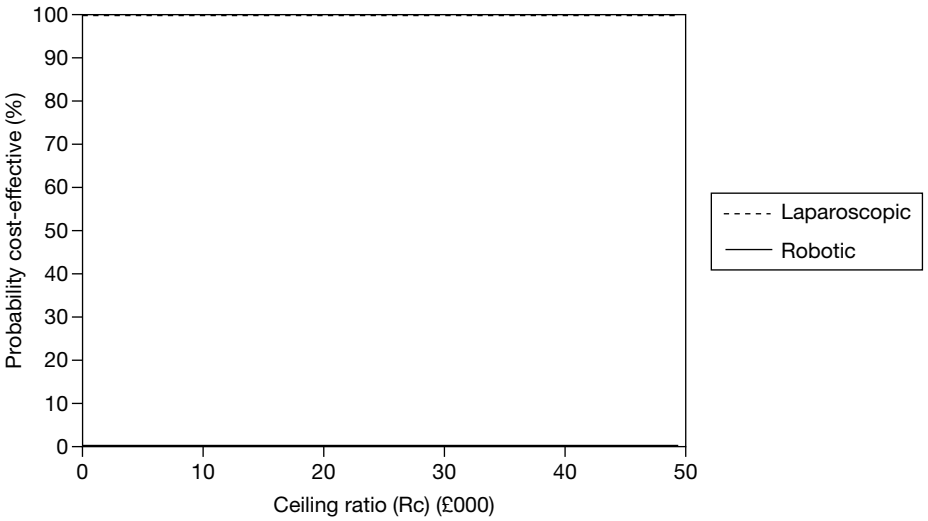

FIGURE 84 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (50 procedures).

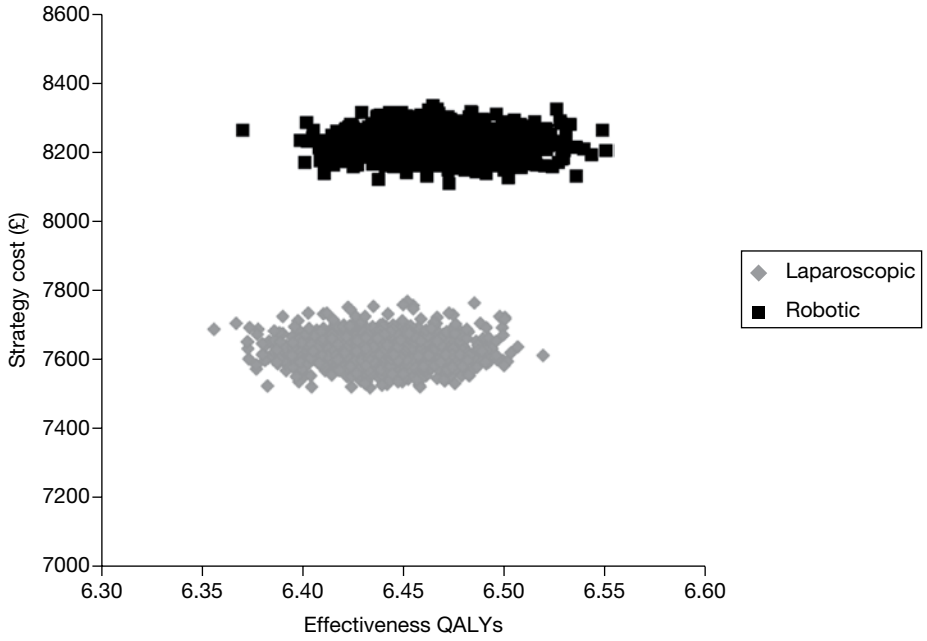

FIGURE 85 Distribution of costs and QALYs for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (200 procedures using the least expensive procurement plan for the robotic system).

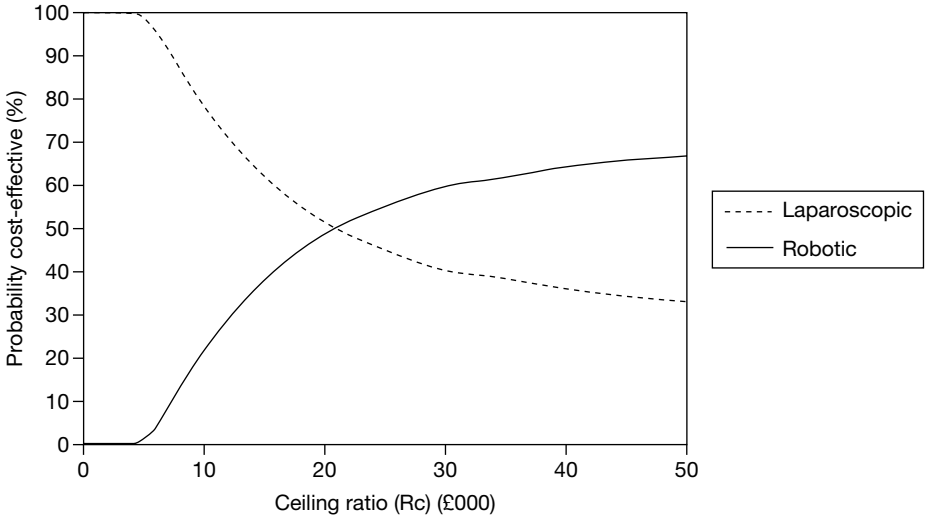

FIGURE 86 Cost-effectiveness acceptability curve for each intervention following sensitivity analysis over 10 years with rates for positive margin status set at OR 0.955 (200 procedures using the least expensive procurement plan for the robotic system).

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Feedback

The HTA programme and the authors would like to know your views about this report.

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We look forward to hearing from you.

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ISSN 1366-5278