Laparoscopic remotely assisted radical prostatectomy

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee with the assistance of Ms Antje Smala and Ms Mia Mudge from M-TAG Pty Ltd, a unit of IMS Health. Ms Ann Jones of M-TAG Pty Ltd, a unit of IMS Health, edited the report. The report was endorsed by the Minister for Health and Ageing on 24 August 2006.

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Medical Services Advisory Committee—role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision-making when funding is sought under Medicare. A team from the Medical Technology Assessment Group (M-TAG) Pty Ltd, a unit of IMS Health, was engaged to conduct a systematic review and economic evaluation of laparoscopic remotely assisted radical prostatectomy(LRARP). An Advisory Panel with appropriate expertise then evaluated this evidence and provided advice to MSAC.

MSAC's assessment of laparoscopic remotely assisted radical prostatectomy

This report addresses the safety, effectiveness and cost-effectiveness of LRARP for the treatment of clinically localised prostate cancer with curative intent relative to open radical prostatectomy (ORP).

Clinical need

The current management strategies used for clinically localised prostate cancer include no initial treatment, radiotherapy, or radical prostatectomy. In Australia, open radical prostatectomy (ORP) is the most commonly performed surgical procedure with curative intent. Compared with ORP, LRARP may offer a less invasive alternative for the treatment of clinically localised prostate cancer.

Incidence and mortality

Cancer of the prostate gland is the most common cancer in Australian men. In 2001, prostate cancer accounted for 23.4 per cent (n=11,191) of all new cancers diagnosed in males (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2004). This equates to an age-standardised rate of 128.5/100,000 and a lifetime risk of 1 in 11.

The age-standardised prostate cancer incidence rates per 100,000 have increased over recent years. This increased incidence has been largely attributed to the use of the prostate specific antigen (PSA) assay test which has increased detection and reporting of asymptomatic prostate malignancies (Smith et al 1998).

The risk of prostate cancer increases with age. Between the ages of 0–39, the age-specific rate was zero. At the age of 40, the incidence of prostate cancer was 21/100,000. The rate continued to increase with age and reached the peak rate in men 70–74 years old. Thereafter, the age-specific rate declined with increasing age (Australian Institute of Health and Welfare (AIHW) 2005a).

In Australia, for the period 1992 to 1997, the relative one-year survival after diagnosis of prostate cancer was 95 per cent (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2005). The five-year relative survival proportion for the same period was 82.7 per cent. There was a significant increase in five-year relative survival rates between the periods 1982 to 1986 and 1992 to 1997 for the age groups: 40–49, 50–59, 60–69, 70–79 and 80–89 years (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2005). The introduction of prostate specific antigen (PSA) assay for prostate cancer in the 1990s influenced this increase in survival through detecting a large number of early stage disease patients hence causing a stage migration phenomenon.

Safety

The results from the comparative studies showed that LRARP was associated with substantially lower estimated blood loss (EBL) and number of transfusions required compared with OPR. In studies with applicable patient populations (clinically localised prostate cancer) and certain surgeon experience, the overall complication rate

post-surgery was significantly lower in LRARP patients (5%) compared with ORP patients (16.3%). The rates of individual events were generally low (≤3.3% in LRARP and ≤4% in ORP). No deaths were reported in either treatment group. Significantly more patients who had undergone ORP (4%) experienced fever or pneumonia compared with those who had undergone LRARP (0%). No other significant differences in event rates were reported.

The non-comparative safety data were heterogeneous due to the variability in number of subjects included, type of study and population included. As expected, the ranges for EBL and transfusions were much broader than those reported in comparative studies. The proportion of patients experiencing postoperative complications in LRARP patients ranged from nil to 32.5 per cent. The studies reporting a nil rate included very few patients (≤5) whereas the study reporting the highest rate included 40 patients.

It can therefore be concluded that compared with ORP, LRARP is at least equally as safe, if not safer.

Effectiveness

The evidence available for the assessment of comparative efficacy of LRARP and ORP (with comparative surgeon experience) consisted of two cohort studies that included a patient population applicable to this review. One of these studies had some methodological issues and the other study included only a small sample. Another two studies with uncertainties (regarding applicability of patient population and comparative surgeon experience) were also included. No randomised controlled trials were available.

Primary efficacy outcomes

None of the studies reported any of the primary efficacy outcomes, that is, long-term survival rates/tumour-free survival, or death rates. Secondary efficacy outcomes assessed in this review included disease recurrence, positive margin rate and quality of life.

Disease recurrence

There were no significant differences between groups in biochemical recurrence rates, based on rising PSA levels post-surgery, in the only study reporting unbiased results. In this study, the three-month biochemical recurrence rate was the same in both treatment groups (~5%). However, the clinical importance of these immature results is questionable. Based on advice from the Advisory Panel, almost all cases of early detectable PSA post-surgery (within three months) are due to metastatic disease. To enable a fair comparison between procedures, biochemical recurrence rates one year after surgery, where local recurrence is a contributor to the rate, is warranted.

Positive margins

The data relating to positive margins in organ-confined cancers showed that there were no significant differences in the rates between patients who had undergone LRARP (4.5%) and those who had undergone ORP (9.0%; risk difference –5%; 95% CI: [15, 6]). The rates of total margin positivity, irrespective of pathological tumour stage, were similar between ORP and LRARP patients in both studies.

Quality of life

There were two studies identified that reported post-surgery urinary continence data (Ahlering et al 2004b; Tewari et al 2003b). The short term results from Ahlering et al (2004b) showed that a similar proportion of patients to those who had undergone ORP and LRARP were continent of urine three months after surgery (~76%). The study by Tewari et al (2003b) included only a subset of the population in the analyses, and few details of the selection of patients were provided. This study may therefore be prone to selection bias. Consequently, caution should be exercised in the interpretation of these results. The results from this study pertaining to urinary continence showed that while patients who had undergone LRARP achieved continence sooner than those who had undergone ORP, over time, this difference disappeared. Tewari et al (2003b) also reported erectile function and sexual function data. These results are also subject to the bias previously described. Patients who had undergone LRARP had a faster rate of return of erectile function and sexual intercourse after surgery compared with patients who had undergone ORP.

The mean postoperative pain score (using a visual analogue scale) as reported by Tewari et al (2003b) on the first postoperative day was significantly lower in patients who had undergone LRARP compared with those who had undergone ORP ($p<0.05$).

Effectiveness conclusion

The available data comparing LRARP with ORP in patients with clinically localised prostate cancer are not sufficiently mature to provide evidence of primary efficacy including long-term survival rates/tumour-free survival, or death rates. Studies of higher quality and with longer follow-up are warranted. Based on secondary efficacy outcomes, there appear to be no differences in biochemical recurrence rates and margin positivity. The results from this review indicated that LRARP might offer advantages in terms of less pain after surgery compared with ORP. Furthermore, the data pertaining to urinary continence, erectile dysfunction and sexual intercourse presented in one study indicated that LRARP patients regained urinary continence sooner and had a higher rate and faster resumption of erectile function and sexual intercourse. However, as previously mentioned, these results were based on a subset of the entire cohort, and lack of details regarding the selection of subjects renders these analyses prone to bias. It is difficult to determine the direction of bias. Consequently, although a difference between LRARP and ORP in terms of functional outcomes cannot be ruled out, it cannot be confidently confirmed either.

Cost comparison

LRARP is a new technology. Currently, there is scant information available about the long-term costs and treatment outcomes. Comparative health economics evaluations have not yet been published.

This assessment report provides an assessment of treatment costs associated with the use of LRARP and estimates of the aggregated financial implications for the Medicare Benefits Scheme (MBS) and to society.

Costs

The current evidence available for the assessment of comparative efficacy of LRARP and ORP is very limited. One of two available studies may have been prone to selection bias and the other study included only a small population. Because of these limitations, there is no current evidence, free from potential bias, demonstrating a difference in effect between the treatment approaches. Therefore, a cost comparison of LRARP and ORP was performed for this review. The direct treatment costs associated with each procedure are compared and presented. The comparison showed that LRARP is associated with markedly higher direct treatment costs than ORP ($15,469 versus $11,207 respectively). This difference is driven primarily by the high equipment costs associated with LRARP and with the need for a conjoint surgeon. The shorter hospital stay following LRARP (about 2 days versus 7.5 days following ORP) does not offset these additional costs.

Financial implications

The cost structure of LRARP procedures is different from ORP, with more costs for Medicare, but mainly for other healthcare funders, such as private hospitals. Therefore, the financial implications for funding LRARP have been presented separately for Medicare and for other healthcare services funders. It has been shown that the net impact for Medicare will be $685,800 per year. The net impacts for the other healthcare funders will be $3.15 million per year. These figures are based on provision of 300 LRARP procedures per annum by each of the three available da Vinci® systems presently commissioned in Australia. Each additional system implemented and increased patient throughput will increase these costs. To date, neither of the systems in current operation has attained predicted performance in terms of patient throughput. Costs would be lower if the da Vinci® system was used for other types of surgeries in addition to prostatectomies.

Cost-effectiveness

It is not possible to reliably estimate the cost-effectiveness of LRARP because of the lack of robust comparative effectiveness data. An indicative cost utility analysis was performed based principally on the questionable data from Tewari et al (2003b). Because of the uncertainties of the underlying data, this analysis is presented in **Appendix H** rather than in the main body of the report.

Recommendation

MSAC recommended that on the strength of evidence pertaining to laparoscopic remotely assisted radical prostatectomy public funding should be supported for this procedure.

- The Minister for Health and Ageing accepted this recommendation on 24 August 2006.-

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of laparoscopic remotely assisted radical prostatectomy (LRARP) which is a surgical procedure that attempts to cure clinically localised prostate cancer.

MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are provided in **Appendix A**. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for LRARP for clinically localised prostate cancer.

Background

Laparoscopic remotely assisted radical prostatectomy

The procedure

Laparoscopic remotely assisted radical prostatectomy (LRARP) is a surgical procedure that attempts to cure clinically localised prostate cancer. The LRARP procedure involves the use of the da Vinci® surgical system, which is a remotely assisted controller-subordinate system. The system incorporates robotic technology, three-dimensional visualisation, a wide range of movement, and 360-degree manoeuvrability of the tips of the instrument (in some planes of movement) through laparoscopic ports. Similar to the conventional laparoscopic procedure, LRARP involves multiple, small incisions in the abdominal wall, through which ports are inserted to enable the introduction of the instruments into the abdominal cavity.

The da Vinci® surgical system comprises a surgeon console, patient-side cart, instruments and image processing equipment. The system incorporates three or four multi-joint arms controlling the binocular endoscope and the endo-wrist instruments. The four-arm configuration is used in 50 per cent of procedures. During different stages of the surgery two lenses—0 degrees and 30 degrees—are used. The 30 degrees lens can be used to look up or down to improve visualisation of the field. The arms and camera are controlled by two finger controls within the mobile console. The operating surgeon is seated at the console. The views from both monitors are merged by a stereoscope, which provides three-dimensional visualisation. Manipulation of the finger-controls is transmitted to a computer that filters, scales and relays the surgeon's movements to the arms and instruments. Joysticks at the tip of the instruments can scale the hand movements to 1:1, 3:1 or 5:1. This scaling allows for finer and more precise execution of certain steps of the operation. Tremors and small, unintended movements that can occur as a result of holding instruments for a prolonged period, are eliminated. There is no measurable delay between the surgeon operating the finger-controls on the console and the movement of the instruments within the patient. The instruments allow 7 degrees of liberty in their movement (Tewari et al 2002). By contrast, conventional laparoscopic instruments allow 4 degrees of freedom (Basillote et al 2004).

The LRARP procedure involves the same level of patient preparation and surgical steps as conventional laparoscopic radical prostatectomy. The chief difference between LRARP and conventional laparoscopic radical prostatectomy is the instrumentation used. A remotely assisted controller-subordinate system is used to perform LRARP, whereas a standard laparoscope is used to perform conventional laparoscopic radical prostatectomy.

As per the conventional laparoscopic procedure, the patient is placed in a head down supine position. The legs are placed in the lithotomy position with enough space between the thighs for the da Vinci® system to be wheeled in. Patients less than 1.8 m tall may be positioned in a frog-leg configuration.

After the abdomen is cleaned, shaved, painted and draped, a pneumoperitoneum is created. The insufflator is set to a maximum pressure of pneumoperitoneum between

12–15 mmHg. Approximately 3–4.5 L of gas volume is introduced before the ports are positioned. The number of ports may vary—five or six is typical. One port is dedicated to the camera lens and is placed at the umbilicus.

There are two ports used for the instrument arms (placed approximately 10 cm from the midline on the line joining the anterosuperior iliac spine to the umbilicus) and two additional ports are placed in the right side for retraction and suction purposes. A sixth port (assistant port) may be placed laterally in the flank slightly inferior to the left port.

Conventional laparoscopic instruments are used by the conjoint surgeon (ie, patient-side surgeon) and include atraumatic graspers, scissors, suction, bipolar cautery and intracorporeal clips. The dissection is done using two instruments: a monopolar hook on the right side and forceps on the left (for right-handed surgeons). During anastomosis two needle drivers are used (Tewari et al 2002).

Lymph node dissection may be performed at the time of the prostate resection if required. The surgical steps of the conventional laparoscopic approach to resection of the prostate may include:

- posterior dissection (dissection of the seminal vesicles and opening Denonvilliers' fascia)
- anterior approach (bladder dissection, entering the endopelvic fascia, ligation of the dorsal venous complex of Santorini)
- bladder neck dissection
- dissection of the lateral surface of the prostate (incision of the prostatic pedicles, preservation of neurovascular bundles)
- apical section (section of the venous complex, incision of the urethra and the rectourethral muscle)
- urethrovesical anastomosis
- leaving the abdomen and closing and dressing the incisions (Guillonneau et al 2000).

This technique is often referred to as the Montsouris technique, and can be modified by the LRARP surgeon. One modification of the Montsouris technique in performing LRARP was described by Tewari et al (2002).

Surgical assistance

For the purpose of this review, it was assumed that one surgeon and one conjoint surgeon are required for the procedure.

The level of surgical assistance required to perform an LRARP varies throughout the literature. In Tewari et al (2002) the console surgeon was assisted by a conjoint surgeon and a patient-side assistant. However, Lee et al (2004) has described their experiences of LRARP with only one assistant (with moderately advanced laparoscopic training plus a

thorough comprehension of the operation). In an Australian study by Costello et al (2005) the surgeon operating the remotely assisted system was supported by a conjoint surgeon. It is therefore likely that the type of surgeon assistance (another surgeon or an assistant) and number of assistants required varies between countries and hospitals, and is dependent on resource availability and experience of the console surgeon.

Nerve-sparing technique

When radical prostatectomy was first introduced, a major reported complication of the surgery was sexual impotence. A better understanding of the autonomic innervation of the corpus cavernosa, pelvic fascia and the anatomy of the striated sphincter continence mechanism has enabled improved techniques of surgery to be developed. In particular, nerve-sparing techniques have been described (Walsh 1998) and have generally been adopted by urological surgeons. This presents surgeons with the opportunity to preserve the neurovascular bundles when possible, or to excise them when required in order to achieve wider margins of the resection. The nerve-sparing techniques have lead to improvements in post-surgery erectile function.

More recently, nerve-sparing techniques have been adapted and many minor variations have been described. For example, Menon et al (2005) describe a new technique whereby the nerve fibres that are spread sparsely over the lateral aspect of the prostate are preserved. Nerve-sparing techniques can be performed unilaterally or bilaterally and can be achieved both with LRARP and open radical prostatectomy (ORP). Whilst technically possible, the nerve-sparing technique is much more difficult to perform with the perineal than the retropubic approach.

Types of surgical systems

There is currently one surgical system—the da Vinci® surgical system—available to perform LRARP. Initially, two surgical systems were available—da Vinci® and Zeus®. The Zeus surgical system was purchased by the da Vinci® system manufacturer and currently operates under the latter name. A voice activated endoscopic robot system for holding cameras in minimal invasive surgery (AESOP®) is also available. However, this system is not remotely assisted and differs substantially from the da Vinci® system. The AESOP system is therefore not considered in this review.

Intended purpose

For the purposes of this review, the evaluation will focus on the intended use of LRARP in the resection of clinically localised prostate carcinomas. LRARP is intended to replace open radical prostatectomy (ORP) for this purpose (MSAC Advisory Panel, July 2005). The flow chart in **Appendix E** outlines the potential clinical pathway for the treatment of clinically localised prostate carcinoma for patients suitable for radical prostatectomy.

Clinical need/burden of disease

Organ-confined prostate cancer is potentially curable with today's treatments. The current treatments used to manage clinically localised prostate cancer include no initial treatment, radiotherapy, or radical prostatectomy (open or conventional laparoscopic). Of these treatments, open radical prostatectomy (ORP) is the most commonly performed surgery in Australia. The ORP procedure requires an incision in the lower abdomen or perineum of the patient whereas the LRARP procedure is performed through multiple, small incisions in the abdominal wall. LRARP may therefore offer a less invasive procedure for patients with clinically localised prostate cancer.

Incidence and mortality

Cancer of the prostate gland, a part of the male reproductive system, is the most common cancer in Australian men. In 2001, prostate cancer accounted for 23.4 per cent (n=11,191) of all new cancers diagnosed in males (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries [AACR] 2004). This equates to an age-standardised rate of 128.5/100,000 and a lifetime risk of 1 in 11.

The age-standardised prostate cancer incidence rates per 100,000 have increased over recent years. The age-standardised prostate cancer incidence rates in 1985, 1990, 1995 and 2001 were 82.8, 102.4, 167.8 and 128.5 per 100,000 men, respectively. This increased incidence has been largely attributed to the use of the prostate specific antigen (PSA) assay test which has increased detection and reporting of asymptomatic prostate malignancies (Smith et al 1998).

The risk of prostate cancer increases with age. The age-specific incidence rate of prostate cancer per 100,000 in 2001 is presented in **Figure 1**. Between the ages of 0–39, the age-specific rate was zero. At the age of 40, the incidence of prostate cancer was 21/100,000. The rate continued to increase with age and reached the peak rate in men 70–74 years old. Thereafter, the age-specific rate declined with increasing age (Australian Institute of Health and Welfare (AIHW) 2005a).

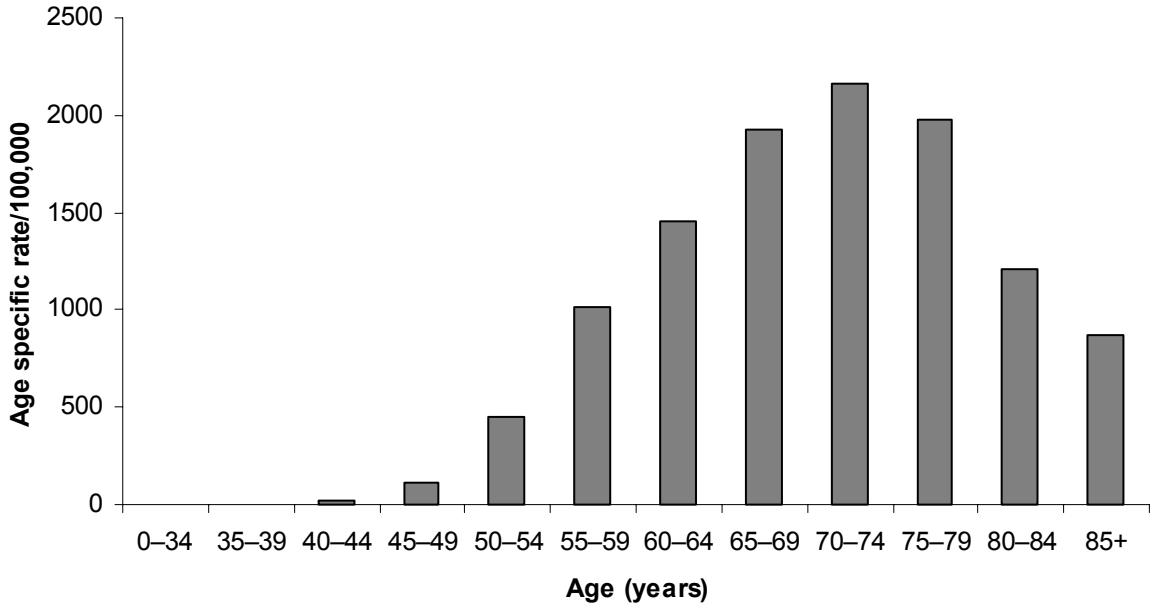

Figure 1 Age-specific rate of prostate cancer per 100,000 in 2001

Source: (Australian Institute of Health and Welfare (AIHW) 2005a).

Years of potential life lost measures the extent of premature mortality, which is assumed to be any death before the age of 79 years. In 2002, the years of potential life lost from any cancer deaths in men was 189,562. The number of years of potential life lost does not reflect only the incidence and survival rates, but also the age at which deaths from this cancer frequently occur. Though the rate of death due to prostate cancer was the second highest of all of the priority cancers in men, comparatively speaking, low numbers of years of potential life lost resulted from this type of cancer (10,850 years). This is likely due to the fact that prostate cancer is more prevalent in older men (Australian Bureau of Statistics (ABS) 2004).

Use of healthcare services

In 2003–2004, there were 12,642 non-same-day and 7905 same-day hospital separations (episodes of care) for malignant prostate neoplasms, equating to a total of 97,326 patient-days (Australian Institute of Health and Welfare (AIHW) 2005b).

In 1996, the Australian government nominated cancer as a National Health Priority Area (NHPA). Priority cancers to be targeted include lung, melanoma (of skin), non-melanocytic skin, cervical, breast, colorectal, prostate and non-Hodgkin's lymphoma. The initiative directs public attention and policy on health areas known to contribute most to the burden of disease in Australia (Australian Bureau of Statistics (ABS) 2004).

Prostate cancer

The prostate gland is part of the male reproductive system that is located in front of the rectum and under the bladder, surrounding the urethra as it exits from the bladder. A normal prostate is about the size of a walnut, doughnut shaped, with the urethra passing through it. The function of the prostate is to produce a secretion that is the fluid part of semen.

Several risk factors for prostate cancer have been identified. These include increasing age, family history in a first-degree male relative, a diet high in fat, elevated androgen levels, race, and cadmium or dioxin exposure (National Cancer Institute 2005).

In the early stages, most prostate cancers are asymptomatic. Symptoms depend on the site of involvement. Late stage local involvement can cause lower urinary tract symptoms, blood in the urine or semen, and incontinence. Metastatic prostate cancer can cause bone pain, weight loss, lethargy, paraplegia, and occasionally, renal failure.

Prostate cancer is a histological diagnosis. The main diagnostic tools used to identify people at increased risk of prostate cancer are serum prostate specific antigen (PSA), digital rectal examination (DRE) and transrectal ultrasonography (TRUS) (Gerber et al 1991). The identified people then usually have multiple core biopsies of the prostate. Multiple systematic ultrasound-guided biopsies detect more cancers than digital- or ultrasound-guided biopsies of suspicious areas (Ellis et al 1994; Hodge et al 1989). Other methods of obtaining tissue for diagnosis are transurethral resection of prostate or fine needle aspiration cytology. Histopathological examination also allows grading of the tumour. There is no clear-cut single clinical diagnostic pathway for prostate cancer because of its varied clinical presentations.

In general, prostate cancer has a long natural history when compared with other common malignancies. Because of this, the assessment of overall health status, life expectancy and tumour characteristics, such as location and stage of disease, has increased significance in decision-making. In addition, there are many competing modalities of treatment, both curative and palliative, with differing and significant morbidities that often have a similar survival outcome. This often means that patient preference has a more significant place in the decision-making process than with other common malignancies.

Organ-confined prostate cancer is curable with today's treatments; locally extensive disease can usually be controlled, but is rarely cured. Metastatic disease is currently not curable.

In Australia, for the period 1992 to 1997, the relative one-year survival after diagnosis of prostate cancer was 95.0 per cent (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2005). The five-year relative survival proportion for the same period was 82.7 per cent. There were significant increases in five-year relative survival between the periods 1982 to 1986 and 1992 to 1997 for the age groups: 40–49, 50–59, 60–69, 70–79 and 80–89 years (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2005). The introduction of PSA assay for prostate cancer in the 1990s influenced this increase in survival through detecting a large number of early stage disease patients, hence causing a stage migration phenomenon.

Existing treatments

Treatments that are currently used to manage clinically localised prostate cancer include no initial treatment (delay of treatment until signs of cancer progression), radiotherapy, or radical prostatectomy (open or conventional laparoscopic). Each of these procedures is described in more detail below.

No initial treatment

No initial treatment, also referred to as 'watchful waiting' in the literature, implies that treatment is reserved for symptoms or complications of prostate cancer, while not necessarily attempting to bring about a cure. There are two groups of patients who may qualify for no initial treatment. One group consists of patients who have miniscule prostate cancer and have a long life expectancy. These patients are monitored regularly through repeat biopsies and PSA level measurements. These patients may require radical therapy with curative intent if the cancer progresses. Another group of patients qualifying for no initial treatment includes older patients, whose therapy may be deferred because there is a low probability that the cancer will affect patients' life expectancies. These patients may undergo palliative treatment.

According to the Advisory Panel, the average time from diagnosis to the need for palliative treatment is approximately five to six years, depending on the characteristics of the tumour.

No initial treatment reduces the risk of potential morbidities due to local treatments. However, leaving the disease untreated reduces the opportunity to cure and prevent metastasis (Commonwealth of Australia 2002). A Swedish population-based, cohort study by Johansson et al (2004) found that whilst most cancers had an indolent course during the first 10–15 years, further follow-up from 15–20 years revealed a substantial reduction in: cumulative progression-free survival (from 45.0 to 36.0%); survival without metastasis (from 76.9 to 51.2%) and prostate cancer-specific survival (from 78.7 to 54.4%). These results support early intervention, particularly in patients with estimated life expectancy of more than 15 years.

A recent randomised controlled trial compared no initial treatment and radical prostatectomy in the management of clinically localised prostate cancer in men with a life expectancy of more than 10 years (Bill-Axelson et al 2005). The 10 year results from this study showed that radical prostatectomy is associated with statistically significant reductions in: mortality due to prostate cancer (relative reduction of 44%); overall mortality (relative reduction of 26%); risk of distant metastasis (40% relative reduction); and risk of local progression (relative reduction 67%). In absolute terms, the reductions in prostate cancer specific mortality and overall mortality after 10 years were moderate (5.3 and 5.0 percentage points, respectively) in favour of radical prostatectomy, but the absolute reductions in the risks of metastasis and local tumour progression were substantial.

Patients most likely to benefit from no initial treatment are those with moderately-to-well defined tumours, low volume disease, low PSA, with life expectancies of less than 10 years and who prefer no treatment after having been informed about the risks and benefits.

Radiotherapy

Radiation therapy utilises x-rays to preferentially damage cancer cells in an effort to eradicate tumours without significantly affecting normal tissue. Radiation therapy with curative intent may be used in patients whose cancer is clinically confined to the prostate and/or surrounding tissues. There are two main types of radiation therapy: external beam radiation therapy (EBRT) and internal radiation (ie, brachytherapy).

External beam radiotherapy (EBRT)

The patients most likely to benefit from EBRT included those with a relatively long life expectancy (greater than 10 years), who have low PSA, low volume and tumours that are moderately differentiated (Commonwealth of Australia 2002).

EBRT typically involves delivery of radiation therapy in brief sessions at the rate of one session each weekday for six to seven weeks. The procedure itself lasts for a few minutes and is painless. The relatively non-invasive nature of radiotherapy has ensured its continued use as one of the primary treatment modalities for localised prostate cancer. Patients who receive EBRT are more likely to be older and have a higher frequency of high-grade tumours and higher initial PSA assays. Recent advancements in EBRT have led to the development of three new methods of treatment—conformal radiotherapy, conformal proton beam radiation therapy, and intensity modulated radiation therapy (IMRT).

Conformal radiotherapy refers to 'shaping' the high dose treatment volume to 'conform' to the prostate gland, whilst excluding adjacent normal dose-limiting structures such as the rectum. This approach uses three-dimensional computed tomography (CT) planning and is becoming a standard method for delivering EBRT. Because it is important that movement is limited during therapy, patients are placed in a body cast moulded from Styrofoam.

Conformal proton beam radiation therapy is similar to conformal radiotherapy except that it uses protons to produce the radiation beam. The proton beams pass through healthy tissue without causing damage to eradicate cancer cells.

IMRT is an advanced form of conformal radiotherapy. It utilises a machine that moves around the patient as it delivers the specified radiation dose. In addition to aiming beams from several directions, the intensity of the beams can be adjusted to minimise the dose of radiation reaching the most sensitive normal tissues while delivering a uniformly high dose to the cancer.

Interstitial brachytherapy

Brachytherapy exists in two forms, low dose rate (LDR) and high dose rate (HDR). Patients most likely to benefit from interstitial radiotherapy are similar to those benefiting from EBRT. That is, patients should have low volume, low grade disease and life expectancies of greater than 10 years (Commonwealth of Australia 2002).

LDR brachytherapy

LDR involves implantation or insertion of small 'sealed sources' containing a radioactive isotope into the prostate gland. This treatment enables high doses of radiation to be delivered precisely to the prostate gland. The type of radiation emitted by the seeds only penetrates 1–2 mm. This has the theoretical advantage of limiting damage to adjacent

tissues. Radioactive seeds are generally implanted via the perineal percutaneous route. This is performed under ultrasound control.

Low dose brachytherapy is indicated for localised prostate malignancy at clinical stages T1–T2, with a Gleason score of less than or equal to six and a PSA of less than or equal to 10 ng/mL at the time of diagnosis (Australian Government Department of Health and Ageing (DoHA) 2005b).

There are several different seed types available worldwide. In Australia, the I^{125} seed is the only one approved for funding under Medicare.

HDR brachytherapy

This form of treatment involves a combination of brachytherapy and EBRT boost. A grid of approximately nine hollow needles attached to a Perspex plate is inserted transperineally into the prostate. Ir–192 wires are then inserted through the hollow needles and left *in situ* for varying times as dictated by computer modelling. The needle grid remains in place for about 48 hours before being removed. Following this, a boost dose of EBRT is given.

Radiotherapy was not selected as a comparator to LRARP in this review. This is because people who choose brachytherapy have usually rejected surgery as a treatment, be that open or conventional laparoscopic radical therapy; hence LRARP is therefore unlikely to displace this therapy.

Radical prostatectomy

Surgery is the usual treatment for patients who are in good health, less than 70 years of age (with greater than 10 years life expectancy) and whose tumours are confined to the prostate gland. Patients most likely to benefit are those with low volume, low PSA and who have no significant surgical risk factors (Commonwealth of Australia 2002).

The objective of this surgical procedure is the removal of all prostate tissue with a clear margin of resection. Surgical removal of the prostate gland is potentially curative only if the entire tumour is removed. The prostate may be surgically removed using a number of techniques, open radical prostatectomy, conventional laparoscopic radical prostatectomy (both described below) and LRARP.

Each type of surgery may be performed as a nerve-sparing or non-nerve-sparing procedure. Nerve-sparing procedures are used to avoid damaging nerves that run beside the prostate. These nerves are involved in sphincter and erectile function. Non-nerve-sparing procedures remove the entire prostate and the tissue surrounding it, including the nerves.

Open radical prostatectomy (ORP)

ORP can be performed through one of two approaches: the perineal or retropubic approach. In the retropubic approach, the prostate gland is removed through an incision in the lower abdomen. The pelvic lymph nodes may be removed and examined at the time of surgery (pelvic lymph node dissection). Retropubic prostatectomy is the most widely performed surgical treatment with curative intent for prostate cancer and allows the surgeon to perform a nerve-sparing procedure. Recovery time after this surgery may be longer than following perineal surgery.

In the perineal approach, the prostate gland is removed through an incision in the perineum (the space between the rectum and base of the penis). Although this approach is considered less invasive, a limitation is that it is much more difficult for the surgeon to perform as a nerve-sparing procedure. The perineal approach also requires a separate incision for pelvic lymph node dissection.

Due to procedural differences between the retropubic and perineal approaches, their safety, efficacy and morbidity profiles differ (Frazier et al 2005; Haab et al 1994). The retropubic approach is associated with greater numbers of blood transfusions and longer operative times (Frazier et al 2005; Haab et al 1994). In the short term (three months after surgery) patients having undergone the perineal approach report higher levels of impotence and incontinence compared with patients having undergone retropubic approach. However, by six months post-surgery these differences appear to be less apparent (Haab et al 1994).

Conventional laparoscopic radical prostatectomy

Although the conventional laparoscopic radical prostatectomy technique was first described in 1992, it was not until 1999 that the procedure entered its initial phase of acceptance thanks to Guillonneau and Vallancien (2000).

This procedure involves multiple, small incisions in the abdominal wall, similar to the LRARP procedure. Trocars are inserted through the incisions to enable the introduction of the laparoscope and various instruments into the abdominal cavity. The laparoscope provides good lighting down into the far reaches of the pelvis. The scope used in conventional laparoscopic radical prostatectomy provides magnified images to a monitor that can be simultaneously viewed by the surgeon and assistants.

Some advantages with the conventional laparoscopic radical prostatectomy procedure include low levels of surgical pain and decreased blood loss. However, there are some inherent limitations of this approach. Due to the design of the instrument, the surgeon is limited to four degrees of freedom of movement. The surgeon requires experience to determine spatial distance due to the two-dimensional view provided by the camera system. Like the LRARP procedure, there is minimal tactile feedback from the instrumentation (Basillote et al 2004).

Transurethral resection of the prostate (TURP)

TURP is an endoscopic procedure that only enables partial removal of the prostate. It only ever provides palliation of prostate cancer, and hence, has not been considered in this review.

Comparator

The Advisory Panel experts advised that in the current situation, the majority of patients with clinically localised prostate cancer undergoing curative therapy would have ORP. As such, should LRARP be listed on the Medicare Benefits Schedule (MBS), this procedure will in most instances replace ORP. The safety, effectiveness and cost-effectiveness of LRARP will therefore be compared with ORP for the purpose of this review. The flowchart detailed in **Appendix E** outlines the clinical pathway and comparator for LRARP.

LRARP is a procedure that aims to cure localised prostate cancer. Hence, it is potentially an alternative therapy for all treatments described in the preceding sections. Notwithstanding, the Advisory Panel recommended that open radical prostatectomy was the appropriate comparator for this review. Radiotherapy was not considered a comparator because the patients who choose radiotherapy usually want to avoid surgery in general; hence, LRARP is unlikely to replace radiotherapy. Conventional laparoscopic radical prostatectomy was rejected as a comparator because relatively few of these procedures are performed in Australia. LRARP is most likely to replace ORP because it is the dominant therapy applied as a surgical protocol aimed at attaining cure of clinically localised prostate cancer. Because of the nature of the LRARAP and its comparator, ORP, the proposed new intervention is considered a substitute treatment and will not be considered or offered as additional treatment.

It is noteworthy that the evidence from this review would not allow conclusions to be made regarding the relative efficacy and safety of laparoscopic radical prostatectomy and LRARP.

Marketing status of the device/technology

The Therapeutic Goods Administration (TGA) lists LRARP on the Australian Register of Therapeutic Goods (ARTG). The TGA governs the use of medicines and medical technologies to ensure they are of an acceptable standard for the protection of consumers.

Current reimbursement arrangement

LRARP is currently reimbursed on the MBS under the radical prostatectomy item numbers. Item numbers for radical prostatectomy and service fees per item number are provided in **Table 1**.

Table 1 **MBS item numbers and service fees of radical prostatectomy**

MBS item number	Service fee
37209	$1117.45
37210	$1379.05
37211	$1674.90

Approach to assessment

The research question

What additional benefits, in terms of effectiveness (including the impact on clinical outcomes) safety, and cost-effectiveness does laparoscopic remotely assisted radical prostatectomy (LRARP) provide in the resection of clinically localised prostate cancers relative to open radical prostatectomy (ORP)?

Review of literature

The medical literature was searched to identify relevant studies and reviews for the period between 1966 and July 2005. Searches were conducted via primary databases as indicated in **Table 2**.

Table 2 **Electronic databases searched for LRARP review**

Database	Period covered/date searched
Medline	1966 to July, week 2, 2005
EMBASE	1988 to 2005, week 29
PreMedline	21 July 2005
Cochrane Library	Issue 3, 2005 (21 July 2005)

Search strategy

The search strategy was developed using the key elements of the clinical question. The search strategy presented in **Table 3** was used to identify articles in Medline®. A similar search strategy using the same search terms was also employed for the EMBASE™ and PreMedline® databases.

Table 3 **Search strategy**

Number	Search terms
1	exp prostatectomy/
2	robotics/
3	1 and 2
4	(robot$ adj5 prostatectom$).ti,ab.
5	(vattikuti adj3 prostatectomy).ti,ab.
6	(da vinci adj3 (robot or surgical)).ti,ab.
7	zeus.ti,ab.
8	6 or 7
9	8 and 1
10	or/3-5,9

Reference lists of publications were also searched for additional relevant citations that may have been inadvertently missed in searches of major databases. In addition to the primary databases, the websites of international health technology assessment (HTA) agencies listed in **Table 4** were also searched.

Table 4 **Health technology assessment agencies and other sites relevant for prostate cancer specifics searched**

HTA database	Web address
Agency for Healthcare Research and Quality (USA)	http://www.ahrq.gov/query/query.htm
American Society of Clinical Oncology	http://www.asco.org/ac/1,1003,_12-002008,00.asp
American Urological Association Annual meeting, San Antonio, USA, 21–26 May 2005	www.auanet.org
Blue Cross Blue Shield Association (USA)	http://www.bcbs.com/tec/index.html
British Columbia Cancer Agency (Canada)	http://www.bccancer.bc.ca/HPI/default.htm
Canadian Coordinating Office for Health Technology Assessment	http://www.ccohta.ca/entry_e.html
Centre for Health Economics (Monash University, Australia)	http://www.buseco.monash.edu.au/centres/che/publications.php
Centre for Health Services and Policy Research (Canada)	http://www.chspr.ubc.ca/cgi-bin/pub
Current Controlled Trials metaRegister and International Standard Randomised Controlled Trial Number (ISRCTN) register (USA)	http://www.controlled-trials.com/mrct/
Danish Centre for Evaluation and Health Technology Assessment	http://www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering/Publikationer/cemtv_-_Publikationsdatabasen.aspx?lang=en
Department of Health (UK)	http://www.dh.gov.uk/PublicationsAndStatistics/Publications/fs/en
Health Economics Research Group (Brunel University, UK)	http://www.brunel.ac.uk/about/acad/herg/publications/
Health Information Research Unit (HIRU) internal database (McMaster University, Canada)	http://hiru.mcmaster.ca/
Health Technology Assessment International	http://www.htai.org/conferences/
International Network of Agencies for Health Technology Assessment	http://www.hta.nhsweb.nhs.uk/
International Society of Technology Assessment in Healthcare (Montreal, Canada)	http://www.istahc.org/
National Cancer Control Initiative (Australia)	http://www.ncci.org.au/supp/publications.htm
National Cancer Institute (USA)	http://www.cancer.gov/
National Guidelines Clearinghouse (USA)	http://www.guideline.gov/
National Health and Medical Research Council (Australia)	http://www.health.gov.au/nhmrc/publications/index.htm
National Health Service (UK)	http://www.nhs.uk/
National Information Center on Health Services Research and Healthcare Technology (USA)	http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
NHS Centre for Reviews and Dissemination	http://www.york.ac.uk/inst/crd/crddatabases.htm
Scottish Intercollegiate Guidelines Network (SIGN)	http://www.sign.ac.uk/guidelines/published/index.html
Swedish Council on Technology Assessment in Healthcare	http://www.sbu.se/www/index.asp

Published literature

The primary search strategy retrieved a total of 423 non-duplicate citations. A secondary database search identified 10 additional citations relevant for this review. Thus, 433 non-duplicate citations were identified. The number of non-duplicate citations retrieved from each database is presented in **Table 5**.

Table 5 **Number of non-duplicate citations retrieved from each database**

	Medline	PreMedline	EMBASE	Cochrane Library	Secondary database	Total
Number of citations	80	13	239	91	10[a]	433

[a] Number of citations identified and included from secondary database searching.

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (2000).

These dimensions (**Table 6**) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of its determination.

Table 6 **Evidence dimensions**

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design[a]
Quality	The methods used by investigators to minimise bias within a study design
Statistical precision	The *p*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used

[a] See Table 7.

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in **Table 7**.

Table 7 Designations of levels of evidence

Level of evidence	Study design
I[a]	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (ie, alternate allocation or some other method)
III-2	A comparative study with concurrent controls:
	non-randomised, experimental trial[b]
	cohort study
	case-control study
	interrupted time series with a control group
III-3	A comparative study without concurrent controls:
	historical control study
	two or more single-arm studies[c]
	interrupted time series without parallel control group
IV	Case-series with either post-test or pre-test/post-test outcomes

Modified from: National Health and Medical Research Council (NHMRC) (2005).
[a] A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence, when it will be assigned a level I rating.
[b] This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie, utilise A versus B and B versus C to determine A versus C).
[c] Comparing single-arm studies (ie, case series from two studies).

Eligibility criteria for studies

The 433 non-duplicate citations were evaluated to determine whether they met the eligibility criteria outlined in **Table 8**. In order for studies to be included in the evaluation of efficacy, studies had to be comparative, whereas this was not a requirement in order to be included in the safety evaluation.

Considering that LRARP is only performed for patients with clinically localised prostate cancer, studies that did not report patients' diagnoses, but reported results of subjects undergoing LRARP, were assumed to include only patients with prostate cancer. If staging of patients' disease was not reported, the applicability of the results from that study to the population of interest is noted throughout the review. In the comparative efficacy and safety sections, only studies with applicable patient populations were pooled.

Table 8 **Study exclusion criteria for efficacy evaluation**

1. Not a systematic review or clinical study
Citations excluded were those describing non-systematic reviews, editorials, letters, news articles, clinical guidelines, economic articles, regulatory documents, surveys and opinion pieces
2. Non-human/pre-clinical studies
Animal studies and preclinical (including laboratory) studies were excluded
3. Wrong intervention
Studies not using LRARP as an intervention were excluded
4. Wrong patient population
Studies must include patients with localised prostate cancer
5. Wrong comparator or no comparator
In order for studies to be eligible for efficacy analysis, the comparator must be open radical prostatectomy
6. Wrong outcomes
Studies had to report at least one of the following outcomes to be eligible for the efficacy evaluation
– long-term survival rates or tumour-free survival
– death rates
– re-treatment rate
– disease recurrence (including biochemical recurrence based on post-surgery PSA levels)
– positive margins
– quality of life (including pain, psychosocial aspects, sexual function/erection and continence)

Search results

The following flow chart (**Figure 2**) summarises the exclusion of studies from the safety and effectiveness review of LRARP. A total of 433 references were identified through the search of the published and unpublished literature, of which seven were included in the effectiveness review. A total of 40 met the criteria to be considered as evidence in the safety review (six comparative studies and 34 non-comparative studies).

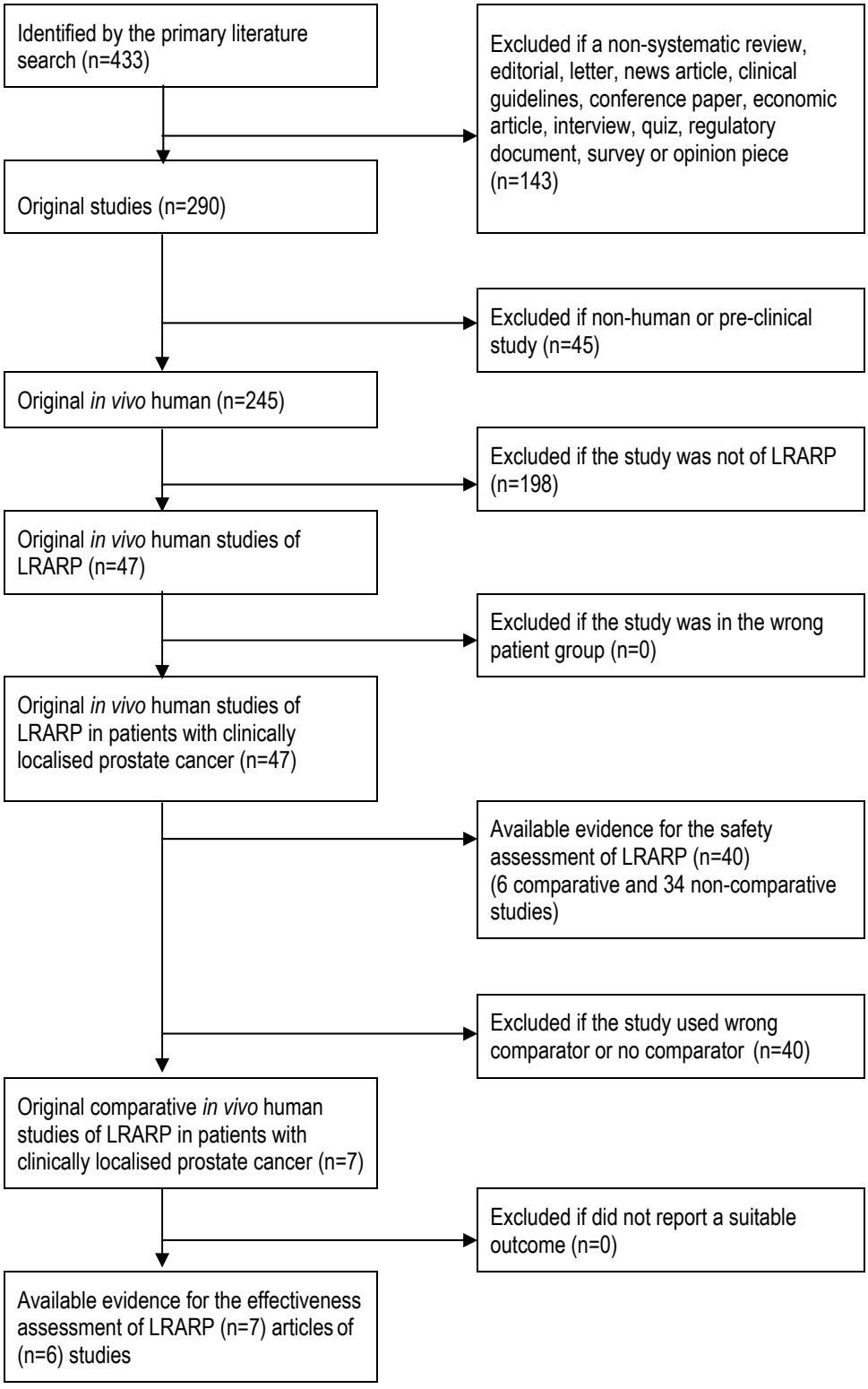

Figure 2 Reasons for exclusion of published reports of LRARP identified by the literature search

Expert advice

An Advisory Panel with expertise in the management of clinically localised prostate cancer was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. MSAC's practice, when selecting members for Advisory Panels, is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the Advisory Panel is provided at **Appendix B.**

Statistical analysis

For baseline data, percentages were presented for dichotomous data and means and standard deviation (or median if only reported) for continuous data. Similarly, for safety and efficacy outcomes, percentages were reported. When only one trial reported the outcome and no *p*-value was reported, the chi-square was used to test for significance if the expected values were greater than five. If the expected values were less than or equal to five, a Fisher's exact test was used. In situations where only percentages were reported, the number of cases and number at risk were calculated. When more than one trial reported the same outcome, data were pooled (including only applicable and 'surgeon experience certain' studies). Dichotomous outcomes are presented using the risk difference (RD) and 95 per cent confidence interval (CI). ReviewManager version 4.2 was used. The method used to calculate RD was the fixed-effects method (FEM) for non-heterogeneous comparisons and the random-effects method (REM) for heterogeneous comparisons. A chi-squared test for heterogeneity was performed on each analysis and was considered significant at $p<0.05$.

Evidence

Evidence for safety has been divided into primary and secondary evidence. The primary evidence contains only comparative trials of LRARP versus ORP (see **Table 7**).
The secondary evidence contains single-arm studies of LRARP, derived either from non-comparative studies or from other comparative studies in which the comparator is not ORP. For a complete listing of both primary and secondary studies included in the safety analyses, see **Appendix C.**

Results from studies containing overlapping patient populations (ie, recruited from the same cohort) are not presented in the safety section. In these cases, the largest inclusive cohort or the study presenting the most complete outcomes were used. In instances where the series with the largest number of patients was presented as an abstract only, the publication presenting the largest number only was included. For completeness, safety results from all studies are presented in **Appendix C**.

Similar to the safety section, results from duplicate studies, or studies containing overlapping patient populations, (ie, recruited from the same cohort) are not presented in the efficacy section. In these cases, the largest inclusive cohort or the study presenting the most complete outcomes were used. No duplicate publications providing further information at different points in time were identified.

No systematic reviews comparing LRARP with ORP were identified and included in this assessment.

Table 9 Relevant published and unpublished studies of LRARP identified for the efficacy and primary safety analyses

Study	Publication status	Study design	Included in safety and/or efficacy
Ahlering (2004b)	Published	Cohort, with historical control	Safety and efficacy
Balaji (2005)	Abstract	Cohort study	Safety
Binder (2002)	Published	Comparative case-series	Safety and efficacy[a]
Farnham (2005)	Abstract	Prospective cohort	Safety
Kella (2005)	Abstract	Comparative case-series	Efficacy[a]
VUI study			
Tewari (2003b)	Published	Prospective, consecutive cohort study	Safety and efficacy
Menon (2002b)	Published	Prospective cohort study	Safety
Springhart (2005)	Abstract	Prospective cohort	Efficacy
DiMarco (2005)	Abstract	Retrospective review of matched LRARP and ORP patients during the same time period	Efficacy

Abbreviation: VUI, Vattikuti Urology Institute.

[a] These studies compared a novice LRARP surgeon's results with an experienced ORP surgeon's results, hence level of experience would have biased the results. These studies are only included in the **Learning curve of LRARP** section and not in the efficacy section.

Comparative studies

The literature search identified seven studies comparing LRARP and ORP. Study design, patient characteristics and an assessment of NHMRC level of evidence, study quality and applicability of these seven studies are presented in **Table 36** of **Appendix D**. Of the seven studies, one compared the positive margin rates of a novice LRARP surgeon with the same surgeon's ORP procedures within a defined period (Kella et al 2005). No other efficacy or safety outcomes were reported. This study did not report comparative efficacy of experienced LRARP and ORP surgeons. This study has been included in the **Learning curve of LRARP** section and is not presented in the efficacy section.

Similarly, the study by Binder et al (2002) reported the initial experience of LRARP and compared this with previous ORP cases performed by experienced ORP surgeons. The level of experience is likely to have biased the results. Again, the results from this study are included in the **Learning curve of LRARP** section and are excluded from the efficacy section.

The study by Tewari et al (2003b) is an extension of the initial study conducted at the Vattikuti Urology Institute (VUI) comparing ORP with LRARP (Menon et al 2002b) and includes more patients followed-up for a longer period of time. Hence, the results from Tewari et al (2003b) were included in the analysis, and data from Menon et al (2002b) were included only if they provided further information on different outcomes or details from different points in time.

Consequently, of the seven studies comparing LRARP with ORP, four studies were included in the assessment of efficacy of LRARP in clinically localised prostate cancer (Springhart et al 2005; DiMarco et al 2005; Ahlering et al 2004b; Tewari et al 2003b). With the exception of Springhart et al (2005), all studies compared LRARP with retropubic ORP. Springhart et al (2005) compared LRARP with perineal ORP, and hence, the results from this study are not pooled with the other studies due to the difference in technique.

The study by Tewari et al (2003b) presents a prospective cohort study comparing the experience at one institution between ORP performed by one group of surgeons and LRARP performed by a single surgeon with a surgical team at the patient's side. This study was consequently designated III-2 level of evidence. The fact that one committed team performed LRARP whereas another performed ORP may have introduced bias in the study due to potential differential experiences between surgeons.

The authors reported that all of the surgeons performing ORP had each conducted at least 100 procedures (with a combined experience of 1400 procedures). They also indicated that 400 LRARPs had been performed between November 2000 and December 2002. However, it is unclear whether the same surgeon included in the study conducted these 400 LRARPs. This makes it difficult to assess whether the level of surgeon expertise is equivalent between groups and if the comparison is fair. It might be reasonable to assume that proficiency would be achieved at the outset of the study, following completion of 100 ORPs and 400 LRARPs. Therefore, whilst the surgeons performing both procedures had differential levels of experience, this is not thought to influence the results to a great degree, as both surgical teams would have reached the learning curve plateau.

The study by Ahlering et al (2004b) compared ORP and LRARP performed by a single surgeon. This was a small cohort study with a historical control group (retrospective cohort) consequently designated III-3 level of evidence. The study used the last 60 (consecutive) cases of open prostatectomy as historical controls. It was deemed that the learning curve of the surgeon in performing LRARP was sufficiently mature to warrant comparison after 45 cases. This is in accordance with the literature (refer to **Learning curve of LRARP** section).

Studies by Di Marco et al (2005) and Springhart et al (2005) did not report levels of experience of LRARP and ORP surgeons. Whilst these articles have been included in the efficacy section, they have been designated 'surgeon experience uncertain' and the data from these studies were not pooled with data from the studies including only experienced ORP and LRARP surgeons.

Springhart et al (2005) did not report clinical staging of patients, and as such, applicability to the population of interest for this review—patients with clinically localised prostate cancer—could not be determined. Results from this study have been designated 'uncertain applicability' throughout the review.

In light of the preceding discussion, only two comparative studies (Ahlering et al 2004b; Tewari et al 2003b) reported results comparing experienced LRARP and ORP surgeons performing procedures on patients with clinically localised prostate cancer ('applicability certain'). Issues regarding potential biases for the different outcomes are discussed.

Baseline demographics and clinical patient characteristics

The baseline demographics and clinical patient characteristics of the studies included in the efficacy section are summarised in **Table 10.**

The mean age of patients in the LRARP and ORP arms ranged from 58.1–62.9 and 60.7–63.1 years, respectively. Patients' ages were generally well balanced between treatment arms. However, in the study by Springhart et al (2005), the patients in the ORP

arm (mean 60.7 years) were slightly older than participants in LRARP arm (mean 58.1 years) although this difference was not statistically significant.

There was no significant difference between treatment arms in PSA levels. However, patients in the study by Ahlering et al (2004b) had PSA levels that were higher than in the other studies.

The majority of patients in the studies by Tewari et al (2003b) and Ahlering et al (2004b) had clinically localised prostate cancer. Only a small proportion of patients were staged at T3a (≤1.5% and ≤4% of LRARP and ORP patients, respectively). Although the study by DiMarco et al (2005) did not report distribution of clinical staging for patients included in the study, it was stated that all patients had clinically localised adenocarcinoma of the prostate. The patient population in this study was therefore designated applicable to this review. The study by Springhart et al (2005) reported that patients were candidates for prostatectomy but there was no further mention of diagnosis or clinical staging of patients. Consequently, data from the study by Springhart et al (2005) were designated 'applicability uncertain' throughout the review.

The Gleason score is used to predict tumour aggression. The higher the Gleason score, the more likely the tumour is to grow rapidly and to metastasise. The majority of patients included in the review studies were classified as having Gleason scores less than or equal to six. In predictive terms, Gleason scores of two to four indicate tumours that are well differentiated, scores of five to six indicate moderately well differentiated tumours, seven equates to moderate to poor differentiation, and eight to ten reflects tumours that are poorly differentiated (DeMarzo et al 2003). Although the mean Gleason score was similar between groups in the study by Tewari et al (2003b), there was a significant imbalance in the distribution of scores. A higher proportion of ORP patients had Gleason scores of 7 or higher compared with LRARP patients (48% versus 34%, respectively). This indicates that ORP patients had more aggressive tumours than LRARP patients. This may have biased the results in favour of LRARP.

Patients undergoing LRARP and open prostatectomy were similar in terms of mean body mass index (BMI). The patients in the studies by Tewari et al (2003b) and Ahlering et al (2004b) were classified as overweight (BMI 25–29.9).

Table 10 **Baseline demographics and clinical characteristics of patients**

Variable	Tewari (2003b)[a]		Ahlering (2004b)		Springhart (2005)		DiMarco (2005)	
	LRARP n (%)	ORP n (%)	LRARP n (%)	ORP n (%)	LRARP n (%)	ORP n (%)	LRARP n (%)	ORP n (%)
Number of subjects	200	100	60	60	37	32	97	194
Age (years) mean (range)	59.9 (40–72)	63.1 (42.8–72)	62.9 (43–78)	62.7 (50–78)	58.1 (7.6)[c]	60.7 (7.1)[c]	61.9 (7.37)[c]	61.9 (7.23)[c]
Serum PSA (ng/mL) mean (range)	6.4 (0.6–41)	6.4 (0.6–41)	8.1 (0.1–62)	8.4 (1.1–39.6)	–	–	5.0 (0.8–33.5)[d]	5.2 (0.6–16.2)[d]
Prostate volume (cm^3) mean (range)	58.8 (18–140)	48.4 (24.2–70)	52.5 (18–135)	50.7 (30–108)	–	–	–	–
Clinical stage								
T1a	(0.5)	(0)			–	–	–	–
T1c	(49)	(59)	38 (63)	36 (60)				
T2a	(10)	(10)	19 (33)	23 (38)				
T2b	(39)	(35)	2 (3.3)	–				
T2c	–	–	–	–				
T3a	(1.5)	(4)	1 (0.7)	1 (2)				
Gleason score	6.5	6.6	–	–	–	–	–	–
Mean ± SD	(67)	(52)	33 (55)	31 (52)			65 (67.0)[e]	133(68.6)[e]
≤ 6	(28)	(35)	20 (33.3)[a]	20 (33.3)[a]			32 (33.0)[f]	61 (31.6)[f]
7	(6)	(13)	7 (11)	9 (15)			–	–
8–10								
Body mass index	27.7 (19–38)	27.6 (17–41)	26.3 (20.6–33.6)	26.5 (20–34.5)	–	–	–	–

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; PSA, prostate specific antigen.

[a] The percentages do not equal 100 in the open prostatectomy arm of the study by Tewari et al (2003b) due to missing data.

[b] Patients sub-classified as 3+4 and 4+3 were combined to determine total number of patients who had Gleason scores of 7.

[c] Standard deviation.

[d] Median. Only includes patients with pathological Gleason score 6 (not ≤ 6).

[f] Includes patients with pathological Gleason scores of 7+.

Results of assessment

Is it safe?

Learning curve of LRARP

It is expected that with increased experience, surgeons performing LRARP would achieve reduced operating time and blood loss, fewer complications and increased surgical precision. The learning curve (or volume) effect must therefore be taken into consideration before comparing LRARP and OPR surgical approaches. In order to make a fair comparison of clinical outcomes, agreement about the proficiency of the procedures must be reached.

The level of experience in performing open radical prostatectomies influences the rate of learning for the LRARP procedure. For example, experienced prostatectomy surgeons converting to LRARP would have different learning curves compared with novice prostatectomists, due to skill transference. In their study investigating the impact of surgical technique and surgeon experience as predictors of positive surgical margins, Kella et al (2005), suggested that a surgeon's surgical experience (measured by case volume) is an important predictor of positive surgical margins after radical prostatectomy. The results also suggested that without compromising cancer-related outcomes during this transition, it was possible for an experienced oncological surgeon to translate low positive surgical margin rates gained from experience with open radical prostatectomy (6.5%) to similarly low rates with LRARP (6.9%). The investigators used univariate and multivariate logistic regression models to test the relationships.

Results from a small study by Wood et al (2004) suggested that experience with retropubic radical prostatectomies is more important than experience with the conventional laparoscopic approach when learning to perform LRARP. This study compared the LRARP learning experience of a surgeon who was a trained open radical prostatectomist (>700 procedures) but with limited experience with conventional laparoscopic prostatectomies, with another surgeon who was trained in conventional laparoscopic prostatectomy (>400 procedures) with limited open radical prostatectomy experience. The results showed that compared with the surgeon with laparoscopic experience, the experienced open surgery surgeon had shorter mean operating time (347 minutes versus 244, respectively); lower mean estimated blood loss (440 mL versus 155, respectively); and lower conversion rate (20% versus 10%, respectively). Of note, the experienced ORP surgeon had a lower rate of negative surgical margins compared with the surgeon with laparoscopic experience (70% versus 75%, respectively). This is counterintuitive to the conclusion of the study. It should be noted that this was a very small study and results would need to be confirmed in a larger sample.

A study by Ahlering et al (2003) reported that a laparoscopically naïve, yet experienced open approach surgeon, successfully transferred open surgery skills to LRARP over the course of 8–12 cases. This is illustrated in **Figure 3**. The learning curve plateaued after 11–20 cases at a mean operating time of 200 minutes. At cases 36–45, the operating time was 167 minutes.

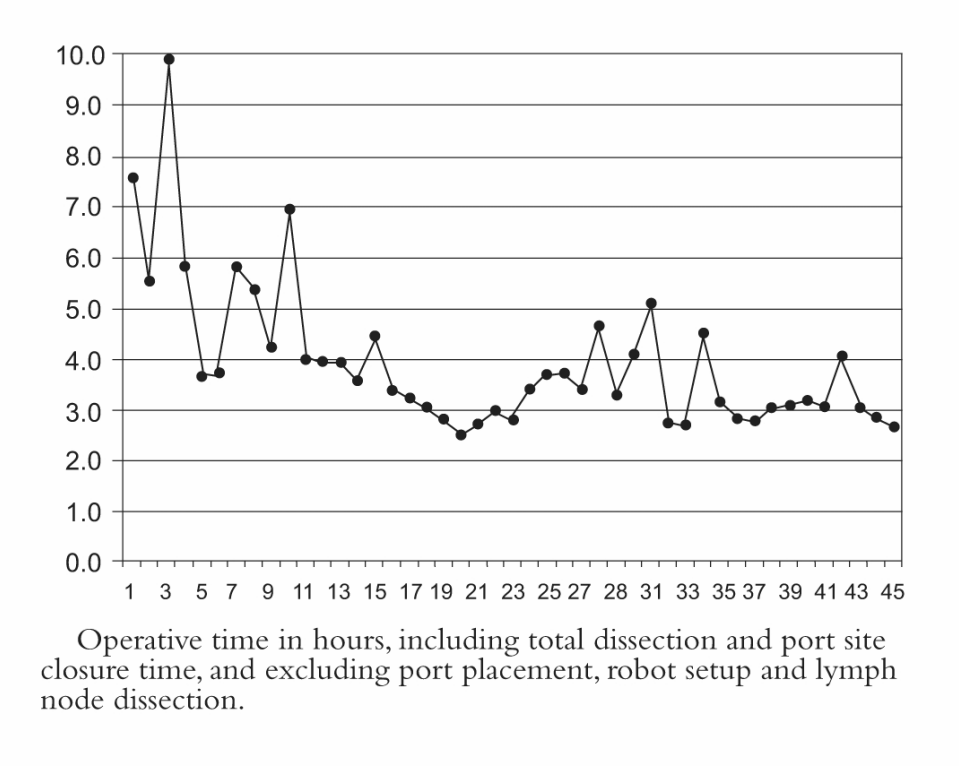

Figure 3 Operating time (y-axis) over cases (x-axis) from Ahlering et al (2003)

Reprinted from *Journal of Urology*, 170, Ahlering TE, Skarecky D, Lee D, Clayman RV, 'Successful transfer of open surgical skills to a laparoscopic environment using robotic interface: initial experience with laparoscopic radical prostatectomy', 1738–1741, Copyright (2003), with permission from the American Urological Association.

Similarly, in the study by Patel et al (2005), the operating time during the initial experience with LRARP decreased with increased surgeon experience (**Figure 4**). The mean operating times for the initial 50 cases and for the last 50 cases (150–200) were 202.2 and 106.4 minutes, respectively. In this study, operating time did not decrease much beyond case 100 minutes. Furthermore, estimated blood loss for the initial 50 cases was markedly higher (151.2 mL) compared with the last 50 cases (48.3 mL) and decreased with surgeon experience, again levelling off after 50 cases (**Figure 5**). The team consisted of a trained laparoscopic surgeon and a skilled open surgeon.

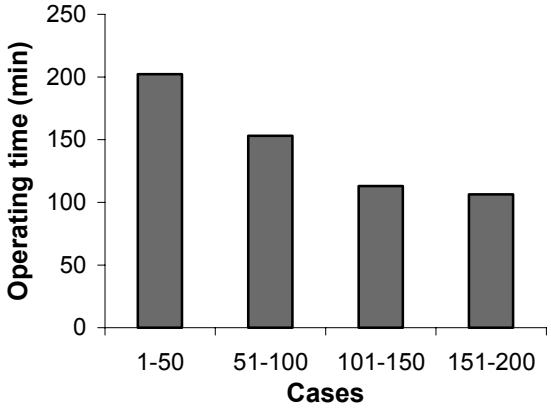

Figure 4 Operating time for the initial 200 cases in Patel et al (2005)

Reprinted from *Journal of Urology*, 174, Patel VR, Tully AS, Holmes R, Lindsay J. 'Robotic radical prostatectomy in the community setting—the learning curve and beyond: initial 200 cases,' 269–272, Copyright (2005), with permission from the American Urological Association.

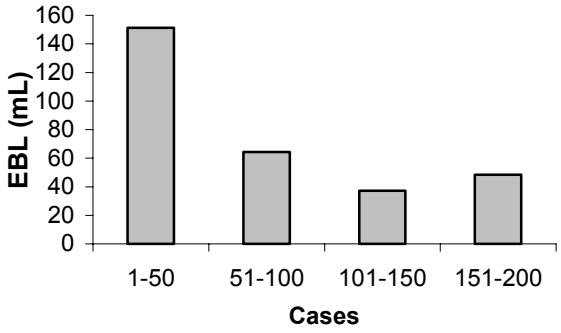

Figure 5 Estimated blood loss for the initial 200 cases in Patel et al (2005)

Abbreviation: EBL, estimated blood loss.
In the study by Binder (2002) the operating time also decreased with increasing experience over the initial 55 cases of LRARP performed. However, the figure presenting operating time over cases was illegible, rendering the interpretation of these results difficult.

Reprinted from *Journal of Urology*, 174, Patel VR, Tully AS, Holmes R, Lindsay J. 'Robotic radical prostatectomy in the community setting—the learning curve and beyond: initial 200 cases,' 269–272, Copyright (2005), with permission from the American Urological Association.

In a recent study presented at the 2005 American Urological Association (AUA) meeting, Patel et al (2005) reported a surgeon learning curve of 20–25 cases. The study included the initial experience of 450 cases performed with LRARP.

In summary, it appears that the case volume of experience may be a predictor of the learning curve for the LRARP procedure. The data presented indicate that a surgeon naïve to LRARP may reach reproducible operating times and blood loss outcomes proficiency after 20–50 cases, depending on previous experience. It is not clear how the learning curves of a novice and an experienced ORP surgeon compare. Some of these observations are based on data from abstracts; hence, caution should be exercised in the interpretation of these results.

Comparative safety

The comparative studies identified in the literature search that reported safety outcomes in patients who had undergone LRARP and ORP are presented in **Table 35** in **Appendix C**. It should be noted that some studies did not report clinical stage and/or diagnosis of patients, and as such, applicability of these studies could not be determined. However, considering that LRARP is performed only for patients with prostate cancer, it can be assumed that all patients have diagnoses of prostate cancer, and these studies should be included. **Table 35** indicates whether the results are applicable to this review or if applicability is uncertain (see the 'Comments' column). Some of the comparative studies did not report the level of experience of surgeons who performed LRARP and ORP; thus, it is not possible to assess whether the comparison is fair or if experience has biased the results. These studies are designated 'surgeon experience uncertain' whereas studies with known and comparable surgeon experience have been designated 'surgeon experience certain'. The pooled rates estimates include only applicable and 'surgeon experience certain' studies.

Operative variables

The operative variables are summarised in **Table 11**. Patients who underwent ORP had significantly higher estimated blood loss (EBL) compared with those who underwent LRARP in all of the studies. In the LRARP arm, the mean EBL ranged from 103–328 mL, whereas in the ORP arm the range was 418–1136 mL.

As expected in light of the results pertaining to EBL, the transfusion rates were higher in ORP patients (range 1.7–67%) than LRARP patients (range 0–25%). However, the studies that met the criteria for pooling (Ahlering et al 2004b; Tewari et al 2003b) were significantly heterogeneous and pooling the data from these studies is not statistically sound. In the study by Tewari et al (2003b) the proportion of patients who required intra-operative blood transfusion was 67 per cent in the ORP arm versus zero per cent in the LRARP arm ($p<0.0001$). In the study by Ahlering et al (2004b) only 1.7 per cent of ORP and zero per cent of LRARP patients required blood transfusion. The variability in transfusion rates in the studies is likely to reflect differences in transfusion practices used at different hospitals and in different countries.

None of the LRARP patients were converted to ORP in the comparative trials with certain applicability. However, two LRARP patients in the study by Binder et al (2002) ('uncertain applicability') were converted to ORP due to excessive surgery time or complications.

Postoperative variables

The postoperative variables are summarised in **Table 12**. Patients in the ORP arm had a significantly higher drop in haemoglobin (Hb) compared with those in the LRARP arm post-surgery ($p\leq0.001$). Although ORP patients had a mean Hb discharge significantly lower than LRARP patients (101 g/L versus 130 g/L; $p<0.05$), the means in both groups were below the range considered normal Hb in males (140–180 g/L).

The study by Farnham et al (2005) reported percentage change in discharge hematocrit and mean perioperative hematocrit change (results not reported in **Table 12**). These results showed that there was a significant difference in discharge hematocrit (36.8% versus 32.8% for LRARP and ORP patients respectively; $p<0.001$). Similarly, the mean perioperative change in hematocrit showed that the LRARP patients had less of a

reduction compared with ORP patients (8.0% versus 10.7% point decrease, respectively; $p<0.001$). However, the mean hematocrit values were not reported so these percentage changes have limited clinical relevance.

The mean catheterisation time was significantly shorter in patients who had undergone LRARP compared with those who had undergone ORP (7 versus 15.8 days; $p<0.05$) in the report by Tewari et al (2003b), but not in data presented by Ahlering et al (2004b). The clinical significance of this difference in catheterisation time is, however, questionable. This is because the studies did not use an objective definition for catheter removal time. The different length of catheterisation time between ORP and LRARP may be due to surgeon preference rather than the technique used.

Postoperative complications

Common postoperative complications were pooled for studies including only applicable and surgeon experience-certain results. The pooled postoperative complication rates are presented in **Table 13**. Additional postoperative complications reported in only one study are presented in **Table 14**.

A significantly higher proportion of ORP patients (16.3%) had a complication compared with LRARP patients (5.0%; $p=0.0004$) based on the pooled estimate including only applicable and surgeon experience-certain studies. The risk difference of developing a postoperative complication was 12 per cent in favour of LRARP.

In one surgeon experience-uncertain study (DiMarco et al 2005), the rate of early complications (ie, any urological or incision complication that occurred less than 30 days post-surgery) was significantly higher in LRARP patients compared with ORP patients ($p=0.017$). No further details of these early complications, and resolution thereof, were provided. These results were contradictory to the pooled estimates including only applicable and surgeon experience-certain.

Deaths

There were no deaths reported in either treatment arm of the study by Tewari et al (2003b). None of the other studies made mention of any patient deaths.

Ileus

The incidence of ileus (slow return of intestinal mobility) was similar between treatment groups. Ileus was reported in 1.5 per cent of LRARP and 1.9 per cent of ORP patients. No further details of the resolution of postoperative ileus were reported.

Deep vein thrombosis

Overall, the incidence rates of deep vein thromboses were very low. The pooled analysis showed that 0.4 per cent and 1.25 per cent of LRARP and ORP treated patients had deep vein thromboses.

Postoperative bleeding/re-exploration

The rate of bleeding was marginally higher in patients who had undergone ORP compared with those who had undergone LRARP (2.5% versus 0.4%, respectively). In the study by Ahlering et al (2004b) one patient experienced an episode of delayed bleeding (14 days postoperatively and seven days after catheter removal) which was cauterised cystoscopically.

Fever/pneumonia

Tewari at al (2003b) reported that significantly more patients who had undergone ORP experienced fever or pneumonia after surgery compared with those who had undergone LRARP ($p<0.05$). No LRARP patients had fever or pneumonia, whereas four (4%) ORP patients did.

Other postoperative complications

The rates of other postoperative complications (**Table 14**) were low with no significant differences reported between treatment groups.

Table 11 Operative variables in LRARP and ORP patients

Variable	LRARP	ORP	*p*-value[a]	Applicability of results/comparability of surgeon experience
Estimated blood loss, mean (range) (mL)				
Tewari (2003b)	153 (25–750)	910 (200–500)	<0.001	Applicable, surgeon experience certain
Ahlering (2004b)	103 (25–400)	418 (150–1200)	≤0.001	Applicable, surgeon experience uncertain
Balaji (2005)	328	1136	<0.05	Applicability uncertain, surgeon experience uncertain
Farnham (2005)	191	664	<0.001	Applicability uncertain, surgeon experience uncertain
Intra-operative blood transfusion, total n (%)				
Tewari (2003b)	0/200 (0)	67/100 (67)	<0.0001	Applicable, surgeon experience certain
Ahlering (2004b)	0/60 (0.0)	1/60 (1.7)	NS	Applicable, surgeon experience certain
Farnham (2005)	1/176 (0.5)	3/103 (2.9)	NS	Applicability uncertain, surgeon experience uncertain
DiMarco (2005)	5/97 (5.2)	48/194 (24.7)	<0.0001	Applicable, surgeon experience uncertain
Binder (2002)	14/50 (28)	19/50 (38)	0.288	Applicability uncertain, surgeon experience uncertain
Conversions, n (%)				
Tewari (2003b)	0/200 (0.0)	NA	NA	Applicable, surgeon experience certain
Ahlering (2004b)	0/60 (0.0)	NA	NA	Applicable, surgeon experience certain
Binder (2002)	2/55 (3.60)	NA	NA	Applicability uncertain, surgeon experience uncertain
Total	0/260 (0.0)	NA	NA	Only includes applicable and surgeon experience certain studies

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; NA, not applicable; NS, not significant; ORP, open radical prostatectomy.

[a] As reported in the article or calculated for the purpose of this review using chi-square.

Table 12 Postoperative variables in LRARP and ORP patients

Variable	LRARP n (%)	ORP n (%)	*p*-value[a]	Applicability of results/comparability of surgeon experience/comments
Hb drop, mean (range) (g/dL)				
Ahlering (2004b)	1.6 (0.2–3.4)	3.3 (0.3–6.1)	≤0.001	Applicable, surgeon experience certain
Discharge Hb, mean (range) (g/L)				
Tewari (2003b)	130 (73–151)	101 (69–146)	<0.05	Applicable, surgeon experience certain
Catheterisation (days), mean (range)				
Tewari (2003b)	7 (1–18)	15.8 (7–28)	<0.05	Applicable, surgeon experience certain
Ahlering (2004b)	7	9	NS	Applicable, surgeon experience certain

Abbreviations: Hb, haemoglobin; LRARP, laparoscopic remotely assisted radical prostatectomy; NS, not significant; ORP, open radical prostatectomy.
[a] As reported in the article.

Table 13 Pooled postoperative complication rates in LRARP and ORP patients

Postoperative complications	LRARP n (%)	ORP n (%)	RD (95% CI)[a]	*p*-value[a]	Applicability of results/comparability of surgeon experience/comments
Total number of complications					
Tewari (2003b)	9/200 (4.5)[b]	20/100 (20.0)			Applicable, surgeon experience certain
Ahlering (2004b)	4/60 (6.7)	6/60 (10.0)			Applicable, surgeon experience certain
DiMarco (2005)	15/97 (15.5)	14/194 (7.7)		0.017[c]	Applicable, surgeon experience uncertain. Refers to any urological or incision complication that occurred <30 days after surgery
Total	13/260 (5.0)	26/160 (16.3)	–0.12 (–0.18, –0.05)	0.0004	Only includes applicable and surgeon experience certain studies
Ileus					
Tewari (2003b)	3/200 (1.5)	3/100 (3.0)			Applicable, surgeon experience certain
Ahlering (2004b)	1/60 (1.7)	0/60 (0.0)			Applicable, surgeon experience certain. Prolonged ileus
Total	4/260 (1.5)	3/160 (1.9)	–0.01 (–0.03, 0.02)	0.73	
Deep vein thrombosis					
Tewari (2003b)	1/200 (0.5)	1/100 (1.0)			Applicable, surgeon experience certain
Ahlering (2004b)	0/60 (0.0)	1/60 (1.7)			Applicable, surgeon experience certain
Total	1/260 (0.4)	2/160 (1.25)	–0.01 (–0.03, 0.01)	0.41	
Bleeding/re-exploration					
Tewari (2003b)	1/200 (0.5)	4/100 (4.0)			Applicable, surgeon experience certain
Ahlering (2004b)	1/60 (1.7)[d]	0/60 (0.0)			Applicable, surgeon experience certain
Total	2/260 (0.8)	4/160 (2.5)	–0.02 (–0.05, 0.01)	0.23	

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RD, risk difference.
[a] Calculated for the purpose of this review using ReviewManager version 4.2.
[b] The article reports a total of 5 complications, however upon adding up all the complications, the total is 9.
[c] As reported in the article.
[d] One delayed episode of bleeding (14 days postoperatively and 7 days after catheter removal) that was cauterised cystoscopically.

Table 14 Additional postoperative complications in LRARP and ORP patients

Postoperative complications	LRARP n (%)	ORP n (%)	*p*-value	Applicability/ surgeon experience/comments
Aborted				
Tewari (2003b)	2/200 (1.0)	1/100 (1.0)	NS	Applicable, surgeon experience certain
Death				
Tewari (2003b)	0/200 (0.0)	0/100 (0.0)	NS	Applicable, surgeon experience certain
Rectal injuries				
Tewari (2003b)	0/200 (0.0)	1/100 (1.0)	NS	Applicable, surgeon experience certain
Wound dehiscence/hernia				
Tewari (2003b)	2/200 (1.0)	1/100 (1.0)	NS	Applicable, surgeon experience certain
Fever/pneumonia				
Tewari (2003b)	0/200 (0.0)	4/100 (4.0)	< 0.05	Applicable, surgeon experience certain
Lymphocele				
Tewari (2003b)	0/200 (0.0)	2/100 (2.0)	NS	Applicable, surgeon experience certain
Obturator neuropathy				
Tewari (2003b)	0/200 (0.0)	2/100 (2.0)	NS	Applicable, surgeon experience certain
Myocardial infarction				
Tewari (2003b)	0/200 (0.0)	1/100 (1.0)	NS	Applicable, surgeon experience certain
Pulmonary embolism				
Ahlering (2004b)	1/60 (1.7)	0/60 (0.0)	NS	Applicable, surgeon experience certain
Pulmonary complication secondary to asbestosis				
Ahlering (2004b)	0/60 (0.0)	1/60 (1.7)[a]	NS	Applicable, surgeon experience certain
Urine leak				
Ahlering (2004b)	1/60 (1.7)[b]	0/60 (0.0)	NS	Applicable, surgeon experience certain
Urinary retention				
Menon (2002b)	1/30 (3.3)	1/30 (3.3)	NS	Applicable, surgeon experience certain
Exaggeration of arthritis				
Menon (2002b)	1/30 (3.3)	0/30 (0.0)	NS	Applicable, surgeon experience certain
Encroachment on the orifice				
Tewari (2003b)	0/200 (0.0)	2/100 (2.0)	NS	Applicable, surgeon experience certain. Ureteral stent placement in the initial operation was necessitated

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; NS, not significant.
[a] Responded to conservative therapy after 8 days of hospitalisation.
[b] Responded to conservative treatment.

Non-comparative safety

The non-comparative studies identified in the literature search that reported safety outcomes in patients who had undergone LRARP are presented in **Table 35** in **Appendix C**. It is noteworthy that some studies did not report clinical stage and/or diagnosis of patients, and as such, applicability of the results of these studies to the population under review could not be determined. However, considering LRARP is performed only in patients with prostate cancer, it can be assumed that all patients were diagnosed with prostate cancer, and these studies should be included. Results from the studies have been designated 'applicable' or 'applicability uncertain' throughout the review.

Results from studies containing overlapping patient populations (ie, recruited from the same cohort) are not presented in the safety section. In these cases, the largest inclusive cohort, or the study presenting the most complete outcomes have been used. If the series with the largest number of patients was presented only as an abstract, the largest peer reviewed publication was included. For completeness, results from all studies reporting safety outcomes are presented in **Appendix C**.

Operative and postoperative variables

Operative and postoperative variables for patients who have undergone LRARP are presented in **Table 15**. The mean estimated blood loss (EBL) ranged from 75.1–1013 mL. The mean EBL was higher in studies with fewer patients compared with the studies with a larger cohort. This is expected, as to a certain degree, blood loss is a function of surgeon experience. The mean EBL range is much broader than the means reported in the comparative studies (153–328 mL).

The rate of transfusions ranged from 0 per cent to 32.5 per cent. The study with the highest transfusion rate also had the highest EBL. Catheter removal time was reported to be 2.7 days in the study reporting shortest time and three weeks in the study reporting the longest time. The study reporting catheter removal time of three weeks was a case study including only one patient who underwent LRARP.

The rate of conversion from LRARP during the procedure ranged from 0–15.5 per cent. There were eight studies that reported 0 per cent conversions and two studies reported conversion rates that were less than 6 per cent. Some patients were converted to ORP, one patient was converted to conventional laparoscopic radical prostatectomy and two patients were converted to laparotomy.

Postoperative complications

Postoperative complications of LRARP patients reported in non-comparative studies are summarised in **Table 15.** The proportion of patients experiencing postoperative complications ranged from 0 per cent to 32.5 per cent. Due to the heterogeneity of the studies, the overall complication rates were not pooled. The two studies reporting 0 per cent postoperative complications only included one and five cases. The study reporting the highest rate of postoperative complications reported two cases of pulmonary embolism that were considered serious, and one case of deep vein thrombosis which was considered a major complication. Other complications in this study included obturator nerve injury, venous plexus bleeding, urinary tract infection and prolonged anastomic leak.

In summary, a total of three cases of deep vein thrombosis (major complication) and two cases of pulmonary embolism (serious event) were reported in the non-comparative studies. Some urinary related complications reported included extravasation (n=2), prolonged catheterisation secondary to urinary leak (n=8), and urinary retention (n=2). There were five bladder neck restenoses and two bladder neck contractures reported. Reports also include three patients with ileus and one with paralytic ileus. Bleeding was reported in four cases and port hernia in three cases. Rectal injuries were sustained by two patients. Complications related to anastomosis include anastomotic disruption (n=3) and prolonged anastomotic leak (n=4). The non-comparative studies that reported postoperative complications included a total of 687 subjects.

Table 15 Non-comparative operative and postoperative safety variables of LRARP

Study	N	EBL, mean (mL)	Transfusion rates n/N (%)	Death rates n/N (%)	Catheter removal time mean (SD) (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Applicability of results/comments
Abbou (2001)	1	300	–	–	3	–	–	Applicable
Ahlering (2003)	45	134 (range 25–350)	0/45 (0.0)	–	–	0/45 (0.0)	6/45 (13.3)	Applicable. Urinary extravasation (n=2) treated conservatively; prolonged hospitalisation because of leg pain due to prolonged operative time and stirrup placement (n=1), bleeding from port site (n=1), DVT (n=1), anastomotic disruption (n=1)
Ball (2005)	110	–	–	–	–	–	6/90 (6.7)	Applicability uncertain. Prolonged catheterisation secondary to urinary leakage was required in 6 (6.7%) of the patients. This was in the initial 90 patients, subsequently, the technique during anastomosis was changed and no further urinary leakage or short term complications were reported
Bentas (2003)	40	570 (SD: 499)	13/40 (32.5)	0	16.7 (9.3)	2/40 (5.0)	13/40 (32.5)	Applicable. Pulmonary embolism (n=2) considered serious; DVT (n=1) considered major complication. The rest of the complications were considered minor: obturator nerve injury (n=1); trocar injury to epigastric artery (n=1); venous plexus bleeding (n=2); UTI (n=2); prolonged anastomotic leak (n=4). Two patients were converted to laparotomy. None of the complications were considered related to use of the da Vinci® system
Costello (2005)	122	–	4/122 (3.3)	–	8.4 (5–33)	0/122 (0.0)	19/122 (15.6)	Applicable. Prolonged D/T leak (n=6); bladder neck restenosis (n=5); acute urinary retention (n=2). Remaining complications were n=1; clot retention requiring readmission, pneumaturia (settled with extended catheterisation), anastomosis breakdown (settled with conservative management), rectal injury (over-sewn), pelvic haematoma plus recto-urethral fistula, paralytic ileus (settled with conservative management)
Dakwar (2003)	45	476	–	–	8.7	7/45 (15.6)	–	Applicability uncertain
Dinlenc (2004)	1	–	–	–	8	–	–	Applicability uncertain. A self-suctioning drain was left in the pelvis for 48 hours. No other complications reported
Eto (2005)	1	500	–	–	7	–	–	Applicable
Gettman (2003)	4	1013	–	–	2.7	0/4 (0.0)	–	Applicable
Hu (2005)	208	313	5/208 (2.4)	–	–	0/208 (0.0)	–	Applicability uncertain. Intra-operative complication rate was 2.4%
Joseph (2005b)	50	206	0/50 (0.0)	0	–	–	4/50 (8.0)	Applicable. Three bladder neck contractures treated by urethral dilation, two urinary leaks treated by prolonged catheterisation

Study	N	EBL, mean (mL)	Transfusion rates n/N (%)	Death rates n/N (%)	Catheter removal time mean (SD) (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Applicability of results/comments
Kaouk (2003)	1[a]	300	–	–	3 (weeks)	0/1 (0.0)	0/1 (0.0)	Applicable
Kong (2005)	5	245	–	–	–	–	–	Applicable
Lee (2005)	231	122	0/231 (0.0)	–	7	–	21/231 (9.1)	Applicability uncertain. Overall complication rate included 3 major complications: DVT, a rectal injury & an incarcerated inguinal hernia
Meininger (2005)	20	NR	NR	–	–	0/20 (0.0)	–	Applicability uncertain. No operative complications
Mikhail (2005)	120	323	–	–	6.4	7/120 (5.8)	–	Applicability uncertain. Five patients were converted due to difficult dissection, one patient due to incidental bladder tumour and one patient due to bladder perforation
Pasticier (2001)	5	800	0/5 (0.0)	–	6.5	–	0/5 (0.0)	Applicable. All but one patient left hospital without the catheter, and in this case, the catheter was removed after nine days. Patient had stress incontinence
Patel et al (2005)	200	75.1	0/200 (0.0)	0/200 (0.0)	7.9 (5–21)	–	2/200 (1.0)	Applicable. *Postoperative complications*: 1 patient readmitted for postoperative gross hematuria — diagnosed with pelvic haematoma (resolved). One bladder neck contracture occurred which required dilation. *1% operative complications (2/200):* 2 small rectal injuries that were closed with a 3-layer closure. Neither patient had any adverse outcomes from the injury
Perer (2003)	1	300	–	–	–	–	–	Applicability uncertain
Rassweiler (2001)	6	–	1/6 (16.7)	–	5[a]	–	–	Applicable. No intra-operative complications
Sarle (2005)	1	400	–	–	–	–	–	Applicability uncertain. No intra-operative complications
Sim (2004)	17	494	3/17 (17.6)	0/17 (0.0)	9.8 (6.1)	0/17 (0.0)	1/17 (5.9)	Applicability uncertain. One patient had pulmonary atelectasis that resolved on the third postoperative day after chest physiotherapy. 3 patients also had moderate urinary incontinence
Tewari (2005b)	530	153	0/530 (0.0)	NR	7	–	8/500 (1.6)	Applicable. Port hernia (n=3), ileus (n=3), delayed bleeding (n=1), DVT (n=1)
Wilson (2005)	191	–	4/191 (2.1)	–	7	1/191 (0.0)	–	Applicability uncertain. Converted to conventional laparoscopy radical prostatectomy. Approximately 2% received at least one unit of blood transfused in the postoperative period
Wolfram (2003)	81	300[b]	10/81 (12)	–	14	–	–	Applicability uncertain

Abbreviations: EBL, estimated blood loss; DVT; deep vein thrombosis; UTI, urinary tract infection; NR, not reported

[a] Two patients underwent conventional laparoscopic radical prostatectomy with only partial assistance by the da Vinci® system. These patients were excluded from the analysis.

[b] Median.

Is it effective?

Primary efficacy outcomes

None of the studies reported any of the primary efficacy outcomes, that is, long-term survival rates/tumour-free survival, or death rates.

Secondary efficacy outcomes

Secondary efficacy outcomes assessed in this review included disease recurrence, positive margin rate and quality of life. Note that the quality of life endpoints, considered as secondary efficacy endpoints in this review, could also be interpreted as safety outcomes.

Disease recurrence (biochemical)

Disease recurrence in prostate cancer can be measured in terms of prostate specific antigen (PSA) biochemical recurrence post-surgery. Following radical prostatectomy, PSA levels should be undetectable unless there is either local or metastatic residual disease. Rising PSA levels are increasingly used as a surrogate endpoint of clinical outcomes, considering the long-term follow-up required to effectively measure clinical failure or mortality. Detectable PSA levels post-radical prostatectomy is generally considered a reliable indicator of residual disease (Commonwealth of Australia 2002). Based on advice from the Advisory Panel, it was determined that a threshold nadir of <0.1 ng/mL is commonly used to define freedom of biochemical disease. If the post-surgery PSA is raised, the disease invariably progresses and will likely result in recurrence in the event that the patient lives long enough.

It is estimated that around 35 per cent of patients will develop biochemical recurrence within 10 years following radical prostatectomy (Roehl et al 2004; Hull et al 2002; Han et al 2001; Amling et al 2000). However, the natural history of prostate cancer after biochemical recurrence is rather long, and biochemical relapse may precede clinical failure by months or years. In a cohort study of men who had undergone radical prostatectomy, and who had subsequent biochemical recurrences, the median time from recurrence to metastasis was eight years, and from metastasis to death was five years (Pound et al 1999). Another study of risk factors in men with recurrence after radical prostatectomy, demonstrated that prostate specific antigen doubling time (PSADT), pathological Gleason score, and time from surgery to biochemical recurrences, are risk factors for prostate cancer-specific mortality (Freedland et al 2005).

For the purpose of this review, the biochemical recurrence rates, rather than biochemical disease-free rates as presented in the studies, are reported. This rate was calculated by subtracting the biochemical disease-free rates from 100.

Ahlering et al (2004b) and Tewari et al (2003b) reported biochemical disease-free rates post-surgery. The immature, three-month results from the analysis of biochemical recurrence rates for patients who have undergone LRARP and ORP reported by Ahlering et al (2004b) are presented in **Table 16**. There were no significant differences between groups in biochemical recurrence rates. In this study, the three-month biochemical recurrence rate was the same in both treatment groups (5%). However, the clinical importance of these immature results is questionable. The Advisory Panel advised

that almost all cases of early detectable PSA post-surgery (ie, within three months) are due to metastatic disease. In order to enable a fair comparison between LRARP and ORP, biochemical recurrence rates one-year post-surgery, where local recurrence is a contributor to the rate, is warranted.

Table 16 Biochemical recurrence rate measured in terms of post-surgery PSA levels

Study (author)	3 month biochemical recurrence rate		RD (95% CI)[b]	*p*-value[b]
	LRARP n (%)	ORP n (%)		
Ahlering (2004b)	3/60 (5.00)[a]	3/60 (5.0)[a]	0.00 (–0.08, 0.08)	NS

Abbreviations: CI, confidence interval; LRARP, laparoscopic remotely assisted radical prostatectomy; NS, not significant; ORP, open radical prostatectomy; PSA, prostate specific antigen; RD, risk difference.

[a] The study reported that the biochemical disease free rate was 5.3% for ORP and 5.5% for LRARP(defined as PSA <0.1 ng/mL). This would translate to a biochemical recurrence rate of 95%. However, the author of the study was contacted and in a response confirmed that there was an error in the study. Rather the biochemical recurrence rate is around 5% and the biochemical disease free rate is 95%.

[b] Calculated for the purpose of this review using ReviewManager version 4.2.

In the study by Tewari et al (2003b), there was a significant differential follow-up period for patients who had undergone LRARP and ORP (mean 236 days versus mean 556 days, respectively; $p<0.05$). Time from surgery to biochemical recurrence is a predictor of prostate cancer-specific mortality, and in particular, survival is found to increase with increasing time from surgery to recurrence (Freedland et al 2005). Therefore, the differential follow-up between LRARP and ORP has likely biased the results in favour of LRARP. Indeed, the results showed that a lower proportion of LRARP patients experienced biochemical recurrence compared with ORP patients (8% and 15%, respectively). These results are dismissed due to the issues in follow-up and are not pooled with other studies.

Positive margins

A positive surgical margin is defined as the presence of tumour at the inked margin of the resected specimen. This can result from incising into the extraprostatic extension of the tumour or by inadvertent incision into an otherwise organ-confined cancer (PT2+) (Wieder et al 1998). A positive margin has been found to be a significant predictor of biochemical recurrence in patients with T2N0 after open radical prostatectomy (Lattouf et al 2003; Gorgonos et al 2003; Blute et al 1997). However, controversy exists regarding the clinical significance of positive surgical margins as an outcome and prognostic factor in prostate cancer (Hull et al 2002). Furthermore, it is generally difficult to interpret differences in positive margin rates between studies and surgical procedures as the proportion of positive margins in a given series can be dominated by patient selection and the method of pathologic analysis rather than by the surgical procedure *per se* (Guillonneau et al 2003; Menon et al 2003c).

The rates of margin positivity in the studies included for efficacy assessment are presented in **Table 17**. The data representing positive margins in organ-confined cancers showed that there were no significant differences in the rate between patients who had undergone LRARP (4.5%) and those who had undergone ORP (9.0%; RD: –5%; 95% CI: [–15, 6]). The rates of total margin positivity, irrespective of pathological tumour stage, were similar between ORP and LRARP patients in both studies.

Table 17 Margin positivity

Author (year)	LRARP n (%)	ORP n (%)	RD (95% CI)[b]	*p*-value[b]	Comment
Ahlering (2004b)					
PT2a + PT2b[a]	2/44 (4.5)	4/44 (9.1)	–0.05 (–0.15, 0.06)	0.40	Applicable. Surgeon experience certain
PT3a + PT4	8/16 (50.0)	8/16 (50.0)	0.00 (–0.35, 0.35)	1.00	
Total positive margin	10/60 (16.7)	12/60 (20)	–0.03 (–0.17, 0.11)	0.64	
DiMarco (2005)					
Total positive margin	16/97 (16.5)	36/194 (18.6)	–0.02 (–0.11, 0.07)	0.66	Applicable. Surgeon experience uncertain

Abbreviations: CI; confidence interval; LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RD, risk difference.
[a] Organ-confined tumours.
[b] Calculated for the purpose of this review using ReviewManager version 4.2.

In the Vattikuti Urology Institute (VUI) study as reported by Tewari et al (2003b), organ-confined cancer margins were considered positive if there was tumour present at the inked margin in the open series. In the LRARP patients, the apical margin was considered positive if cancer was detected in the intra-operative distal biopsies. The difference in definition of positive margins between treatment groups is likely to favour results towards LRARP having lower margin positivity rate. The results from this study were therefore not pooled with the other study. Indeed, lower rates of margin positivity were reported in LRARP patients. A total of 6 per cent[1] versus 23 per cent of LRARP and ORP patients respectively, with organ-confined cancer, had a positive margin (includes both focal [≤1 mm] and extensive [>1 mm] margin positivity). However, it is likely that the differential definition of margin positivity between treatment arms artificially inflated the difference in rates.

Quality of life

There were two studies of certain applicability and certain surgeon experience, reported quality of life (or functional) results (Ahlering et al 2004b; Tewari et al 2003b). A study of uncertain applicability and uncertain surgeon experience reported urinary continence data (Springhart et al 2005). In this study, the Expanded Prostate Cancer Index Composite (EPIC) was used as a validated patient self-assessment instrument to collect continence data.

A subset of all patients was included in the analysis of urinary continence and sexual function in the study by Tewari et al (2003b). Of the 300 subjects included, a subset of 120 patients participated in a telephone interview following surgery. This survey was conducted by a third party interviewer who asked patients about pre-operative sexual function, ability to obtain an erection, recent sexual intercourse (within four weeks), use of sildenafil and the number of pads or liners used to manage urinary incontinence. The article failed to report how many of the 120 patients surveyed had undergone LRARP and ORP. No further details of how patients were selected were provided. This may have introduced selection bias.

[1] The rate of positive margins tabulated in the article was 6% in LRARP, whereas in the text of the article, 9% is reported.

Considering the lack of details provided about the selection of subjects, it is difficult to determine the direction of this potential bias. It is unknown whether the investigators selected patients who would produce the desirable results, whether patients were self-selected or if the remainder of the cohort was lost to follow-up. If it is true that the investigators selected patients based on their prior knowledge of who would produce the desired results, bias is likely in favour of LRARP. If the analysis included only self-selected patients, it is likely that the subjects who responded to the survey were more interested, or otherwise had more vested interests in these results, compared with those who did not participate in the survey. This situation would be expected to introduce non-differential bias, (ie biasing the results towards the null). If the remainder of the cohort was lost to follow-up, and it is unknown how many patients were in each group, it is difficult to determine the direction of potential bias. Caution should therefore be exercised in the interpretation of the results from this study.

In the study by Ahlering et al (2004b), urinary continence data were obtained during clinic visits by using patient self-reported questionnaires or by telephone surveys performed by a non-clinical research associate.

Urinary continence

Urinary continence data were reported in two studies including patients with 'certain applicability' to this review (Ahlering et al 2004b; Tewari et al 2003b). The study by Ahlering et al (2004b) assessed patients' urinary continence at three months post-surgery (defined as no use of pads). A similar proportion of patients who had undergone ORP and LRARP (75.0% verus 76.7%, respectively) were continent of urine three months after surgery (**Table 18**).

Table 18 Urinary continence at three months post-surgery in Ahlering et al (2004b)

Author (year)	LRARP n (%)	ORP n (%)	RD (95%CI) [a]	*p*-value[a]	Comments
Ahlering (2004b)	46/60 (76.7)	45/60 (75.0)	0.02 (–0.14, 0.17)	0.83	Applicable Surgeon experience certain

Abbreviations: CI; confidence interval; LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RD, risk difference.

[a] Calculated for the purpose of this review using ReviewManager version 4.2.

In the study by Tewari et al (2003b), urinary continence was defined as using no pads or using a liner for security reasons only. Patients who had undergone LRARP achieved urinary continence sooner after surgery than those who had undergone ORP. The 50 per cent return of urinary continence occurred in 44 and 160 days, respectively ($p<0.05$). The survival analysis of the probability of return to urinary continence in both groups is presented in **Figure 6**. After approximately 400 days of follow up, most patients (~90%) were continent of urine, and the difference between groups was minimal. The Kaplan-Meier curve takes into account the differential follow-up between patients who had undergone ORP and LRARP. However, the possible introduction of selection bias must be borne in mind when interpreting these results.

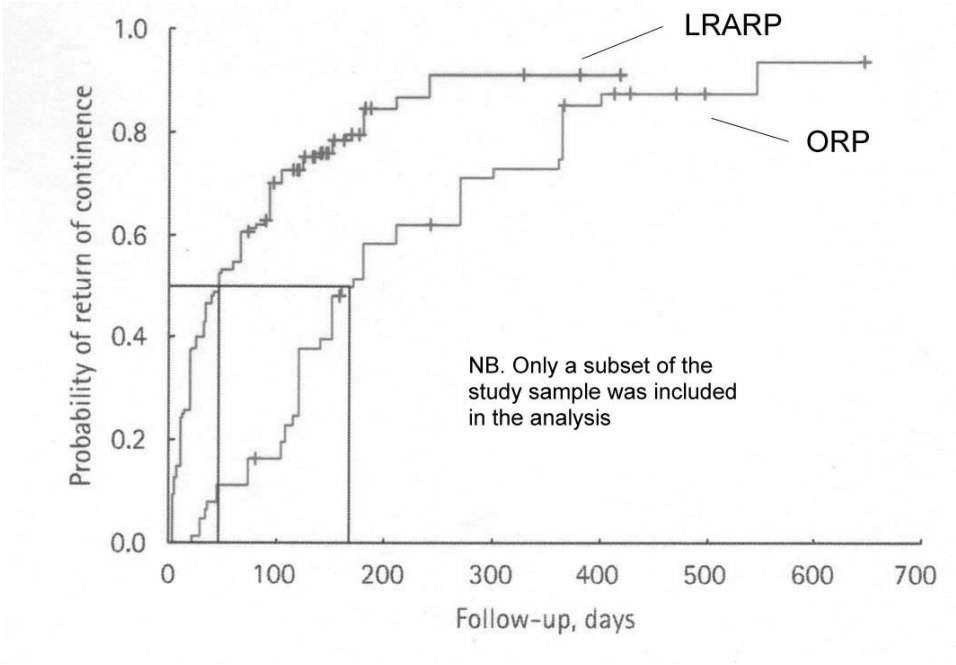

Figure 6 Kaplan-Meier analysis of return of continence in the ORP and LRARP groups

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

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There was one study that included patients of uncertain applicability to this review (staging not detailed) reported the proportion of patients who were continent over time (Springhart et al 2005). The comparative surgeon experience in this study was uncertain. The mean pre-operative urinary summary scores were balanced across groups.

There were two different urinary continence criteria used: patients using no pad or one pad per 24-hour period; and patients experiencing leakage less than once a week. The results from this study are presented in **Figure 7**. There were no significant differences at any time using either criterion for urinary continence between patients who had undergone LRARP or ORP. It was noted that the perineal approach was used to perform ORP in this study. It is unknown whether nerve-sparing techniques were used to perform ORP and LRARP. Therefore, the results from this study should not be compared with those of LRARP versus retropubic ORP studies in which nerve-sparing techniques were used. The abstract does not detail surgeon experience, so it is difficult to determine if surgeon experience may have biased the results.

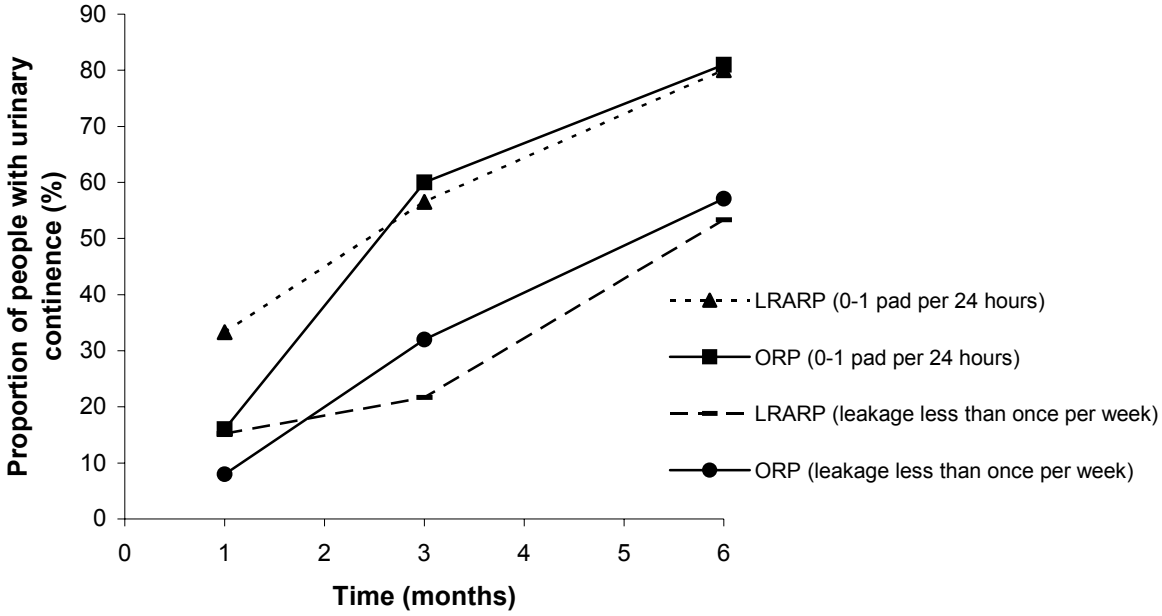

Figure 7 Proportion of patients with urinary continence over time based on two criteria

Source: Springhart et al (2005).

Sexual function

In the study by Tewari et al (2003b) sexual function data (ability to achieve erections and to have an erection strong enough for sexual intercourse) were also collected during telephone surveys. Only patients who classified themselves as having normal pre-operative erections and sexual intercourse and those who had a bilateral nerve-sparing procedure were included in this analysis. Of note, baseline Sexual Health Inventory for Men (SHIM) scores was not assessed. It is therefore unclear how comparable patients in the ORP and LRARP groups were at baseline in terms of erectile function. This is a limitation of the erectile function and intercourse results from this study. Furthermore, the possible introduction of selection bias, as discussed previously, should be taken into account in the interpretation of these results.

The Kaplan-Meier curves describing the probability of return of erections and sexual intercourse are presented in **Figure 8** and **Figure 9**, respectively. Patients who had undergone LRARP had faster return of erectile function after surgery compared with patients who had undergone ORP. Patients achieved a 50 per cent return of erectile function at a mean follow-up of 180 and 440 days after LRARP and ORP, respectively ($p<0.05$). Similarly, resumption of sexual intercourse was also significantly faster in LRARP patients ($p<0.05$). The 50 per cent probability of return of sexual intercourse was achieved at a mean follow-up of 340 days in the LRARP patients. However, at 700 days, the ORP patients had still not achieved this.

Furthermore, 42 per cent versus 65 per cent of LRARP and ORP patients, respectively, were known to be using sildenafil at the time the analysis was conducted in the study by Tewari et al (2003b).

Sexual function was not assessed in the study by Ahlering et al (2004b) due to insufficient follow-up in the LRARP group.

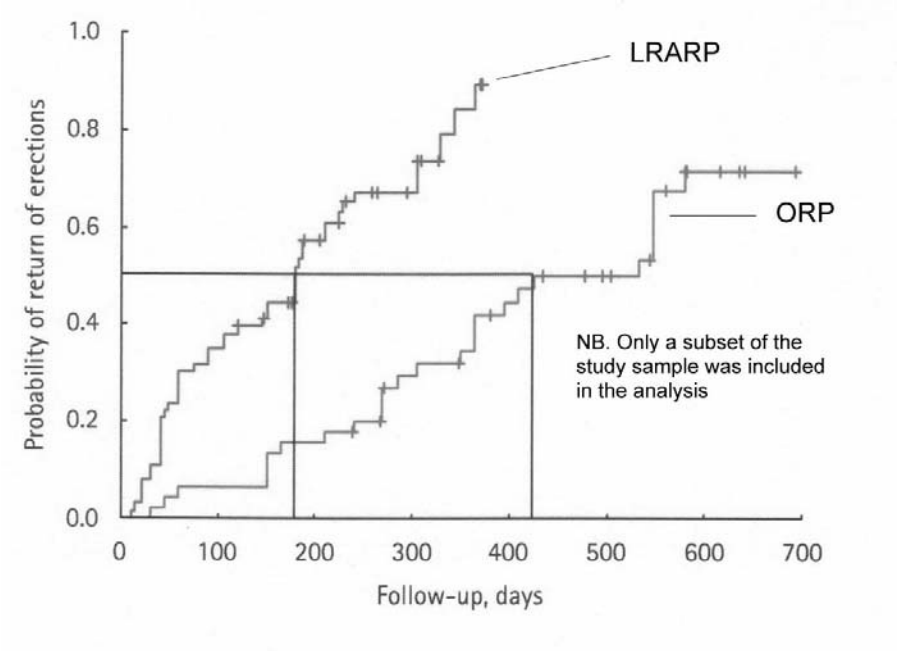

Figure 8 Kaplan-Meier analysis of return of erections in the ORP and LRARP groups

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

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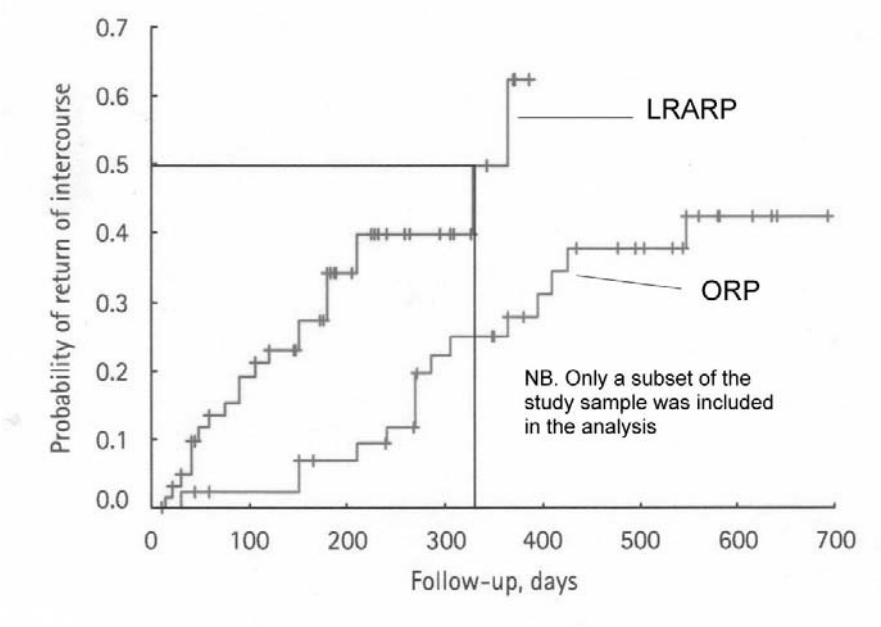

Figure 9 Kaplan-Meier analysis of return of intercourse in the ORP and LRARP groups

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

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Pain scores

In the study by Tewari et al (2003b), the mean postoperative pain score (using a visual analogue scale) on the first postoperative day was significantly lower in patients who had undergone LRARP compared with those who had undergone ORP ($p<0.05$). These results are presented in **Table 19**.

Table 19 Mean postoperative pain scores (based on the visual analogue scale) in the first postoperative day

Postoperative pain score	LRARP	ORP	*p*-value
	n (%)	n (%)	
Tewari (2003b)	3 (1–7)	7 (4–10)	< 0.05

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

What are the economic considerations?

Laparoscopic remotely assisted radical prostatectomy (LRARP) is a new technology. Currently, there is scant information available about the long-term costs and treatment outcomes. Comparative health economics evaluations have not yet been published.

This section of the assessment report provides:

- an assessment of treatment costs associated with the use of LRARP (see the **Cost comparison of LRARP and ORP** section)

and

- estimates of the aggregated financial implications for the Medicare Benefits Scheme (MBS) and to society (see the **Financial impact of a positive recommendation for LRARP** section).

The current evidence available for the assessment of comparative efficacy of LRARP and ORP is very limited: it consists of two cohort studies with comparable surgeon experience and included a patient population applicable to this review. One of these studies may have been prone to selection bias and the other study included only a small population. Because of these limitations, there is no current evidence, free from potential bias, demonstrating a difference in effect between the treatment approaches. Therefore, a cost comparison of LRARP and ORP was performed for this review. The direct treatment costs associated with each procedure are compared and presented. The comparison showed that LRARP is associated with markedly higher direct treatment costs than ORP ($15,469 versus $11,207). This difference is driven primarily by the high equipment costs associated with LRARP and with the need for a conjoint surgeon. The shorter hospital stay following LRARP (about two days versus 7.5 days following ORP) does not offset these additional costs.

The cost structure of LRARP procedures is different from ORP, with more costs for Medicare, but mainly for other healthcare funders, such as private hospitals. Therefore, the financial implications for funding LRARP have been presented separately for Medicare and for other healthcare services funders. It has been shown that the net impact for Medicare will be $685,800 per year. The net impacts for the other healthcare funders will be $3.15 million per year. These figures are based on provision of 300 LRARP procedures per annum by each of the three available da Vinci® systems (the proprietary name of the remotely assisted laparoscopic prostatectomy technology) presently commissioned in Australia. Each additional system implemented and increased patient throughput will increase these costs. To date, neither of the systems in current operation has attained predicted performance in terms of patient throughput. Costs would be lower if the da Vinci® system was used for other types of surgeries in addition to prostatectomies. Based on forecasted figures for the number of radical prostatectomies provided, overall expenditure will increase over time.

An indicative cost utility analysis was performed based on a potentially more rapid recovery of urinary continence and increased rates of sexual potency, as reported by Tewari et al (2003b). The results of the analysis are presented in **Appendix H**.

Methods and results of all evaluations are presented in the following subsections.

Available studies

A search of the literature identified no published cost, cost-effectiveness or cost-benefit studies for LRARP in Australia. Australia is not unique in this position— there have not yet been studies published based on other countries' cost-effectiveness or cost-benefit analyses of LRARP. Published studies by Lotan et al (2004), Joseph et al (2005a), and Bernstein et al (2005) compare various aspects of alternative treatments without considering their effectiveness.

Lotan et al (2004) performed a comparative cost analysis for open, laparoscopic and remotely assisted radical prostatectomies from the perspective of the USA's Medicare system. The incremental cost per patient undergoing one of these three surgical approaches was reported. The cost-structure presented in this study is shown in **Table 20**. Overall costs per patient were calculated to be about $7609 (US$5554)[2] for those undergoing ORP; $8276 (US$6041) for conventional laparoscopic radical prostatectomy; and $9974 (US$7280) for LRARP including da Vinci® system purchase costs; and $9191 (US$6709) excluding da Vinci® system purchase costs. It was noted that the study's tabulated item costs do not equate to the reported total costs per patient (Lotan et al 2004).

The authors reported that the high maintenance and equipment costs for LRARP are not offset by the shorter hospital stay and shorter operation time.

Table 20 Costs per patient and cost-structure for three prostatectomy surgical approaches

Costs per treatment ($) Cost item	ORP	Conventional laparoscopic radical prostatectomy	LRARP (da Vinci® systems purchase cost included)
Operating room	3326	3940	3019
Equipment	103	730	2334
Surgeon's professional fees	2184	2313	2313
Hospital room + board	1354	704	649
Intravenous fluids/medications	206	107	99
da Vinci® system cost per case (purchase and maintenance)	–	–	1174
Total	$7609	$8276	$9974

Based on Lotan et al (2004).
Abbreviations: ORP, open radical prostatectomy; LRARP, laparoscopic remotely assisted radical prostatectomy.
Note: National cost data reported in US$ were converted into AUD$ by using OECD Purchasing Power Parities (PPPs).
Note: Cost data published in the article do not sum to the reported total costs.

[2] All national cost data have been converted to AUD$ by considering Organization for Economic Co-operation and Development (OECD) Purchasing Power Parities (PPPs).

Table 21 LRARP equipment costs for disposables and reposables

Item	Costs per procedure ($)
Cautery da Vinci® system (hook)	193
Large needle driver (2)	767
Round tip scissors	229
Bipolar (optional)	343
Cadiere forceps	233
Drape instrument (2)	97
Drape camera arm	49
Drape camera	36
Suction	44
Veress needle	30
Visiport 5–12 mm trocar [a]	92
Snap-on clips (1)	121
Specimen retrieval bag (1)	101
Total	$2334

Based on Lotan et al (2004).
Note: National cost data reported in US$ have been converted into AUD$ by using OECD Purchasing Power Parities (PPPs).
[a] Some reusable trocars were used and therefore do not contribute to these costs.

Joseph et al (2005a) presented a study that assessed the costs for LRARP from the perspective of a private tertiary care hospital in the USA. The total costs were $12,470 (US$9102) per patient; $4040 (US$2949) contributed to fixed costs and $8430 (US$6153) for variable costs. The average costs of reposables and disposables per case were $1559 and $2160 (US$1138 and US$1577), respectively. Reimbursed cost per case was $12,267 (US$8954) causing the hospital a net loss for every patient treated. The initial purchase, maintenance and repair costs for the da Vinci® system were not included in this calculation.

Bernstein et al (2005) analysed costs and revenue for three different surgical prostatectomy approaches—retropubic, perineal and remotely-assisted. The authors did not report whether the retropubic surgeries were performed using open or laparoscopic approaches. The reported costs were $7430 ± $1956 (US$5423 ± $1428) per patient (perineal); $8560 ± $2195 (US$6248 ± $1602) per patient (retropubic); and $9675 ± $1710 (US$7062 ± $1248) per patient (remotely-assisted). Considering the local reimbursement conditions, the largest margin for the hospital was for perineal surgery ($2137, US$1560) and lowest for remotely-assisted surgery ($126, US$92).

Cost comparison of LRARP and ORP

Costs of LRARP

Costs for the procedure were calculated by using configuration and cost information provided by both the Advisory Panel and the Applicant.

For this cost calculation, LRARPs were assumed to be provided as inpatient procedures in tertiary care hospitals, although Lee et al (2005) recently reported LRARP provided as a day care facility procedure.

The total costs for LRARP include capital costs, equipment cost per procedure, direct medical and non-medical costs and indirect costs.

Major capital equipment

Capital costs are those required to purchase major medical facilities and equipment required to perform the service under evaluation. For this assessment, 'capital expenditure' refers to the outlay required to purchase the da Vinci® system. Capital costs are typically investments made at a single point in time (often at the outset); whereas running costs occur throughout the equipment's life cycle.

Capital costs for equipment and buildings are subject to depreciation, reflecting that their value decreases over time (due to technological and material wear). Depreciation can be calculated using one of three approaches—linear, progressive or degressive.

Opportunity costs also contribute to overall capital costs. They represent costs of resource options that are no longer available, leading to selecting next-best and (frequently) less cost-effective options.

To calculate the current value of an investment, all costs and benefits are discounted to their current values. Discounting is a method to adjust costs and benefits occurring at different points in time to their present values. The underlying principle for discounting is that costs and benefits arising in the future have a lower value than they would if they arose today.

In general, the da Vinci® system purchasing and maintenance costs are not covered by Medicare but by other healthcare funders. The Applicant provided cost data.
A purchasing cost of $2.945 million for a four-arm da Vinci® system was considered for the base case analysis.[3]

Maintenance costs generally equate to five to ten per cent of system costs. The Applicant provided annual maintenance cost estimate of $294,500, following a one-year warranty period.

To calculate capital cost, a linear depreciation over an estimated equipment life span of seven years with a residual value of zero, was applied. Maintenance costs are proposed for seven years—a one-year warranty period, followed by an additional six years of maintenance costs. Opportunity costs are considered as interest to be paid for the undepreciated investment costs and maintenance costs (7.25%, based on data provided by Medfin Finance, Sydney). A discount rate of 5 per cent per annum has been applied to the undepreciated investment costs, maintenance costs, opportunity costs, as well as a returned benefit in terms of LRARP procedures performed.

Based on the calculation described, capital costs amount to $2709 per treatment procedure.

[3] Based on advice from the Advisory Panel, 50% of all LRARP procedures are performed using a four-arm configuration. This four-arm system also allows surgeries to be performed using a three-arm configuration. The three-arm system is not available in Australia.

Table 22 Calculation of capital costs per LRARP procedure

	Life cycle year						
	1	2	3	4	5	6	7
Investment							
Value of investment	$2,945,000	$2,524,286	$2,103,572	$1,682,858	$1,262,144	$841,430	$420,716
Depreciation, per year [a]	$420,714	$420,714	$420,714	$420,714	$420,714	$420,714	$420,714
Maintenance costs, per year [b]	$0	$294,500	$294,500	$294,500	$294,500	$294,500	$294,500
Interest costs of investment and maintenance [c]	$213,513	$204,362	$173,860	$143,358	$112,857	$82,355	$51,853
Total costs per year	$634,227	$919,576	$889,074	$858,572	$828,071	$797,569	$767,067
Present value of costs [d]	$603,784	$834,055	$768,160	$706,605	$649,208	$594,986	$545,385
Total present value of costs	$4,702,183						
Return on investment							
Number of procedures	300	300	300	300	300	300	300
Present value of procedures [e]	286	272	259	247	235	224	213
Total present value of procedures	$1736						
Present capital costs per procedure	$2709						

Abbreviation: LRARP, laparoscopic remotely assisted radical prostatectomy.
Notes: MedFin Finance normally finances for a maximum period of five years. For this calculation, it has been assumed that agreement could be reached on a seven-year financing period.
[a] Linear depreciation, no residual value, lifetime seven years.
[b] First year: warranty period, no maintenance costs.
[c] Calculated by considering an interest rate of 7.25% for purchase and maintenance costs.
[d] Discounted at 7.25% per annum to reflect current value of investment.
[e] Discounted at 5% to reflect current value of procedures.

Equipment cost per treatment

Equipment costs comprise of elements for disposable, reusable and reposable instruments and devices. Many LRARP instruments are reposables: they can be used repeatedly but have a finite number of uses (8, 10 or 30). This number is counted and controlled electronically by the system.

Both the Advisory Panel and the Applicant provided information on da Vinci® system configuration and costs. Resulting costs amount to $4014 per procedure (see **Table 23**).

Table 23 Equipment costs

Item	Cost per item ($)	Quantity per procedure	Probability of use	Cost per procedure ($)
Instrument arm drape (three-arm configuration)	$84.67	2	1	$169.34
Instrument arm drape (four-arm configuration)	$84.67	1	0.5 [a]	$42.34
Camera arm drape	$84.67	1	1	$84.67
Camera drape	$60.48	1	1	$60.48
da Vinci® system cannula seal (three-arm configuration)	$36.29	2	1	$72.58
da Vinci® system cannula seal (four-arm configuration)	$36.29	1	0.5 [a]	$18.15
Cautery spatula	$483.87	1	0.5	$241.94
Cautery hook	$483.87	1	0.5	$241.94
Round tip scissors	$471.74	1	1	$471.74
Large needle drivers	$532.22	2	1	$1,064.44
Precise bipolar forceps	$653.18	1	1	$653.18
Prograsp forceps	$532.22	1	0.5 [a]	$266.11
10–12 mm Endopath (512B) trocar and cannula	$150.00	2	1	$300.00
Ethicon 5 mm Apple Port	$45.30	2	1	$90.60
Ethicon 5 mm Apple Port	$45.30	1	0.5 [a]	$22.65
Seal reducer	$12.00	2	1	$24.00
Endo Pouch Retriever 10 mm	$190.00	1	1	$190.00
Total				$4,014.16

[a] Used for four-arm configuration only. Half of all procedures are performed using a four-arm configuration.

Professional fee per surgery

LRARP is currently reimbursed on MBS item numbers 37209, 37210 and 37211 for radical prostatectomies. The average fee was calculated by analysing the distribution of MBS item services 37209, 37210 and 37211 performed between July 2004 and June 2005 (Australian Government Medicare Australia 2005).

Considering these data, the weighted average fee for service in the year July 2004–June 2005, was $1513 per procedure. It has been assumed that a conjoint surgeon would receive 75 per cent of this payment. The total service fee for LRARP has been estimated as $2648 per procedure. This assumption has been further explored in the **Cost summary** section.

Table 24 Estimation of service fee for surgery

	Service description	Value	Reference
	Total excision of prostate		
A	Number of procedures [a]	154	Medicare Australia 2005
B	Proportion of procedures	4%	Calculated
C	Service fee	$1117.45	MBS item 37209, 100%
	Prostatectomy, radical		
D	Number of procedures [a]	1267	Medicare Australia 2005
E	Proportion of procedures	32%	Calculated
F	Service fee	$1379.05	MBS item 37210, 100%
	Prostatectomy, radical, with pelvic lymphadenectomy		
G	Number of procedures [a]	2523	Medicare Australia 2005
H	Proportion of procedures	64%	Calculated
I	Service fee	$1674.90	MBS item 37211, 100%
J	Weighted average fee for principal surgeon	$1513	J=B*C + E*F + H*I
K	Assumed fee for conjoint surgeon	$1135	K=J * 75%, based on Advisory Panel estimates
L	Weighted average fee, in total	$2648	L=J + K

Abbreviation: MBS, Medicare Benefits Schedule.
[a] For the period July 2004 to June 2005.
NB. MBS fees for services as by 1 November 2005.

Costs for associated medical services

Costs for anaesthesia associated with LRARP have been estimated by considering MBS service fees as described in **Table 25** (Australian Government Department of Health and Ageing 2005b).

Since some anaesthesia fees are based on the duration of surgery, average anaesthesia time has been derived from available comparative and non-comparative studies. The weighted average was calculated to be 205 minutes (3:25 hours). Details of the references consulted appear in **Table** 37 in **Appendix F**.

Studies reporting on initial surgeries and from small series' of patient numbers were included in the assessment of time required for surgery. This approach allowed consideration of a possible prolonging learning curve effect. Where studies were identified that reported on similar patient samples or authors represented the same institution, the publication reporting the largest sample has been selected for averaging. Where both peer-reviewed papers and abstracts reported similar data or patient samples, the peer-reviewed data were selected for inclusion.

These data are anticipated to be influenced by the underlying definition of time for surgery, for example, whether da Vinci® system set up time was included, or only the time from dissection to completing the final suture of the anastomosis for the procedure was reported.

A separate fee for the control of postoperative pain has not been included in the cost calculation. Advice from clinical members of this review's Advisory Panel indicates that postoperative pain is normally managed using oral analgesics, and occasionally, with intramuscular injections of narcotics. This means that additional care for pain is not normally part of patient management for this procedure.

Table 25 Estimation of costs for anaesthesia

	Service description	Value	Reference
A	Anaesthesia, pre-examination in preparation for the operation	$37.15	MBS item 17603, 100%
B	Initiation of anaesthesia for radical prostatectomy	$171.50	MBS item 20845, 100%
C	Anaesthesia during surgery (3:16 to 3:30 hours) [a]	$291.55	MBS item 23117, 100%
D	Total anaesthetic costs, per treatment	$497.20	D=(A+B+C)

Abbreviation: MBS, Medicare Benefits Schedule.
[a] Modifying age condition not considered.

Based on advice from the Advisory Panel, it was considered that 2 per cent of all patients undergoing LRARP receive two units of packed red blood cells (PRBCs) on average. Unit costs for PRBCs were obtained from the National Blood Authority (verbal communication, 28 November 2005). Costs are wide-ranging—$184 to $474—depending on the value-added nature of the blood product, such as buffy coat removed, leucocyte depleted etc. These costs represent the most accurate costs available for Australia. An average of $329 per unit was considered for cost calculations (**Table 26**).

Table 26 LRARP blood transfusion costs

	Service description	Value	Reference
A	Transfusion probability	2%	Advisory Panel
B	Number of transferred units per patient	2	Advisory Panel
C	Compatibility tests including cross-match, grouping checks, haemoglobin levels (for up to 6 units)	$113.40	MBS item 65099, 100%
D	Administration of blood, already collected	$72.20	MBS item 13706, 100%
E	Packed red blood cells, per unit, on average	$329.00	National Blood Authority (2005 data)
F	Total transfusion costs, per treatment	$16.87	F=A*((B*C)+(D+E))

Abbreviation: MBS, Medicare Benefits Schedule.

Costs for other associated medical services have been assumed to be equal to ORP and/or already included in other costs (see calculation of hospital service costs below).

Cost of hospital services

The cost of hospitalisation has been determined using both fixed and marginal costs derived from the National Hospital Cost Data Collection (NHCDC) for public and private sector hospitals (Australian Refined Diagnosis Related Groups [AR-DRG] version 4.2, round 7, 2002–2003) (Australian Government Department of Health and Ageing (DoHA) 2005a; Australian Government Department of Health and Ageing [DoHA] 2003). The diagnosis related group (DRG) M01Z ('Major male pelvic procedures') was considered as the most relevant. The equation used for the calculation of hospital cost is:

$$\text{Cost of hospitalisation} = \text{Fixed cost} + (\text{daily marginal cost} \times \text{length of stay})$$

The cost components were evaluated individually to determine whether they were fixed or marginal costs. Rather than using the true economic definitions of fixed and marginal costs, consideration has been given to the timing and frequency of the stated item or procedure. Hence, items such as emergency department and pathology costs are considered fixed costs, since these would likely occur at admission and are not influenced by length of stay.

The mean cost per episode has been weighted by the proportion of services provided in each hospital sector (public, private). Weighted daily costs were multiplied by the average length of hospital stay following LRARP. The literature indicated that patients stay in hospital for 1.4 days on average (range 1 to 7 days) (see **Table** 37 in **Appendix F** for the supporting literature). The Advisory Panel has advised that the Australian the length of stay is considered to be two days.

The fixed cost equals $4563.43 and the daily marginal cost amounts to $510.05.
The equation becomes:

$$\text{Cost of hospitalisation} = \$4563.43 + (\$510.05 \text{ per day} \times 2 \text{ days})$$

resulting in total hospital service costs of $5583.53 per LRARP procedure.
Calculation details are presented in **Table 38** in **Appendix G**.

A possible overestimation of hospital costs that may be caused by using DRG-based costs has been addressed in the sensitivity analysis (see **Sensitivity analysis**).

Cost for non-inpatient healthcare

Data from the comparative studies showed that average catheter removal time was seven days (see the **Comparative safety** section). The catheter removal time reported in the non-comparative studies ranged from 2.7 days to three weeks. The study reporting catheter removal time of three weeks was a case study of one patient who underwent LRARP (see the **Non-comparative safety** section). Therefore, the literature data indicate that the majority of patients leave hospital with indwelling catheters.
The Advisory Panel's advice is that in Australian clinical practice, indwelling catheters are removed between days five and eight post-surgery.

LRARP component cost summary

Table 27 summarises the component costs presented above and shows estimated overall direct costs per LRARP procedure.

Table 27 LRARP component costs

	Item	Costs	Reference
Major capital costs			
A	Capital costs	$2709	See Table 22
Equipment costs			
B	Reusable, reposable and disposable equipment per procedure	$4014	See Table 23
Direct treatment costs			
C	Proposed professional fee	$2648	See Table 24
D	Cost of associated medical services	$514	See Table 25 and Table 26
E	Cost of hospital services	$5584	See Cost of hospital services
F	Direct treatment costs per procedure	$8746	F=C + D + E
G	Total direct cost per procedure	$15,469	G=A + B + F

Note: Numbers may not add due to rounding.

Costs of ORP

ORP does not require provision of special major clinical equipment. An assumption was made that limited equipment costs are included in the DRG allocations.

Professional fee per surgery

The service fee for ORP reimbursed by Medicare has been derived from the Medicare Australia (formerly known as the Health Insurance Commission [HIC]) statistics for Medicare Benefits Schedule (MBS) items 37209, 37210 and 37211. Calculation details are presented in **Table 24**. Costs are considered to be $1513 per procedure.

Unlike LRARP, ORP requires an assistant surgeon, but not the services of a conjoint surgeon. The fee for the assistant surgeon is one-fifth of the surgeon's fee for the procedure (MBS item no 51303). This amounts to $311.59 per procedure (calculated as weighted average based on the number of provided MBS items 37209, 37210, 37211).

Costs for associated medical services

Costs for anaesthesia associated with ORP surgery have been estimated by considering MBS service fees as described for LRARP. Based on the findings of comparative studies by Tewari et al (2003b) and Ahlering et al (2004b), it has been assumed that there are no differences in the time required to perform both surgeries. It might also be expected that the time needed to perform ORP relates to surgeon experience. For the base case costs analysis, the surgery time was assumed to be similar to LRARP, with costs for anaesthesia at $497.20 per procedure. In a separate scenario (see **Cost summary**) the time needed for open surgery was reduced to 2:30 hours.

An assumption that an average transfusion volume of two units PRBCs were required by 35 per cent of ORP patients was made to calculate blood transfusion costs (**Table 28**).

Table 28 ORP blood transfusion costs

	Service description	Value	Reference
A	Transfusion probability	35%	Advisory Panel
B	Number of transferred units per patient	2	Advisory Panel
C	Compatibility tests including cross-match, grouping checks, haemoglobin levels (for up to 6 units)	$113.40	MBS item 65099, 100%
D	Administration of blood, already collected	$72.20	MBS item 13706, 100%
E	Packed red blood cells, per unit, on average	$329.00	National Blood Authority (2005 data)
F	Total transfusion costs, per treatment	$295.26	F=A*((B*C)+(D+E))

Abbreviation: MBS, Medicare Benefits Schedule.

Costs of hospital services

ORP hospitalisation costs were derived from the National Hospital Cost Data Collection (Australian Government Department of Health and Ageing [DoHA] 2005a). The Australian Refined Diagnosis Related Groups (AR-DRG) health classification system captures the average costs including any additional costs that may be incurred, such as anaesthesia, or applied health interventions such as physiotherapy, as well as the cost for the hospital stay. Based on the reported number of separations for AR-DRG M01Z, the weighted average cost per patient was approximately $8590 in 2002–2003 (**Table 29**).

Table 29 ORP hospital service costs

	AR-DRG	Description	Hospital sector	ALOS	Number of separations	Average costs ($)
A	M01Z	Major male pelvic procedures	public	7.49	722	$10,782
B	M01Z	Major male pelvic procedures	private	7.56	2182	$7865
C	Weighted average			7.54	–	$8590

Abbreviations: AR-DRG, Australian Refined Diagnosis Related Groups, ALOS, average length of stay.

Average DRG costs may be driven by other costs such as high frequency procedures or by procedures with high cost weights. The greater the differences in cost structures of the covered procedures or conditions, the less precisely the DRGs represent the costs of a specific procedure or condition.

Data relating to DRG M01Z from 2000–2001 indicated that the most frequently provided surgical service covered by this DRG was radical prostatectomy. It can therefore be assumed that DRG M01Z accurately reflects the costs for ORP.

ORP cost component summary

Table 30 summarises the total component costs for ORP that total $11,207 per procedure.

Table 30 ORP component costs

Item		Costs	Reference
Direct treatment costs			
A	Professional fee	$1513	See Table 24
B	Assistant surgeon	$312	1/5 of surgeon's fee (MBS item no 51303)
C	Cost of associated medical services	$792	See Table 25 and Table 28
D	Cost of hospital services	$8590	See Table 29
F	Direct treatment costs per procedure	$11,207	F=A + B + C + D + E

Abbreviations: MBS, Medicare Benefits Schedule; ORP, open radical prostatectomy
Note: Numbers may not add up due to rounding

Cost summary

Table 31 compares treatment costs per LRARP or ORP procedure.

Table 31 Costs summary for LRARP and ORP

Item	LRARP	ORP	Increment
Capital cost	$2709	–	$2709
Equipment cost	$4014	[a]	$4014
Professional fee [b]	$2648	$1825	$823
Cost of associated medical services	$514	$792	–$278
Cost of hospital services	$5584	$8590	–$3006
Direct costs per procedure	$15,469	$11,207	$4262

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.
[a] Equipment costs for ORP are not zero — they are included in the cost of hospital services.
[b] Including the fee for the conjoint surgeon (LRARP) and an assistant surgeon (ORP).
Note: Numbers may not add up due to rounding.

Considering lower average operation times for LRARP and ORP would affect the MBS fees for anaesthesia only because they are time-related. Tewari et al (2005b) reported LRARP operation times of 160 ± 28 minutes (2:40 ± 0:28 hours) for the largest patient sample (n=530). The Advisory Panel considered that the average required operation time for ORP might also reach 2:30 hours, similar to LRARP. Therefore, the anaesthesia costs for both procedures would be reduced by $85.75 (MBS item 23112 instead of 23117: $205.80, 100 per cent) to $411.45 rather than $497.20 for each procedure.
Total direct treatment costs would be $15,383 for LRARP and $11,121 for ORP.

Considering different fees for the LRARP conjoint surgeon would affect the overall costs for LRARP: if the conjoint surgeon were to receive 100 per cent of the principal surgeon's fee, the total costs per LRARP procedure would be $15,847. If the conjoint surgeon received 50 per cent of the principal surgeon's fee, the total costs per LRARP procedure would be $15,091.

Resource allocation

Table 32 shows a break down of future service funder costs for ORP and LRARP within the healthcare system should LRARP be listed on the MBS. Costs of procedures, anaesthesia, blood transfusion (except unit costs) and outpatient treatment have been allocated to Medicare. Other costs associated with treatment such as purchase and equipment cost, hospitalisation and so forth, are borne by other healthcare funders including public and private hospitals. A detailed allocation of costs for other healthcare funders was beyond the scope of this assessment. LRARP funding provokes a significant increase in overall costs per procedure for other healthcare funders.

Table 32 Allocation of direct costs among healthcare funders should LRARP be listed on the MBS

Procedure	Medicare costs	Costs for other healthcare funders	Total direct costs
LRARP	$3149	$12,320	$15,469
ORP	$2387	$8820	$11,207

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

Discussion

Currently, there is no evidence, free from potential bias, of a difference in effect between LRARP and ORP. Therefore, a direct treatment cost comparison was provided.
The comparator procedure was ORP, since approximately 95 per cent of all radical prostatectomies are performed via open approach surgeries. Results indicate that LRARP is associated with markedly higher direct treatment costs. This is mainly due to extra costs for reposable and disposable equipment needed for each procedure. Additional costs for a conjoint surgeon, da Vinci® system purchasing and maintenance costs also contribute to increased direct treatment costs. These additional costs are only partially offset by savings associated with a markedly shorter hospital stay (approximately two days versus 7.5 days) and a reduced need for blood transfusions.

Financial impact of a positive recommendation for LRARP

Based on rising incidence figures for diagnoses of prostate cancer (see the **Incidence and mortality** section) and an increasing proportion of the affected male population, it is to be expected that the overall number of patients eligible for radical prostatectomy will further increase over time.

A detailed aggregation of the extent of service utilisation and resulting costs of an increased funding for LRARP to Medicare and other healthcare funders is provided below. Projections of financial impact have been based on the number of expected services rather than on epidemiological evidence.

This calculation is based on the following data and assumptions:

- The expected number of services has been projected based on the past number of relevant MBS services provided. It has been assumed that the number of services provided will follow the patterns observed during past years.

- Based on Advisory Panel advice, the proportion of open procedures plus remotely-assisted procedure has been assumed to be at 98 per cent and constant over the next three years.

- The number of available da Vinci® systems will not increase during the next three years and will remain stable at three systems.

- The number of procedures performed with each da Vinci® system is stable at 300, as provided by the Applicant.

- The costs per patient undergoing either LRARP or ORP are assumed to be stable over the next three years.

The expected numbers of services during the next three years were forecast based on the past growth of MBS services 37209 (*prostate, and/or seminal vesicle/ampulla of vas, unilateral or bilateral, total excision of, …;* –13 per cent); 37210 (*prostatectomy, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction, …;* +42.3 per cent) and 37211 (*prostatectomy, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction, with pelvic lymphadenectomy, …;* +17.6 per cent). The results are presented in **Figure 10**.

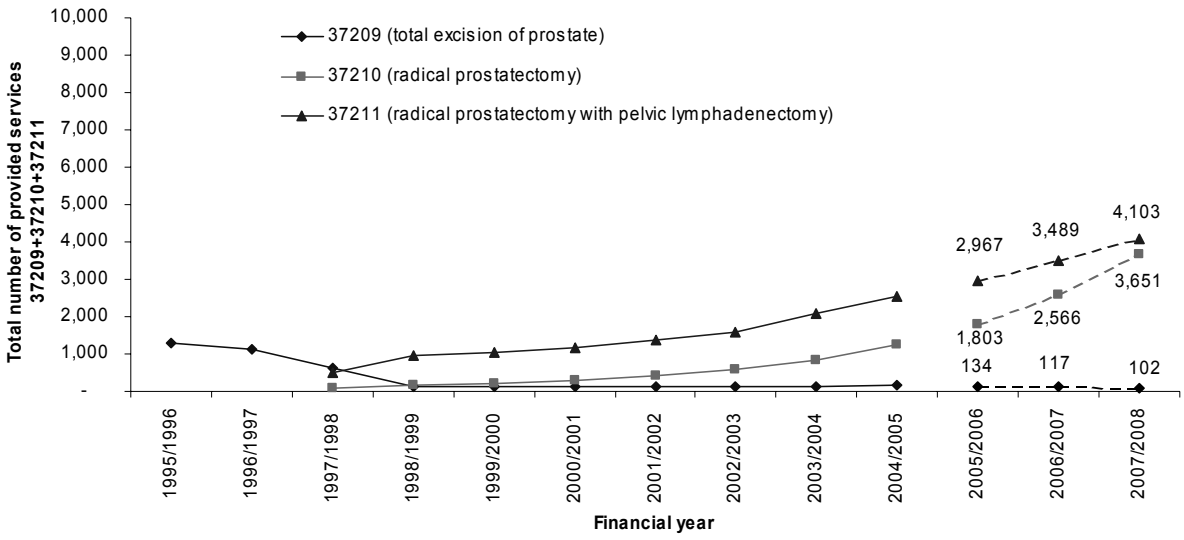

Figure 10 2005–2008 forecasts of MBS-provided prostate excisions and radical prostatectomies

The aggregated financial impact of an increased funding for LRARP for Medicare and other healthcare funders is shown in **Table 33** and **Table 34**.

Table 33 Aggregated financial impact of LRARP to Medicare

		Year 1	Year 2	Year 3	Reference
A	Total patient population undergoing RP (projected)	4904	6172	7856	Medicare Australia statistics
B	Proportion of ORP/LRARP procedures	98%	98%	98%	Advisory Panel
C	Number of ORP/LRARP procedures	4806	6049	7699	C=A * B
D	Cost per procedure	$2387	$2387	$2387	See Table 32
E	Current annual costs	$11,471,922	$14,438,963	$18,377,513	E=C * D
F	Number of da Vinci® systems in Australia	3	3	3	Advisory Panel
G	Number of LRARP procedures per da Vinci® system	300	300	300	Applicant
H	Number of LRARP procedures	900	900	900	H=F * G
I	Cost per LRARP procedure	$3149	$3149	$3149	See Table 32
J	LRARP costs in total	$2,834,100	$2,834,100	$2,834,100	J=H * I
K	Number of remaining ORP procedures	3906	5149	6799	K=C – H
L	Cost per ORP procedure	$2387	$2387	$2387	See Table 32
M	ORP costs in total	$9,323,622	$12,290,663	$16,229,213	M=K * L
N	Future annual costs	$12,157,722	$15,124,763	$19,063,313	N=J + M
O	Incremental costs	$685,800	$685,800	$685,800	O=N – E

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RP, radical prostatectomy.

Table 34 Aggregated financial impact of LRARP across other healthcare funders

		Year 1	Year 2	Year 3	Reference
A	Total patient population undergoing RP (projected)	4904	6172	7856	Medicare Australia statistics
B	Proportion of ORP procedures	95%	95%	95%	Advisory Panel
C	Number of ORP procedures	4806	6049	7699	C=A * B
D	Cost per ORP procedure	$8820	$8820	$8820	See Table 32
E	Current annual costs	$42,388,920	$53,352,180	$67,905,180	E=C * D
F	Number of da Vinci® systems in Australia	3	3	3	Advisory panel
G	Number of LRARP procedures per da Vinci® system	300	300	300	Applicant
H	Number of LRARP procedures	900	900	900	H=F * G
I	Cost per LRARP procedure	$12,320	$12,320	$12,320	See Table 32
J	LRARP costs in total	$11,088,000	$11,088,000	$11,088,000	J=H * I
K	Number of remaining ORP procedures	3906	5149	6799	K=C – H
L	Cost per ORP procedure	$8820	$8820	$8820	See Table 32
M	ORP costs in total	$34,450,920	$45,414,180	$59,967,180	M=K * L
N	Future annual costs	$45,538,920	$56,502,180	$71,055,180	N=J + M
O	Incremental costs	$3,150,000	$3,150,000	$3,150,000	O=N – E

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RP, radical prostatectomy.

LRARP will not reduce the overall number of radical prostatectomies provided in the coming years. LRARP will replace a limited proportion of all radical prostatectomies provided. Due to higher costs for Medicare, this substitution will contribute to higher costs.

Assuming a constant number of 900 LRARP procedures provided per year (three da Vinci® systems each providing 300 procedures annually), the financial impact of a positive recommendation of LRARP to Medicare can be estimated by multiplying the incremental costs per LRARP procedure with the number of performed LRARP services, resulting in additional costs to Medicare of $685,800 per year. These additional costs will continue for each subsequent year.

Each additional da Vinci® system installed in an Australian hospital, with a similar annual throughput of 300 procedures, results in additional annual costs of $228,600. An increased performance of da Vinci® systems would cause higher costs than considered in the projections provided and vice versa. It should be noted that the number of LRARP procedures provided in Australia is currently lower than the 900 procedures considered in the economic analysis — the present rate is about 170 per year; however, an increase should be expected in the near future. The Advisory Panel predicts that if unlimited resources were made available, it would be likely that LRARP procedures would make up the majority of radical prostatectomies performed in private hospitals. The uptake of LRARP would potentially be constrained by the need to train surgeons to use the technology and adequate patient throughput to maintain surgeons' LRARP procedure skills.

Additional costs of $3.15 million per year for healthcare funders other than Medicare can be expected. A significant component of this amount relates to the substantial

proportion of disposable equipment required to perform LRARP. Costs would be lower where the da Vinci® system may be used to perform other types of surgeries in addition to prostatectomies.

It is noteworthy that the overall costs for radical prostatectomies are expected to rise within the next few years. Although the number of services has not been projected based on epidemiological evidence, this scenario is supported by recent AIHW prostate cancer incidence projections (AIHW 2005c).

Conclusions

Safety

The results from the comparative studies showed that LRARP was associated with substantially lower estimated blood loss (EBL) and number of transfusions required compared with ORP. In studies with applicable patient populations and certain surgeon experience, the overall complication rate post-surgery was significantly lower in LRARP patients (5%) compared with ORP patients (16.3%). The rates of individual events were generally low (≤3.3% in LRARP and ≤4% in ORP). No deaths were reported in either treatment group. Significantly more patients who had undergone ORP (4%) experienced fever or pneumonia compared with those who had undergone LRARP (0%). No other significant differences in event rates were reported.

The non-comparative safety data were heterogeneous due to the variability in number of subjects included, type of study and population included. As expected, the ranges for EBL and transfusions were much broader than those reported in comparative studies. The proportion of LRARP patients experiencing postoperative complications ranged from nil to 32.5 per cent. The studies reporting a nil rate included very few patients (≤5) whereas the study reporting the highest rate included 40 patients.

It can therefore be concluded that compared with ORP, LRARP is at least equally as safe, if not safer.

Effectiveness

The evidence available for the assessment of comparative efficacy of LRARP and ORP (with comparative surgeon experience) consisted of two cohort studies that included a patient population applicable to this review. Of these studies one had some methodological issues, and the other study included only a small sample. A further two studies with uncertainties (regarding applicability of patient population and comparative surgeon experience) were also included. No randomised controlled trials were available.

None of the studies reported any primary efficacy outcomes, that is, long-term survival rates/tumour-free survival, or death rates. Secondary efficacy outcomes assessed in this review included disease recurrence, positive margin rate and quality of life.

There were no significant differences between patients who had undergone LRARP and ORP in biochemical recurrence rates, based on rising PSA levels post-surgery, in the only study reporting unbiased results. The three-month biochemical recurrence rate was the same in both treatment groups (~5%). However, the clinical importance of these immature results is questionable. Based on expert advice from the Advisory Panel, almost all cases of early detectable PSA post-surgery (within three months) can be attributed to metastatic disease. To allow a fair comparison between procedures, biochemical recurrence rates 12 months after surgery, where local recurrence is a contributor to the rate, is warranted.

The data relating to positive margins in organ-confined cancers showed that there were no significant differences in the rates between patients who had undergone LRARP (4.5%) and those who had undergone ORP (9.0%; RD: –5%; 95% CI: [15, 6]). The rates of total margin positivity, irrespective of pathological tumour stage, were similar between ORP and LRARP patients in both studies.

In one of the studies, a similar proportion of patients, 75 per cent versus 76.7 per cent of those who had undergone ORP and LRARP respectively, were continent of urine three months after surgery (Ahlering et al 2004b). The study by Tewari et al (2003b) reported longer-term data pertaining to urinary continence data. However, this study included only a subset of the population in this analysis, and few patient selection details were provided. This study may be prone to selection bias. Consequently, caution should be exercised in the interpretation of these results. The results showed that patients who had undergone LRARP achieved continence sooner after surgery than those who had undergone ORP. The 50 per cent return of continence occurred in 44 and 160 days, respectively ($p<0.05$). However, after approximately 400 days there was no difference between groups and most patients were continent of urine (~90%).

The study by Tewari et al (2003b) also reported postoperative erectile function and sexual function data. Again, only a subset of the population was included in the analyses. Patients who classified themselves as having normal pre-operative erectile function and sexual intercourse, and those who had a bilateral nerve-sparing procedure only were included. The direction of possible selection bias is difficult to determine. Hence, there is considerable uncertainty surrounding the results from these outcomes. The results showed that patients who had undergone LRARP had a faster return of erectile function after surgery compared with patients who had undergone ORP. Patients achieved a 50 per cent return of erectile function at a mean follow-up of 180 and 440 days after LRARP and ORP, respectively ($p<0.05$). Similarly, the return of sexual intercourse was also significantly faster in LRARP patients ($p<0.05$). The 50 per cent probability of return of sexual intercourse was achieved at a mean follow-up of 340 days in the LRARP patients. However, the ORP patients had still not achieved this at 700 days.

The mean postoperative pain score (using a visual analogue scale) on the first postoperative day was significantly lower in patients who had undergone LRARP compared with those who had undergone ORP ($p<0.05$).

It can therefore be concluded that the available data comparing LRARP with ORP in patients with clinically localised prostate cancer are not sufficiently mature to provide evidence of primary efficacy including long-term survival rates/tumour-free survival, or death rates. Studies of higher quality and with longer follow-up are warranted. Based on secondary efficacy outcomes, there appear to be no differences in biochemical recurrence rates and margin positivity. The results from this review indicated that LRARP might offer advantages in terms of less pain after surgery compared with ORP. Furthermore, the data pertaining to urinary continence, erectile dysfunction and sexual intercourse presented in one study indicated that LRARP patients regained urinary continence sooner and had a higher rate and faster resumption of erectile function and sexual intercourse. However, as previously mentioned, these results were based on a subset of the entire cohort, and lack of details regarding the selection of subjects renders these analyses prone to bias. It is difficult to determine the direction of bias. Consequently, although a difference between LRARP and ORP in terms of functional outcomes cannot be ruled out, neither can it be confidently confirmed.

Cost comparison

Since no bias-free evidence that could be used to account for any differences in effect was available, a comparison of direct treatment costs was provided. The results indicated that LRARP is associated with markedly higher direct treatment costs. The total direct costs were calculated to be $15,469 per LRARP procedure versus $11,207 per ORP procedure. This difference is mainly caused by extra costs for reposable and disposable equipment needed for each procedure. Additional costs for a conjoint surgeon as well as da Vinci® system purchasing and maintenance costs also contribute to increased direct treatment costs. These additional costs are only partially offset by savings associated with a shorter hospital stay (approximately two days versus 7.5 days) and a reduced need for blood transfusions.

The key assumptions in the cost comparison analysis were:

- The considered da Vinci® system purchase, maintenance and equipment costs for the LRARP procedure reflect the costs in the Australian setting.
- The average hospital length of stay of two days following LRARP reflects current clinical practice in the Australian setting.

The total costs for the healthcare system are presented separately for Medicare and other healthcare funders: The additional annual costs are calculated to be $685,800 for Medicare and $3.15 million for other healthcare funders.

The key assumptions for the calculation of the financial impact were:

- The future number of MBS services will follow the patterns observed during past years.
- The number of available da Vinci® systems will not increase during the next three years and will remain stable at three systems.
- The number of procedures performed with each da Vinci® system is stable at 300, as provided by the Applicant.
- The costs per patient undergoing either LRARP or ORP are assumed to be stable over the next three years.

Should the number of da Vinci® systems be increased, the incremental cost for each additional system for Medicare would be $228,600 per annum and $1.05 million for other healthcare funders.

Recommendation

The MSAC has considered the safety, effectiveness and economic issues of laparoscopic remotely assisted radical prostatectomy (LRARP) compared with open radical prostatectomy. This procedure is being utilised under current funding arrangements in the public and private sectors in Australia. MSAC finds the procedure is at least as safe as and possibly safer than open radical prostatectomy. The procedure is likely to be as effective and may have some advantages over open radical prostatectomy. At present there is uncertainty about the comparative cost-effectiveness.

MSAC recommends that current funding arrangements for LRARP remain the same at the present time.

- The Minister for Health and Ageing accepted this recommendation on 24 August 2006.-

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	**Expertise or affiliation**
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Mary Turner	Australian Health Ministers' Advisory Council representative
Dr Kwun Fong	thoracic medicine
Dr Debra Graves	medical administrator
Professor Jane Hall	health economics
Professor John Horvath	Chief Medical Officer, Department of Health and Ageing
Ms Samantha Robertson	Department of Health and Ageing representative
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Donald Perry-Keene	endocrinology
Dr Ray Kirk	health research
Dr David Gillespie	gastroenterology

Dr Ewa Piejko	general practice
Ms Sheila Rimmer	consumer health issues
Dr David Wood	orthopaedic surgery
Professor Frederick Khafagi	nuclear medicine
Professor Ken Thomson	radiology
Dr Douglas Travis	urology

Appendix B Advisory Panel

Advisory Panel for MSAC application 1091
Laparoscopic remotely assisted radical prostatectomy

Dr Paul Craft (Chair) MBBS, MPH, FRACP Director Medical Oncology Unit Canberra Hospital	Member of Medical Services Advisory Committee
Mr Manish Patel MBBS, MMed, FRACS Urological Oncologist Westmead Private Hospital	Nominee of Australian and New Zealand Association of Urological Surgeons
Mr Justin Peters MBBS, FRACS Senior Consultant Urologist Royal Melbourne Hospital	Nominee of Australian and New Zealand Association of Urological Surgeons
Dr Doug Travis MBBS FRACS (UROL) Head of Urology Western Network, Melbourne	Member of Medical Services Advisory Committee
Mr Keith Williams Diploma in Youth Leadership from the YMCA College of Youth Leadership	Nominee of Consumers' Health Forum of Australia

Evaluators for application 1091

Ms Mia Mudge BAppSci Senior Heath Outcomes Analyst	M-TAG Pty Ltd, a unit of IMS
Ms Antje Smala BAgEng(Hons) BEng(Hons) Senior Health Economist	M-TAG Pty Ltd, a unit of IMS

Members from the Department of Health and Ageing for application 1091

Ms Alex Lloyd Senior Project Manager	Health Technology Section

Appendix C Studies included in the review of safety

The comparative and non-comparative studies that were included in this review of safety are listed in **Table 35.** Some study details and safety outcomes are summarised. It should be noted that some studies did not report clinical stage and/or patient diagnoses, and as such, applicability of these studies could not be determined. However, considering that LRARP is performed only in patients who have prostate cancer, it can be assumed that all patients' diagnoses are for prostate cancer and these studies should be included. It is noted in **Table 35** whether the results are applicable to this review or if applicability is uncertain ('uncertain applicability'). Some of the comparative studies did not report the comparative experience of surgeons who performed LRARP and ORP. It is therefore not possible to estimate whether the comparison is fair or if experience has biased the results. These studies are labelled 'surgeon experience uncertain' whereas studies with known and comparable surgeon experience are identified as 'surgeon experience certain'.

Studies in which patients were recruited from the same centre(s) and reported by the same author(s) have been grouped together and are separated by broken lines. These studies, while they may contain different numbers of patients, are likely to have considerable overlap in terms of included patients, and if not identified would result in double-counting of events. During data extraction, no assumptions were made about the occurrence of an event; entries in data fields were based on whether a publication explicitly stated that an event had occurred or not, that is, a zero value was assigned *only* if reported. In comparative trials, even if one treatment arm reported an event, unless the other treatment arm explicitly stated that the event had not occurred, '–' was entered into the field.

Table 35 Studies included in the comparative and non-comparative safety analyses

Author (year)	N	Study design	Patient population/	EBL mean (mL)	Transfusion rates n/N (%)	Deaths n/N (%)	Catheter removal, mean (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Comments
Comparative safety										
Ahlering (2004b)	60	Cohort with historical control	Prostate cancer (T1–T3)	103	0/60 (0.0)	–	7	0/60 (0.0)	4/60 (6.7)	Applicable, comparative surgeon experience certain
Binder (2002)	50	Comparative case-series	Diagnosis not clear	–	14/50 (28.0)	–	–	–	–	Applicability uncertain, comparative surgeon experience uncertain
Tewari (2003b)	200	Prospective, consecutive cohort study	Most had clinically localised prostate cancers	153	0/200 (0.0)	0/200 (0.0)	7	0/200 (0.0)	9/200 (4.5)	Applicable, comparative surgeon experience certain
DiMarco (2005)	97	Retrospective review of matched LRARP and ORP patients during the same time period	Clinically localised prostate adenocarcinoma	–	5/97 (5.2)	–	–	–	–	Applicable, comparative surgeon experience uncertain
Balaji (2005)	29	Cohort	Prostate cancer, but staging is not detailed	328	–	–	–	–	–	Applicability uncertain, comparative surgeon experience uncertain
Farnham (2005)	176	Prospective cohort	Prostate cancer, but staging is not detailed	191	1/176 (0.5)	–	–	–	–	Applicability uncertain, comparative surgeon experience uncertain
Non-comparative safety studies										
Abbou (2001)	1	Case report	T1c tumour	300	–	–	3	–	–	Applicable
Ahlering (2003)	45	Case series	Clinically localised prostate cancer (one patient with T3a)	134	0/45 (0.0)	–	–	0	6/134 (4.5)	Applicable. Urinary extravasation (n=2) treated conservatively; prolonged hospitalisation because of leg pain due to prolonged operative time and stirrup placement (n=1), bleeding from port site (n=1), DVT (n=1), anastomitic disruption (n=1)
Ahlering (2004a)	140	Case series, consecutive	Prostate cancer (T1c-T3) <1% with T3	Group 1: 129 Group2: 102	–	–	–	–	–	Applicable. Reports results separately for cases 1–50 (group 1) & cases 51–140 (group 2). Reported that no complaints or clinical complications were reported regarding stable migration

Author (year)	N	Study design	Patient population/	EBL mean (mL)	Transfusion rates n/N (%)	Deaths n/N (%)	Catheter removal, mean (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Comments
Ahlering (2005)	48	Case series	Not stated	Group 1: 90 Group 2: 90	0	–	–	–	Group 1: 1/25 (4) Group 2: 2/25 (8)	Applicability uncertain. Reports results for LRARP using standard technique (group 1) & temporary vascular occlusion (group 2). No patients had postoperative delayed bleeding
Ball (2005)	110	Case series	Not stated	–	–	–	–	–	6/90 (6.7)	Applicability uncertain. Prolonged catheterisation secondary to urinary leakage required in 6/90 patients (6.7%) initially treated. Anastomosis technique was subsequently changed. No further urinary leakage or short-term complications reported
Bentas (2003)	40	Case series	Clinically localised prostate cancer (T1b–T2b)	570	13/40 (32.5)	0	16.7	2/40 (5.0)	13/40 (32.5)	Applicable. Pulmonary embolism (n=2) considered serious; DVT (n=1) considered a major complication. Remaining complications were considered minor: obturator nerve injury (n=1); trocar injury to epigastric artery (n=1); venous plexus bleeding (n=2); UTI (n=2); prolonged anastomotic leak (n=4). Two patients were converted to laparotomy. No complications were considered related to da Vinci® system
Binder (2001)	10	Case series	Clinically localised prostate cancer (T1b–T2b)	–	1/10 (10.1)	–	18[a]	1/10 (10.0)	–	Applicable. Laparoscopy abandoned (n=1) because of difficulty in controlling hemostasis (see conversion). 9 (90%) patients experienced mild to moderate stress incontinence post-catheterisation
Costello (2005)	122	Case series	Prostate cancer T1a–T3a	–	4/122 (3.3)	–	8.4	0/122 (0.0)	19/122 (15.6)	Applicable. Prolonged D/T leak (n=6); bladder neck restenosis requiring BNI (n=5); acute urinary retention (n=2). Other complications (n=1) clot retention (readmitted), pneumaturia (settled with extended catheterisation), anastomosis breakdown (conservative management), rectal injury (over-sewn), pelvic haematoma & recto-urethral fistula,

Author (year)	N	Study design	Patient population/	EBL mean (mL)	Transfusion rates n/N (%)	Deaths n/N (%)	Catheter removal, mean (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Comments
										paralytic ileus (conservative management)
Dakwar (2003)	45	Case series	Not stated	476	–	–	8.7	7/45 (15.6)	–	Applicability uncertain
Dinlenc (2004)	1	Case report	Prostate adenocarcinoma	–	–	–	8	–	–	Applicability uncertain. Self-suctioning drain left in pelvis for 48 hours. No other complications reported
Eto (2005)	1	Case report	Clinically localised prostate cancer (T1c)	500	–	0	7	–	–	Applicable
Gettman (2003)	4	Consecutive, case series	Localised prostate cancer	1013	–	–	2.7	0/4 (0.0)	–	Applicable
Hu (2005)	208	Retrospective cohort	Not stated	313	5/208 (2.4)	–	–	0/208 (0.0)	–	Applicability uncertain. Intra-operative complication rate 2.4%
Joseph (2003)	50	Retrospective cohort	Clinically localised prostate cancer (T1c-T2b)	206	0/50 (0.0)	0	–	–	4/50 (8.0)	Applicable. 3 bladder neck contractures treated by urethral dilation, 2 urinary leaks treated by prolonged catheterisation
Kaouk (2003)	1[b]	Case report	Clinically localised prostate cancer (T1c)	300	–	–	3 (weeks)	0/1 (0.0)	0/1 (0.0)	Applicable
Kong (2005)	5	Case series	Clinically localised prostate cancer	245	–	–	–	–	–	Applicable
Lee (2005)	231	Case series	Clinical stage not reported	122	0/231 (0.0)	–	7	–	21/231 (9.1)	Applicability uncertain. Overall complication rate included 3 major complications: DVT; rectal injury; incarcerated inguinal hernia
Meininger (2005)	20	RCT (comparing two techniques)	Not stated	–	–	–	–	0/20 (0.0)	–	Applicability uncertain. No operative complications
Vattikuti Institute Menon (2002a)	40	Prospective cohort (CLRP versus LRARP)	Clinically localised prostate cancer	256	0/40 (0.0)	0/40 (0.0)	–	–	2/40 (5.0)	Applicable. Transient ileus (n=1) treated conservatively (bowel rest & IV fluids) for 72 hours. One patient with severe arthritis had a frozen knee

Author (year)	N	Study design	Patient population/	EBL mean (mL)	Transfusion rates n/N (%)	Deaths n/N (%)	Catheter removal, mean (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Comments
Menon (2003b)	100	Case series, prospective	Clinically localised prostate cancer	150	–	–	4.2	–	4/100 (4)	Applicable
Menon (2003a)	100	Case series	Not stated	149	0/100 (0.0)	0/100 (0.0)	–	0/100 (0.0)	8/100 (8.0)	Applicability uncertain. Port site haematoma (n=1), urinary retention (n=1), constipation (n=2), ileus (n=1), DVT (n=1), incisional hernia (n=1)
Menon (2003c)	200	Case series	Clinically localised prostate cancer (T1c–T2b)	153	0/200 (0.0)	–	7	–	8/200 (4)	Applicable. Port hernia (n=3), ileus (n=3), delayed bleeding (n=1), DVT (n=1)
Tewari (2003a)	250	Case series	Clinically localised prostate cancer	150	–	–	4.2	–	10/250 (4.0)	Applicable
Tewari (2005b)	530	Case series	Clinically localised prostate cancer	153	0/530 (0.0)	–	7	–	8/500 (1.6)	Applicable. Port hernia (n=3), ileus (n=3), delayed bleeding (n=1), DVT (n=1)
Mikhail (2005)	120	Prospective case series	Not stated	323	–	–	6.4	7	–	Applicability uncertain. Five patients were converted due to difficult dissection, one due to incidental bladder tumour & one due to bladder perforation
Pasticier (2001)	5	Consecutive case series	Clinically localised prostate cancer (T1c–T2a)	800	0/5 (0.0)	–	6.5	–	0/5 (0.0)	Applicable. One patient left hospital with a catheter –removed after 9 days – patient had stress incontinence
Patel et al (2005)	200	Case series	Clinically localised prostate cancer (T1c–T2b)	75.1	0/200 (0.0)	0/200 (0.0)	7.9	–	2/200 (1.0)	Applicable. *Postoperative complications*; one patient was readmitted for postoperative gross hematuria and was diagnosed with a pelvic hematoma from a ruptured anastomotic stitch. Hematuria resolved & the anastomosis healed without intervention. One bladder neck contracture occurred which required dilation *1% operative complications (2/200):* two small rectal injuries that were closed with a 3-layer closure. Neither of the patients had any adverse outcomes from the injury

Author (year)	N	Study design	Patient population/	EBL mean (mL)	Transfusion rates n/N (%)	Deaths n/N (%)	Catheter removal, mean (days)	Conversion rates n/N (%)	Postoperative complications n/N (%)	Comments
Patel (2005)	450	Prospective case series	Prostate cancer (clinical stage not reported)	47	–	0/450 (0.0)	7.2	–	–	Applicability uncertain. Intra-operative complication rate=1%
Perer (2003)	1	Case report	Prostate cancer (clinical stage not reported)	300	–	–	–	–	–	Applicability uncertain
Rassweiler (2001)	6	Case report	Prostate cancer T2a–T3 (1 patient T3)	–	1/6 (16.7)	–	5[a]	–	–	Applicable. No intra-operative complications
Sarle (2005)	1	Case report	Adenocarcinoma of the prostate	400	–	–	–	–	–	Applicability uncertain. No intra-operative complications
Sim (2004)	17	Case series	Adenocarcinoma of the prostate	494	3/17 (17.6)	0/17 (0.0)	9.8	0/17 (0.0)	1/17 (5.9)	Applicability uncertain. One patient had pulmonary atelectasis that resolved postoperative day 3, following chest physiotherapy. 3 patients had moderate urinary incontinence
Wilson (2005)	191	Cohort (CLRP versus LRARP)	Prostate cancer	–	4/191 (2.1)	–	7	1/191 (0.0)	–	Applicability uncertain. Converted to CLRP. Approximately 2% received at least one unit of transfusion in the postoperative period
Wolfram (2003)	81	Case series	Not stated	300[a]	10/81 (12)	–	14	–	–	Applicability uncertain

Abbreviations: CLRP, conventional laparoscopic radical prostatectomy; DVT, deep vein thrombosis; EBL, estimated blood loss; LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; RCT, randomised controlled trial.

Appendix D Studies included in the review of efficacy

The studies included the analysis of efficacy are outlined in **Table 36**. Of the studies included in the table, one reported only the learning curve of LRARP and compared the positive margin rates of a novice LRARP surgeon with the same surgeon's ORP procedures within a defined period (Kella et al 2005). This study did not report comparative efficacy of experienced LRARP and ORP surgeons. It has been included in the **Learning curve of LRARP** section and is not presented in the efficacy section. This study did not report safety outcomes.

Similarly, the study by Binder et al (2002) reported the initial surgeon experience of LRARP and compared this with previous ORP cases performed by experienced ORP surgeons. The level of experience is felt likely to have biased the results. Again, the results from this study are included in the **Learning curve of LRARP** section but not the efficacy section. The study reported some safety data and was included in the safety section. In general, the reporting in this study was very poor.

Two studies (Springhart et al 2005; DiMarco et al 2005) did not report the level of experience of LRARP and ORP surgeons. Whilst these articles have been included in the efficacy section, they have been designated 'surgeon experience uncertain' and data from these studies were not pooled with studies including only experienced ORP and LRARP surgeons. The results from DiMarco et al (2005) reported safety outcomes and was included in the safety section. Conversely, Springhart et al (2005) did not report safety outcomes.

Studies by Binder et al (2002) and Springhart et al (2005) did not report diagnosis or clinical staging of patients, indicating that applicability to the population of interest for this review of clinically localised prostate cancer could not be determined. Results from these studies have been classified as having uncertain applicability throughout the efficacy section.

Tewari et al (2003b) presented an extension of an initial study conducted at the Vattikuti Urology Institute (VUI) that compared ORP with LRARP (Menon et al 2002b). Tewari et al (2003b) included more patients who were followed-up for a longer period of time. Hence, the results from Tewari et al (2003b) were included in the analysis, and data from Menon et al (2002b) were included only when they provided further detail about different outcomes or were from different points in time.

No systematic reviews comparing ORP and LRARP were identified in the literature search.

In light of theses results, only two comparative studies (Ahlering et al 2004b; Tewari et al 2003b) reported results that compared experienced LRARP and ORP surgeons performing procedures on patients with clinically localised prostate cancer (applicability certain). Issues regarding potential biases for different outcomes are discussed in the efficacy section.

Table 36 Characteristics and quality assessment of studies included in the efficacy analysis

Author (year)	Study design	Setting	N	Study population	Surgical approach	NHMRC level	Study quality	Applicability
Published studies								
Ahlering (2004b)	Cohort, with historical control *Objective*: To compare the results from one trained open-approach surgeon with the same surgeon performing LRARP (after 45 initial learning cases)	1 site, USA	120	The last 60 open radical prostatectomies performed at the centre (consecutive) and LRARP cases 46–105 (consecutive) Majority of patients had clinical localised prostate cancer	LRARP (similar to Vattikuti Institute prostatectomy technique)[b] ORP (standard retropubic approach)	III-3	Not randomised. Patients were assigned to one of the two treatment arms based on their personal preferences and no attempts were made to pre-select patients for LRARP Loss to follow-up not reported Study groups were comparable at baseline in terms of the distribution of prognostic factors Follow-up was insufficient for primary clinical outcomes to occur	Majority (98.7%) of patients included were applicable to patient population in the research question (clinically localised prostate cancer, T1–T2) Applicable
Binder (2002)	Comparative case-series *Objective*: not stated	1 site, Germany	100[a]	Pair wise comparison of the first 50 patients undergoing LRARP and patients undergoing ORP Diagnosis and clinical staging is not stated	LRARP: the first 37 procedures performed as combined ascending and descending approach. Seven of these were extraperitoneal approach Subsequent 17 surgeries were performed using a modified Guillonneau and Vallancien technique ORP: standard retropubic technique	III-3	Loss to follow-up not reported. Difficult to assess number of subjects included in the analysis for each outcome Data very poorly reported No information on baseline demographics or patient/tumour characteristics. This may have introduced serious confounding bias The surgeon performing LRARP was novice whereas the ORP surgeon was experienced. Results from this study can therefore be used to assess the learning curve of LRARP in a novice, but does not enable a fair comparison to be made between surgical techniques. The level of experience is likely to introduce confounding bias. Results included in **Learning curve of LRARP** and safety section	Applicability can not be assessed since there is no reporting of clinical staging and patients' characteristics Applicability uncertain

Author (year)	Study design	Setting	N	Study population	Surgical approach	NHMRC level	Study quality	Applicability
							The first 30 LRARPs were performed by 1 of 2 surgeons, whereas the last 25 were performed by 1 surgeon Measurement of outcomes was not blinded Follow-up was insufficient for primary clinical outcomes to occur Overall, the methodology is very poorly reported and the quality of this study is consequently poor	
Tewari (2003b)	Prospective, consecutive cohort study *Objective*: To prospectively compare surgical, oncological and functional outcomes of LRARP and ORP	1 site, USA	300	Prostate cancer patients with Gleason scores ≥6; surgical candidates with 10 years life expectancy Majority of patients had clinically localised prostate cancer	LRARP (Vattikuti Institute prostatectomy) ORP (retropubic, the anatomical technique by Walsh)	III-2	Lost to follow-up. 2 (1%) LRARP and 1 (1%) ORP patients were aborted. It is unclear whether these patients were lost to follow-up The mean number of days of follow-up was significantly lower in LRARP patients than in ORP patients (236 versus 556 days respectively, $p<0.05$). This may have introduced bias in favour of LRARP both for safety and efficacy (particularly the PSA recurrence rates) Measurement of outcomes was not blinded Follow-up was insufficient for primary clinical outcomes to occur Study groups were comparable at baseline in terms of the distribution of prognostic factors One team performed LRARP whereas eight different surgeons performed ORP ORP surgeons had performed at least 100 procedures each (with a combined experience of 1400	Majority (97.7%) of patients included were applicable to patient population in the research question (clinically localised prostate cancer, T1–T2) Applicable

Author (year)	Study design	Setting	N	Study population	Surgical approach	NHMRC level	Study quality	Applicability
							procedures). 400 LRARPs performed Nov—Dec 2002. It appears that the 200 LRARPs included in the study were included in the 400 total LRARPS performed at the Institute. Therefore, both ORP and LRARP surgeons were experienced Margins on organ-confined cancers were considered positive if there was tumour present at the inked margin in the ORP group. In the LRARP patients, apical margin was considered positive if cancer was seen in the intra-operative distal biopsies. The difference in definition of positive margins between treatment groups is likely to favour results towards LRARP having lower margin positivity rate	
Menon (2002b)	Prospective cohort study *Objective:* To assess whether LRARP enhances the precision of anatomic dissection; and increases the feasibility compared with radical retropubic prostatectomy	1 site, USA	60	Clinically localised prostate cancer patients who elected surgical treatment Patients were considered candidates for LRARP if they were medically fit to undergo surgery, weight <250 lb, waist measurement <45 in, BMI <35. Previous abdominal surgery was not an exclusion criterion	LRARP: either Vattikuti Institute prostatectomy or Montsouris technique ORP (retropubic – the anatomical technique by Walsh)	III-2	One team performed LRARP whereas eight different surgeons performed ORP It appears that the ORP surgeons were experienced whereas the LRARP surgeon was novice. This would bias the results in favour of ORP. The LRARP surgeon was mentored whereas ORP surgeons were not Measurement of outcomes was not blinded The mean PSA level at baseline (considered a prognostic factor) was significantly different between groups with higher value in LRARP patients. This may indicate that these patients were more severe at baseline. This was not accounted	Included patients applicable to the population in the research question (clinically localised prostate cancer, T1–T2) Applicable

Author (year)	Study design	Setting	N	Study population	Surgical approach	NHMRC level	Study quality	Applicability
							for in the analysis and may have confounded the results Follow-up insufficient for primary clinical outcomes to occur	
Unpublished American Urological Association abstracts 2005								
Springhart (2005)	Prospective cohort	1 site, USA	69	Prostatectomy candidates scheduled to undergo either LRARP or ORP between July 2002 and July 2004	LRARP (not stated) ORP (perineal)	III-2	Surgeon experience not mentioned Loss to follow-up not reported Patients' disease staging unknown Study groups were comparable at baseline in terms of age and pre-operative urinary summary score (urinary continence was the assessed outcome) Measurement of outcomes was not blinded	Clinical staging of patients unknown, therefore difficult to determine applicability Applicability uncertain
DiMarco (2005)	Retrospective review of matched LRARP and ORP patients during the same time period	1 site, USA	291	Patients with clinically localised adenocarcinoma of the prostate	LRARP (not stated) ORP (retropubic)	III-3	Subjects were matched for age, PSA, clinical stage & biopsy Gleason score LRARPs & ORPs performed during the same time period Unclear if all patients in the specified time period were included (possible selection bias) Unknown how many surgeons were involved & their experience. Not possible to determine if surgeon skill biased results or in which direction Measurement of outcomes was not blinded Loss to follow-up not reported	Only included patients with clinically localised prostate carcinoma, therefore, the results are applicable to this review Applicable

Author (year)	Study design	Setting	N	Study population	Surgical approach	NHMRC level	Study quality	Applicability
Kella (2005)	Comparative case series Assessing learning curve of LRARP	1 site, USA	350	Prostatectomy candidates	Not stated	III-3	One surgeon performed his first 29 cases of LRARP and performed the rest with ORP. He was a novice LRARP surgeon but experienced ORP surgeon The aim of the study was not to compare ORP and LRARP, rather to determine whether surgical experience regardless of approach predicts positive surgical margins No safety outcomes were reported Therefore, this study is not included in the efficacy section, but is discussed in the section Learning curve of LRARP	Clinical staging of patients unknown, therefore difficult to determine applicability. Applicability uncertain

Abbreviations: AUA, American Urological Association; BMI, body mass index; LRARP, laparoscopic remotely assisted radical prostatectomy; NHMRC, National Health and Medical Research Council; ORP, open radical prostatectomy; PSA, prostate specific antigen.

[a] The number of subjects included appears to vary throughout the article.

[b] Except puboprostatic ligament and dorsal venous complex are completely dissected and divided wit an endovascular stapler.

Appendix E Flow chart

Figure 11 outlines the potential clinical pathway (current and proposed) for the treatment of clinically localised prostate carcinoma for patients suitable for radical prostatectomy with curative intent.

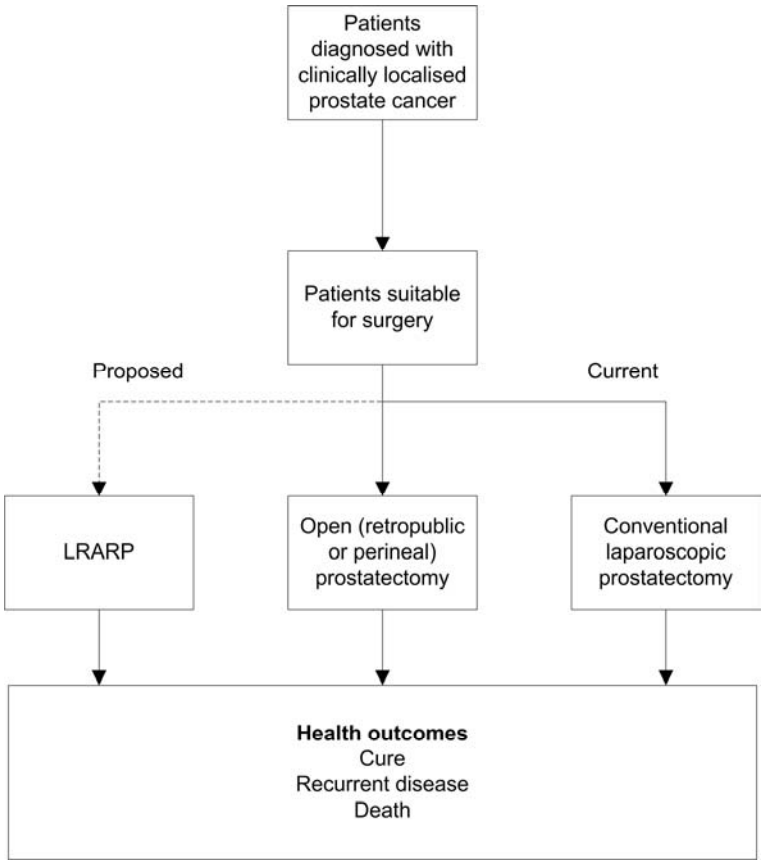

Figure 11 Current and proposed treatment pathways for the management of prostate malignancies

Abbreviation: LRARP, laparoscopic remotely assisted radical prostatectomy.

Appendix F Studies included in economic review

Table 37 features literature data for length of stay (LOS), discharge from hospital, operation time and da Vinci® system set up time.

Table 37 Literature data for LoS, discharge from hospital, operation time and da Vinci® system set up time

Study	Country	N	Duration of hospital stay in days (range)	Patients discharged within 24 hours (%)	Operation time in minutes ± SD (range)	Da Vinci® system set up time in minutes ± SD (range)	Comments
Ahlering (2003)	USA	45	–	–	–	23	Other data than the reported da Vinci® system set up time have not been considered
Ahlering (2004b)	USA	60	1.1	NA	231		
Ahlering (2005)	USA	48	NA (1–4)	NA	NA		Standard technique: hospital stay 1–2 days (n=24), temporary vascular occlusion: 1–4 days (n=24)
Balaji (2005)	–	29	NA	NA	413 ± 29		36% of patients LoS >3 days
Bentas (2003)	D	40	17.1 ± 6.8 [a]	NA	498 ± 168 (246–780)	60 or 96	Da Vinci® system set up time estimated by subtracting the reported time of use of da Vinci® system from the given total operative time ('skin to skin') Inconsistent reports for total operative time (558 and 594 minutes)
Bernstein (2005)	USA	68	1.9 ± 1.05	NA	261 ± 85.2		
Gettman (2003)	F	4	5.3	NA	274		
Hu (2005)	USA	208	NA	NA	204		
Kong (2005)	Korea	5	2.5	NA	154 195		Including preservation of neurovascular bundle: 185 minutes (n=2) W/w non-nerve sparing: 154 (n=2) W/w bilateral pelvic lymphadenectomy: 195 minutes (n=1)
Lee (2005)	USA	231	NA	98	147		Operation time measured from trocar placement until last stitch
Lyon (2005)	USA	120	NA	NA	321		Presenting technique of antegrade nerve preservation (ANP) Lyon et al and Mikhail et al are reporting on the same patient sample
Meininger (2004)	D	10 10	NA	NA	595 ± 73.3 649.4 ± 60.2		Intraperitoneal LRARP, w/w bilateral pelvic lymphadenectomy Extraperitoneal LRARP, w/w bilateral pelvic lymphadenectomy No information about surgeon experience level
Menon (2003c)	USA	200	NA (<1–5)	93	NA (71–315)		Menon et al 2003 & Tewari et al 2005 report the same patient sample

Study	Country	N	Duration of hospital stay in days (range)	Patients discharged within 24 hours (%)	Operation time in minutes ± SD (range)	Da Vinci® system set up time in minutes ± SD (range)	Comments
Menon (2003a)	USA	100	–	–	–	20	Time from anaesthesia to start of dissection. Data other than the reported da Vinci® system set up time were not considered due to inclusion of Menon et al (2003c)
Mikhail (2005)	USA	120	1.8	NA	NA		Mikhail et al and Lyon et al report the same patient sample
Pasticier (2001)		5	5.5 (4–7)	NA	222 (150–381)	93 (76–149)	Operation time from dissection to final stitch of anastomosis
Patel et al (2005)	USA	200	NA (1–3)	95	141	10	
Perer (2003)	USA	1	NA	100	–	–	Data on operation and da Vinci® system set up time were not considered due to Perer et al & Ahlering et al reporting the same population
Rassweiler (2001)	D	6	NA	NA	315 (242–480)	47 (40–55)	Operation time includes pelvic lymph node dissection
Sarle (2005)	USA	1	NA	100	208		Case report for a patient with large median lobe
Sim (2004)	Singapore	17	2.7 ± 1.3 (1–5)		247–43 (170–330) median 240	34 ± 18 (15–60)	Operation times for: Patient 1–8, Montsouris technique: 284 minutes Patient 9–17,Vattikutti technique: 215 minutes
Tewari (2005b)	USA	530	1.2	93	160 ± 28 (71–135)		Considering the reported mean time for surgery, the upper range seems to be wrong but is in line with data reported by Menon et al 2003. The same patient sample is reported by both
Wilson (2005)	USA	191	NA	NA	204 [b)]		Transperitoneal modified Montsouris technique
Wolfram (2003)	D	81	NA	NA	250 (150–390)[b]		Modified Montsouris technique
Weighted average			1.4 (1–7) n_{total} =812	87% (7–100%) n_{total} =1060	205 (71–780) n_{total} =1625	17.13 (10–93) n_{total}=373	

Abbreviation: D, Germany; F, France.

[a] Data on hospital stay have not been considered for averaging, due to being expected to be caused by healthcare system and reimbursement conditions

[b] Median time

Appendix G Economic variables

Hospital service costs per LRARP procedure

Table 38 Estimation of hospital service costs per LRARP procedure

	DRG M01Z Major male pelvic procedures		Classification	Weighted average per day/procedure	Average length of hospital stay (days)	Fixed costs per LRARP procedure	Marginal costs per LRARP procedure
	Public hospitals	Private hospitals					
Number of separations	722	2182					
Average # separations	2904						
Length of stay (days)	7.49	7.56					
Average LoS	7.53						
Costs							
Ward medical	$49.46	$4.47	Marginal	$53.93	2.0		$107.86
Ward nursing	$78.84	4151.67		$230.51	2.0		$461.02
Non-clinical salaries	$13.91	$14.11	Fixed	$28.02	–	$28.02	
Pathology	$119.59	$23.29		$144.88	–	$142.88	
Imaging	$37.79	$21.04		$58.83	–	$58.83	
Allied	$2.79	$4.07	Marginal	$6.86	2.0		$13.72
Pharmacy	$63.15	$92.42	Fixed	$155.57	–	$155.57	
Critical care	$10.36	$61.92	Marginal	$72.28	2.0		$144.56
Operating rooms	$870.43	$1967.86	Fixed	$2838.29	–	$2838.29	
Emergency departments	$7.71	$9.77		$17.48	–	$17.48	
Supplies	$15.63	$49.20	Marginal	$64.83	2.0		$129.66
Special procedure suites	$0.33	$4.07		$4.40	2.0		$8.80
Prostheses	$24.86	$133.75	Fixed	$158.61	–	$158.61	
On-costs	$118.10	$544.75		$662.85	–	$662.85	
Hotel	$11.35	$65.89	Marginal	$77.24	2.0		$154.48
Depreciation	$70.36	$430.54	Fixed	$500.90	–	$500.90	
Total						$4563.43	$1020.10

Based on AR-DRG version 4.2, round 7, 2002–2003
Abbreviation: DRG, diagnosis related group.

Indirect costs

Indirect costs refer to lost productivity during an employee's absence from work due to illness, injury or death. Other possible contributors to productivity losses include decreased workplace productivity or workers' absences to enable them to provide care for family members.

Indirect costs have been calculated based on the human capital approach, meaning that, each lost working day is assigned an average wage value.

LRARP

Based on estimates provided by the Advisory Panel, the length of absence from work has been estimated at about 2.5 weeks (12.5 working days). The considered labour participation and unemployment rates are data for the whole population. (Australian Bureau of Statistics 2005c)These data cannot be specified specifically for patients undergoing radical prostatectomy.

Based on the number of claims for MBS items 37210 and 37211 in 2004-2005, the majority of services were performed for patients aged 55–64 (51% of all services) and 65–74 (33% of all services), respectively (Australian Government Medicare Australia 2005). Considering the age distribution for the affected population, and a probability of lower labour work force participation and earning levels, this calculation approach may contribute to an overestimation of indirect costs. Attempts have been made to address this possibility by considering earnings for all employees (adults and non-adults, full and part-time employees). (Australian Bureau of Statistics 2005b)

The indirect costs per patient undergoing LRARP are calculated to be $1218.

Table 39 Indirect costs due to LRARP

	Description	Value	Reference
A	Weekly wage [a]	$792.90	ABS (2005b)
B	Daily wage	$158.58	B=A/5
C	Unemployment rate	5%	ABS (2005c)
D	Labour force participation rate	64.7%	ABS (2005c)
E	Lost working days [b]	12.5	Expert panel estimate
F	Indirect costs per case	$1218.39	F=B*(1–C)*D*E

Abbreviations: ABS, Australian Bureau of Statistics; LRARP, laparoscopic remotely assisted radical prostatectomy.
a Seasonally adjusted estimates for all employees total earnings in private and public sectors.
b Assumes five working days per week.

ORP

Data showing the number of lost working days due to ORP are not available. Based on estimates from the Advisory Panel, a mean duration of five weeks was assumed (25 working days) contributing indirect costs of $2437 per patient undergoing ORP (see **Table 40**).

Table 40 Indirect costs due to ORP

	Description	Value	Reference
A	Weekly wage [a]	$792.90	ABS (2005b)
B	Daily wage	$158.58	B=A/5
C	Unemployment rate	5%	ABS (2005c)
D	Labour force participation rate	64.7%	ABS (2005c)
E	Lost working days [b]	25	Expert panel estimate
F	Indirect costs per case	$2436.78	F=B*(1–C)*D*E

Abbreviations: ABS, Australian Bureau of Statistics; ORP, open radical prostatectomy

[a] Seasonally adjusted estimates for all employees total earnings in private and public sectors

[b] Assumes five working days per week

Appendix H Indicative cost-utility analysis

Currently, there is no evidence free from potential bias of a difference in effect between the treatment approaches. It should be noted that **no evidence of a difference in effect** is different from **evidence of no difference in effect**. In addition to the cost comparison presented as the main result of this economic assessment, an indicative cost-effectiveness is also presented, showing estimated value for money if the differences observed between LRARP and ORP were true.

This indicative cost-utility analysis found that LRARP could be associated with lower overall direct and indirect costs and an increase in quality-adjusted life years (QALYs) for patients undergoing radical prostatectomy. Uncertainty, mainly concerning cost-assumptions, has been addressed in a range of sensitivity analyses. Results were very sensitive to changes.

The details of the indicative cost-utility analysis are presented in this section.

Effectiveness

Measurement of effectiveness has been proposed to include both the proportion of patients who are continent of urine and those who retain sexual potency (ability to perform sexual intercourse) following LRARP and ORP.

The outcome effect was derived from the Kaplan-Meier (KM) curves presented by Tewari et al (2003b).

Effects on urinary continence from either LRARP or ORP are proposed as indicated at the end of year one following treatment and at the very last observation point (Tewari et al 2003b). The probability of sustaining urinary incontinence following LRARP has been calculated to be 0.91/0.91 (first year/subsequent year) and 0.85/0.94 following ORP.

In relation to sexual potency, the proportions derived from the KM curves were 0.36/0.45 (first year/subsequent year) following LRARP, and 0.20/0.31 following ORP. It has been assumed that treatment effects continue over time to the last observed level.

Patient preferences

Patient preferences, measured as utilities, are quantitative expressions of preferences for, or desirability of, specific health states. Utilities represent the strength of patients' preferences for a specific health outcome, in this context, for example, retaining urinary continence or sexual potency. (Utilities range from 0 [death] to 1 [full health]). They may be expressed in the negative range if patients value a particular health state as being worse than death. Utilities can be derived either from direct measurements, by using techniques such as standard gamble scores or time trade off, or indirectly assigned to health states reported in quality of life (QoL) questionnaires, such as the EuroQoL (EQ-5D).

Several studies have been published that report the preferences of prostate cancer patients. In general, the results are inconsistent. Inconsistencies detected in the literature included definition of the sample population, the measurement/scaling approach, variances in health status descriptions, the point in time that the measurement was applied, and whether patients or their physicians are reporting (Litwin et al 1999). Utilities derived from patient and non-patient populations have been controversially described as being similar, but also quite different. It has also been demonstrated that utilities vary depending on patients' baseline general health as well as on the applied therapy (prostatectomy, radiation, hormone therapy) (Krahn et al 2003; Saigal et al 2001).

Patient preferences data from comparative studies for ORP and LRARP are not available. Hara et al (2003) compared QoL following laparoscopic and open prostatectomy for prostate cancer, but did not report utilities. Tewari et al (2005a) measured QoL in patients undergoing LRARP by using the international prostate symptom score (IPSS).

Because of the limitations in the published data, utilities have been derived from two studies reporting urinary and/or sexual dysfunction following prostatectomy.

Utilities have frequently been reported to be lower for conjoint occurrences of urinary and sexual symptoms than for separate occurrences (Stewart et al 2004; Smith et al 2002). By considering urinary continence and the ability to perform sexual intercourse in separate analyses, a possible conjoint occurrence is not taken into account. Therefore, these separate scenarios do not represent the true treatment outcome in terms of utilities and of QALYs in this population. A combination of both treatment outcomes was not possible due to the event risks having been presented separately by Tewari et al (2003b).

Ability to perform intercourse

Self-reported utilities (n=209) of a longitudinal study sample of US patients undergoing radical prostatectomy are reported by Smith et al (2002). The mean age at recruitment was 67.6 ± 5.9 years and mean time since surgery was 35.4 ± 10.2 months (approximately three years). No co-morbidities were reported for fifty-two per cent of patients, 32 per cent had a single co-morbidity, and 16 per cent of patients had two or more co-morbidities. The majority (76%) of patients were in clinical stages T1 or T2. Utilities were assessed with standard gamble and time trade-off methods and performed as a computer-based self-administered interview. The patient sample was derived from a former QoL study sample. In this sample, only eight of 594 men reported 'urinary bother' without also reporting some form 'sexual bother' (these are the terms used in the study and its report). The authors did not focus on these health states in their utility study due to the low frequency. The three assessed health states were 'urinary and sexual bother', 'sexual bother', and 'no sexual or urinary bother'. Results are shown in **Table 41** (Smith et al 2002).

Table 41 Patient-reported utilities following radical prostatectomy (sexual bother)

	Health state	N	Mean ± SD	*p*-value	Reference
		Standard gamble			
A	Sexual and urinary bother	40	0.822 ± 0.272	0.05 v sexual, <0.0001 vs. none	Smith (2002)
B	Sexual bother	95	0.898 ± 0.199	<0.0001 vs. none	
C	No sexual or urinary bother	74	0.956 ± 0.165	–	
		Time trade-off			
D	Sexual and urinary bother	40	0.767 ± 0.310	<0.05 vs. sexual, 0.015 vs. none	
E	Sexual bother	95	0.869 ± 0.209	0.0002 vs. none	
F	No sexual or urinary bother	74	0.923 ± 0.205	–	

The limitation of these data is that the health status definition of 'sexual bother' does not equate to the treatment outcome 'ability to perform sexual intercourse'. The ability to perform sexual intercourse was one among other definitions included in the health status description in this study.[4] Despite this, utilities values of 0.898/0.956 were applied to patients' abilities to perform sexual intercourse, due to unavailability of more precise data. Utilities gained with standard gamble were considered in the base case analysis, while utilities gained from time trade-off were applied in sensitivity analysis.

Urinary continence

In a recent study, Stewart et al (2004) reported on utilities in men aged 60 and older (n=162), of whom 52 per cent were diagnosed with prostate cancer. Forty-three per cent of study participants were aged 60–69, 45 per cent aged 70–79, and 12 per cent were 80 or more years old. No information was presented for cancer stage and grade. In a complex approach, 27 different health states were rated using computer-assisted standard gamble and time trade-off methods. Results of both methods are presented in combination only. Separate health states were created for symptoms occurring during treatment (see **Table 42**).

Table 42 Patient-reported utilities following radical prostatectomy (urinary incontinence)

	Health state	N	Mean ± SD	Median	Range	Interquartile range	Reference
A	Impotence	150	0.89 ± 0.16	0.91	0.09–1.0	0.86–1.0	Stewart (2004)
B	Urinary incontinence	88	0.83 ± 0.1	0.90	0–1.0	0.78–0.98	
C	Symptoms occurring with prostatectomy	51	0.67 ± 0.29	0.73	0–1.0	0.56–0.90	

Abbreviations: N, number; SD, standard deviation.

In this study, patients' preference to live with sexual impotency is higher (0.89) than the possibility of living with urinary incontinence (0.83). When comparing the utilities reported for sexual impotence, it can be seen that they are comparable with the findings

[4] For the same reason, this utility is also unsuitable to apply in relation to patients who have erectile function. This was also reported by Tewari et al (2003).

of Smith et al (2002) for 'sexual bother'. The utility value reported for urinary incontinence (0.83) has been estimated for further calculations. The reported utility value for all symptoms associated with prostatectomy cannot be estimated because of the inability to separate individual issues from aggregated reporting of compound issues, such as urinary and sexual dysfunction. There is no utility value reported in this study for radical prostatectomy patients not experiencing side effects. Therefore, the utility value reported by Smith et al (2002) has been applied for those patients (0.956, see **Table 41**, row C).

Indicative cost-utility analysis

The cost-utility ratio has been determined as incremental costs per quality-adjusted life year (QALY) gained for patients treated with LRARP rather than ORP.

To provide an indicative estimate of the costs per QALY, a simple Markov model analysis of the decade post-surgery was performed. The selected period reflects the minimum of 10 years remaining life expectancy, which is an indication criterion for patients undergoing LRARP. All costs and outcomes are expected to be realised at the end of each Markov cycle. Therefore, half-cycle correction has not been performed.

Cost data for LRARP and ORP have been estimated, as described in the preceding sections. Detailed costs per patient for the treatment of male urinary incontinence or sexual dysfunction in Australia are not available. Therefore, these costs were estimated from other published sources. Both are chronic conditions that require comprehensive care. It has been assumed that all patients experiencing either condition were treated for the purposes of modelling.

The only identified cost-of-illness study in relation to male urinary incontinence was published by Wilson et al (2001). This US study presents costs separated by age, residence and gender. The authors report a study based on 1995 data and found that annual costs of US$1535 were associated with male patients aged 65 years or older, experiencing urge/mixed urinary incontinence, and who were community-dwelling, while costs for institutionalised patients were US$1650 (Wilson et al 2001). These costs have been averaged and adapted for different price levels between the USA and Australia by estimating OECD purchasing power parities exchange rates. These rates were adapted to current prices by using the Australian Total Health Price Index (Australian Institute of Health and Welfare 2004). Adapted costs are $3058 per urine-incontinent patient. Details of this cost adaptation are shown in **Table 43**.

Table 43 Adaptation of urinary incontinence (UI) treatment costs

	Item	Value	Reference
A	Costs per male patient with UI, age ≥65 years, community-dwelling, 1995, US$	US$1535	Wilson (2001)
B	Costs per male patient with UI, age ≥65 years, institutionalised, 1995, US$	US$1650	
C	Average costs per male patient with UI, age ≥65 years, 1995, US$	US$1593	C=(A + B) / 2
D	OECD PPP 1995 USA	1.00	OECD (2005)
E	OECD PPP 1995 Australia	1.31	
F	Average costs per male UI patient at age ≥65 years, 1995 Australia	$2086	F=(C * E) / D
G	Total health price financial consumption expenditure 1995	72.80	AIHW (2004)
H	Total health price financial consumption expenditure 2003	106.70	
I	Average costs per male UI patient at age ≥65 years, 2003 Australia	$3058	I=(F * H) / G

Abbreviations: AIHW, Australian, Institute of Health and Welfare; UI, urinary incontinence; OECD, Organisation for Economic Co-operation and Development; OECD PPP, Organisation for Economic Co-operation and Development Purchasing Power Parities.

Costs for the treatment of erectile dysfunction have been derived from the UK's most recent study that reported direct National Health Service (NHS) costs for 2000 at £286 per patient (Wilson et al 2002). When all drug costs were excluded (sildenafil citrate, intracavernous injections, transurethral alprostadil, yohimbine)[5], the annual cost per patient amounted to £182. These costs have been adapted to 2005 Australian costs following a similar approach as described for UI costs. Annual costs are considered to be $447 per patient experiencing erectile dysfunction (see **Table 44)**.

Table 44 Adaptation of erectile dysfunction treatment costs

	Item	Value	Reference
A	Costs per male patient 2000 UK	£286	Wilson (2002)
B	Costs per male patient 2000 UK, w/o drug treatment costs	£182	
C	OECD PPP 1995 UK	0.63	OECD (2005)
D	OECD PPP 1995 Australia	1.31	
E	Average costs per patient 2000 Australia	$378	E=(B * D) / C
F	Total health price financial consumption expenditure 2000	90.20	AIHW (2004)
G	Total health price financial consumption expenditure 2003	106.70	
H	Average cost per patient 2003 Australia [a]	$447	H=(E * G) / F

Abbreviations: AIHW, Australian, Institute of Health and Welfare; UK, United Kingdom; OECD, Organisation for Economic Co-operation and Development; OECD PPP; Organisation for Economic Co-operation and Development Purchasing Power Parities.
[a] Drug costs are not included.

Safety data, in terms of urinary continence and ability to perform sexual intercourse, have been derived from the Kaplan-Meier curves presented by Tewari et al (2003b). The safety profile shown at year one post-surgery has been considered for the first year. The treatment benefit shown at the end of the observations has been assumed to continue for years 2 to 10. This approach provides an overestimation of treatment benefit for the first

[5] Sildenafil citrate and tadalafil are currently listed under the Repatriation Pharmaceutical Benefits Scheme (RPBS). The RPBS costs for sildenafil citrate and tadalafil in the financial year 2004–2005 were $66.50 per prescription. The proportion of patients receiving drug treatment and the average annual number of prescriptions per patient is not known. Therefore, the drug treatment costs are not included in the total treatment costs for erectile dysfunction.

year since the treatment benefit steadily increases over time rather than being at the estimated level at the end of the first year.

All causes of mortality for patients aged 60 to 69 years have been estimated (based on the mean age of 63.1 years for the ORP group, and 59.9 years for the LRARP group in the comparative study presented by Tewari et al (2003b). Mortality data have been derived from the Australian Bureau of Statistics (Australian Bureau of Statistics (ABS) 2005a).

Simplified decision trees used for modelling are presented in **Figure 12** and **Figure 13** below. Multiple event probabilities refer to the first/subsequent years. All model input data are listed in **Table 45**.

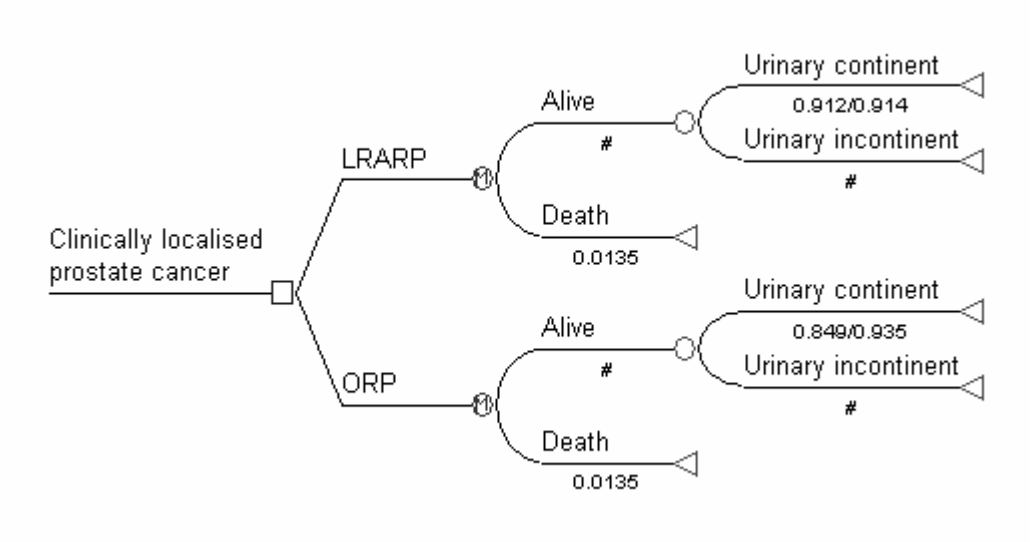

Figure 12 Decision tree model—urinary continence

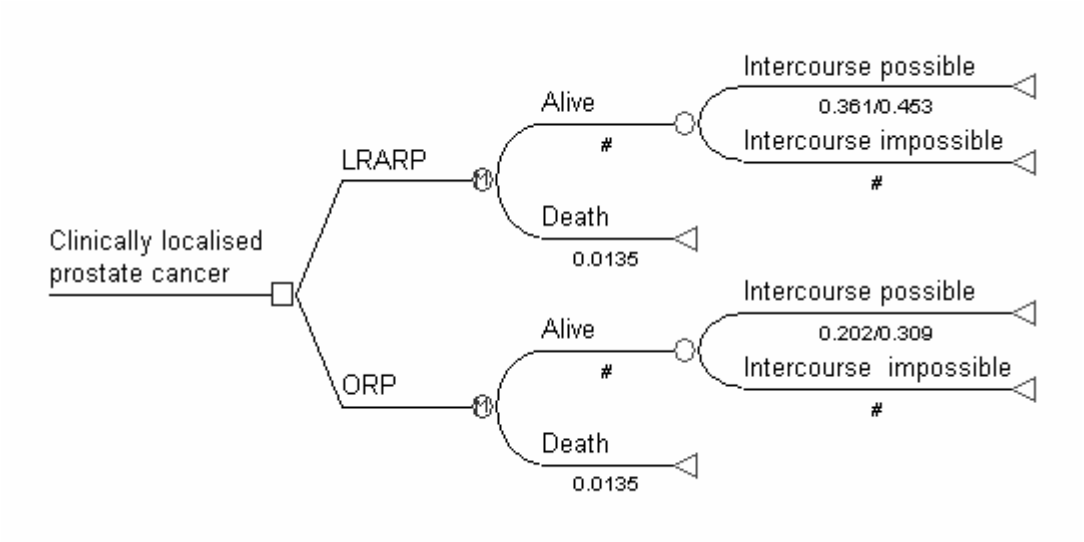

Figure 13 Decision tree model—ability to perform sexual intercourse

Table 45 Decision analysis input variables

		Value	Reference
Epidemiological variables			
A	All cause mortality, age 60–69 (rate)	1.35%	ABS (2005a)
Urinary incontinence			
B	LRARP (probability, first year)	0.91	
C	LRARP (probability, second–tenth year)	0.91	Derived from KM curves presented by Tewari (2003b)
D	ORP (probability, first year)	0.85	
E	ORP (probability, second–tenth year)	0.94	
Ability to perform sexual intercourse			
F	LRARP (probability, first year)	0.36	
G	LRARP (probability, second–tenth year)	0.45	Derived from KM curves presented by Tewari (2003b)
H	ORP (probability, first year)	0.20	
I	ORP (probability, second–tenth year)	0.31	
Costs			
J	LRARP	$15,469	Direct costs as presented
K	ORP	$11,207	Direct costs as presented
L	Urinary incontinence	$3059	Based on Wilson (2001)
M	Sexual dysfunction	$447	Based on Wilson (2002)
N	Discount rate	5%	Per annum
Patient preferences			
O	Urinary incontinence	0.830	Stewart (2004)
P	Sexual intercourse	0.898	Smith (2002)
Q	No side effect	0.956	Smith (2002)

Abbreviations: ABS, Australian Bureau of Statistics; KM, Kaplan-Meier; LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy.

The results of the indicative incremental cost-utility analysis are presented in **Table 46**. LRARP provides more QALYs at higher overall treatment costs per patient.

Table 46 Indicative cost-utility analysis – urinary (in)continence

		LRARP	ORP	Increment
Costs				
A	Costs per patient over 10 years	$17,388	$12,886	$4502
Effectiveness				
B	QALYs realised per person over 10 years	6.93	6.92	0.01
Cost-utility				
C	Cost per QALY gained	–	–	$450,200

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; QALY, quality adjusted life years.

The benefits of both treatment options, and for the first year, are slightly overestimated, due to estimating the proportions of continent patients at the end of the first year. These proportions are lower at outset and accumulate over time and reach the considered level at the end of the first year. This accumulation of treatment benefit has shown to be faster (and to start earlier) in patients undergoing LRARP, resulting in short-term treatment effects superior to ORP. Because of this earlier and faster accumulation of treatment benefit, the findings for the LRARP group are less likely to be overestimated than the findings for the ORP group. In separate analyses of the Kaplan-Meier curves presented by Tewari et al (2003b) performed on a per-day basis (refer to the **Quality of life** section of this document), this overestimation has been quantified to be 0.01 QALY for LRARP

and 0.04 QALY for ORP. Thus, the incremental benefit of LRARP over ORP is higher than shown with the model base case analysis and at 0.04 QALYs gained. Therefore, an additional scenario addressing this issue has been provided in the sensitivity analysis.

The results of another incremental cost-utility analysis based on the ability to perform sexual intercourse are presented in **Table 47**. Again, LRARP provides better therapeutical benefit at higher costs.

Table 47 Indicative cost-utility analysis – ability to perform sexual intercourse

		LRARP	ORP	Increment
	Costs			
A	Costs per patient over 10 years	$17,562	$13,820	$3742
	Effectiveness			
B	QALYs realised over 10 years	6.76	6.66	0.10
	Cost-utility			
C	Cost per QALY gained	–	–	$37,420

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; QALY, quality adjusted life year.

For this analysis, the effect of overestimating treatment benefit has again been proven by analysing the Kaplan-Meier curves presented by Tewari et al (2003b) on a per-day basis. It has been found that for this calculation the model does not overestimate and provides similar results for the first year following surgery.

Sensitivity analysis

A one-way sensitivity analysis was performed by applying changes to uncertain or critical variables used in the indicative cost-utility evaluation. This allows testing of plausible changes in basic assumptions and data, and to determine their influence on the evaluation results. Most of the changes relate to LRARP and ORP procedure costs. The following changes were considered:

Costs

Shared da Vinci® system purchase and maintenance costs:

The da Vinci® system can also be used for other types of surgeries, for example mitral valve repair or coronary artery bypass grafting. In this case, the da Vinci® system purchase and maintenance costs need to be distributed to all these different procedures. Assuming a 30 per cent and 10 per cent utilisation for procedures other than radical prostatectomies, the major capital costs are $1896 and $2438 per procedure. [6]

[6] This proportion is based on estimations for use of the da Vinci ® system at Epworth Hospital which was provided by the Advisory Panel. According to this advice, 30% of the system's use is for surgeries other than radical prostatectomies. Considering that there are presently three da Vinci ® systems in Australia, and assuming that only the system at Epworth is currently used for other types of surgeries, an average utilisation of 10% for other procedures has been considered.

Lowering LRARP hospital costs by 10 per cent, and 20 per cent:

LRARP costs may be overestimated due to some service costs already being included in the DRG cost buckets. Therefore, hospital costs are reduced by 10 per cent and 20 per cent, respectively.

Average hospital length of stay (LOS) following LRARP changed to three days:

In the base case analysis, the average LOS was assumed to be 2.0 days. The impact of the overall hospital stay being prolonged to three days was tested.

Different fee for the conjoint surgeon for LRARP:

The fee for the LRARP conjoint surgeon was set to 50 per cent and 100 per cent of the principal surgeon's fee.

Patient preferences

Applying standard deviations on patient preferences:

Patient preferences for outcomes relating to urinary (in)continence and (in)ability to perform sexual intercourse are increased/reduced by the reported standard deviations (see **Table 41** and **Table 42**).

Application of patient preferences gained with time trade-off (only for cost-utility analysis on the ability to perform sexual intercourse):

Published patients' preferences in regard to the (in)ability to perform sexual intercourse have been obtained with different approaches, standard gamble and time trade-off (see **Table 41**). Due to methodological differences, both approaches provide slightly different results. Patient preferences are set to 0.869 for patients unable to perform sexual intercourse and 0.923 for patients not affected by this side effect.

QALYs

Reducing the calculated number of QALYs (only for cost-utility analysis on urinary (in)continence):

Treatment effect, and therefore QALYs, are overestimated in the modelling due to extrapolating the effect observed at the first anniversary to the one-year period following surgery. The degree of overestimation has been calculated by performing a separate and more detailed evaluation of Kaplan-Meier curves (see **Table 52** and **Table 53**). Overestimation was found for urinary (in)continence but not for the (in)ability to perform sexual intercourse. Overestimation was found to be at 0.01 for LRARP and 0.04 for ORP.

The results of the sensitivity analyses are shown in **Table 48** and **Table 49**.

Table 48 Sensitivity analysis results – indicative cost-utility analysis urinary (in)continence

	Scenario	Incremental costs per QALY gained
A	Base case	$450,200
B	10 % of the da Vinci® system used for other surgeries	$423,100
C	30 % of the da Vinci® system used for other surgeries	$368,900
D	LRARP hospital costs –10%	$394,300
E	LRARP hospital costs –20%	$338,500
F	Average LOS in hospital following LRARP 3 days	$501,200
G	Conjoint surgeon's fee is 50% of the principal surgeon's fee	$412,400
H	Conjoint surgeon's fee is 100% of the principal surgeon's fee	$488,000
I	Patient preference for urinary continence increased by SD [a]	$450,200
J	Patient preference for urinary incontinence changed by ± SD	–$64,314 [b]/ $225,100
K	Both patient preferences increased by SD	–$75,033 [b]
L	Both patient preferences decreased by SD	$112,550
M	Correction for overestimation of QALYs	$112,550

Abbreviations: QALY, quality adjusted life year; LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; SD, standard deviation; LOS, length of stay.
[a] Patients' preference for the urinary continence has not been decreased due to it being lower ranked than the preference for urinary incontinence. This seems not to be very likely.
[b] ORP provides more QALYs at lower costs than LRARP.

Table 49 Sensitivity analysis results – indicative cost-utility analysis sexual intercourse

	Scenario	Incremental costs per QALY gained
A	Base case	$37,420
B	10 % of the da Vinci® system used for other surgeries	$34,710
C	30 % of the da Vinci® system used for other surgeries	$29,290
D	LRARP hospital costs –10%	$31,830
E	LRARP hospital costs –20%	$26,250
F	ALOS in hospital following LRARP 3 days	$42,520
G	Conjoint surgeon's fee is 50% of the principal surgeon's fee	$33,640
H	Conjoint surgeon's fee is 50% of the principal surgeon's fee	$41,200
I	Patient preference for ability to perform intercourse increased by SD [a]	$24,947
J	Patient preference for inability to perform intercourse decreased by SD [b]	$11,339
K	Both patient preferences increased by SD	Not applicable [c]
L	Both patient preferences decreased by SD	$37,420
M	Application of patient preferences gained with time-trade-off method	$124,733

Abbreviations: QALY, quality adjusted life year; LRARP, laparoscopic remotely assisted radical prostatectomy; SD, standard deviation, ALOS, average length of stay.
[a] Patients' preference for the ability to perform sexual intercourse has not been decreased due to it being lower ranked than the preference for inability to perform sexual intercourse. This seems not to be very likely.
[b] Patients' preference for inability to perform intercourse has not been increased due to exceeding the preference reported by patients able to perform intercourse. This seems not to be very likely.
[c] This calculation is not applicable due to both patient preferences reaching 1.0 (perfect health) and causing no incremental difference in provided QALYs.

Discussion

An indicative cost-utility analysis (CUA) has been performed in order to assess the value for money when funding LRARP. This economic evaluation could be regarded as indicative only due to no evidence, free from potential bias, of a difference in treatment effect. The cost-utility model covers a period of 10 years. It considers direct costs related

to the initial surgery for radical prostatectomy, safety outcomes in terms of urinary continence and ability to perform sexual intercourse as well as subsequent costs for treating these conditions and associated patient preferences. The outcomes are considered in separate analyses since combined safety data were not available. The indicative cost-utility analysis shows that in both base case analyses as well as in nearly all of the tested sensitivity scenarios, LRARP provides additional quality-adjusted life years (QALYs) at higher overall costs. When considering indirect costs (as presented in the **Appendix G**), the incremental difference in costs for LRARP and ORP increases. This is caused by lower indirect costs for LRARP due to an assumed earlier return to work following surgery. Areas of uncertainty have been addressed in a range of sensitivity analyses. In most of the scenarios, the key finding that LRARP provides additional benefit at higher treatment costs could be reproduced. Overall, the results of this indicative CUA are very sensitive to changes of key data.

Indicative cost-utility analysis with indirect costs

The cost-utility analyses including indirect costs for urinary (in)continence and ability to performed sexual intercourse are presented in **Table 50** and **Table 51** respectively.

Table 50 Cost-utility analysis including indirect costs— urinary (in)continence

		LRARP	ORP	Increment
Costs				
A	Costs per patient over 10 years	$18,606	$15,323	$3,283
Effectiveness				
B	QALYs realised per patient over 10 years	6.93	6.92	0.01
Cost-utility				
C	Cost per QALY gained	–	–	$328,300

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; QALY, quality adjusted life year

Table 51 Cost-utility analysis including indirect costs—ability to perform sexual intercourse

		LRARP	ORP	Increment
Costs				
A	Costs per patient over 10 years	$18,780	$16,257	$2523
Effectiveness				
B	QALYs realised per patient over 10 years	6.76	6.66	0.10
Cost-utility				
C	Cost per QALY gained	–	–	$25,230

Abbreviations: LRARP, laparoscopic remotely assisted radical prostatectomy; ORP, open radical prostatectomy; QALY, quality adjusted life year

Accuracy of model approach

For estimating the accuracy of the economic model and to quantify an overestimation of treatment benefit assumed for the first year, treatment benefit has been calculated in separate analysis and as area under the curve (AUC) using the Kaplan-Meier curves presented by Tewari et al. (2003b). The results of these calculations are presented in **Table 52** and **Table 53**.

Overestimation was found for urinary (in)continence but not for the (in)ability to perform sexual intercourse. Overestimation of urinary (in)continence was found to be at 0.01 QALYs for LRARP and 0.04 QALYs for ORP.

Table 52 AUC calculation of treatment benefit for urinary (in)continence, year 1

LRARP			ORP		
Time (days)	Continence probability	Continent time (days)	Time (days)	Continence probability	Continent time (days)
2.509	0.0088		20.0717	0.007	
3.3453	0.0911	0.042	20.0717	0.0105	0.000
5.8542	0.1243	0.270	20.908	0.0114	0.009
7.5269	0.1471	0.227	27.5986	0.0123	0.079
11.7085	0.2417	0.813	28.4349	0.0438	0.024
15.0538	0.2539	0.829	33.4528	0.0613	0.264
20.908	0.3748	1.840	34.2891	0.0753	0.057
25.9259	0.3993	1.942	35.1254	0.07705	0.064
33.4528	0.4011	3.012	45.9976	0.0788	0.847
33.4528	0.4273	0.000	45.9976	0.1068	0.000
35.1254	0.4641	0.746	71.9235	0.1138	2.860
42.6523	0.4834	3.566	73.5962	0.1611	0.230
48.5066	0.5219	2.943	103.7037	0.1926	5.325
48.5066	0.5289	0.000	104.54	0.20925	0.168
60.2151	0.5306	6.203	107.8853	0.2259	0.728
60.2151	0.5464	0.000	116.2485	0.2434	1.962
67.7419	0.5482	4.119	120.4301	0.2469	1.025
67.7419	0.6042	0.000	121.2664	0.2504	0.208
77.7778	0.606	6.073	122.1027	0.3765	0.262
81.9594	0.6182	2.560	140.5018	0.394	7.088
91.1589	0.62	5.695	141.3381	0.3949	0.330
93.6679	0.7023	1.659	152.2103	0.3958	4.298
104.54	0.7005	7.626	152.2103	0.4764	0.000
105.3763	0.7198	0.594	158.9008	0.4781	3.193
124.6117	0.7513	14.149	160.5735	0.4956	0.814
125.448	0.7233	0.617	170.6093	0.4991	4.991
133.8112	0.7513	6.166	170.6093	0.5096	0.000
146.356	0.7583	9.469	179.8088	0.5114	4.696
153.8829	0.7828	5.800	181.4815	0.5762	0.910
169.773	0.7933	12.522	211.589	0.6165	17.955
183.1541	0.8406	10.932	212.4253	0.6165	0.516
211.589	0.8459	23.978	245.0418	0.6165	20.108
213.2616	0.8669	1.432	270.9677	0.6182	16.005
241.6965	0.8669	24.650	271.8041	0.7075	0.554
244.2055	0.9089	2.228	301.9116	0.7093	21.328
331.1828	0.9124	79.206	302.7479	0.725	0.600
365	0.9124	30.855	362.1266	0.7443	43.623
			362.963	0.79685	0.645
			365	0.8494	1.677
Urinary continence (days)		273			163
Urinary continence (years)		0.75			0.45
Urinary incontinence (years)		0.25			0.55

LRARP			ORP		
Time (days)	**Continence probability**	**Continent time (days)**	**Time (days)**	**Continence probability**	**Continent time (days)**
Utilities continence		0.956			0.956
Utilities incontinence		0.830			0.830
QALYs continence		0.717			0.430
QALYs incontinence		0.208			0.457
Total QALYs (first year, based on AUC)		0.925			0.887
Total QALYs discounted (first year, based on AUC)		0.881			0.845
Total QALYs discounted (first year, modelled)		0.890			0.880
Difference in QALYs based on AUC and modelled)		-0.01			-0.04
Total QALYs modelled		6.93			6.92
Incremental difference modelled					0.01
QALYs corrected		6.92			6.88
Incremental difference modelled, corrected					0.04

Table 53 AUC calculation of treatment benefit for (in)ability to perform intercourse, year 1

LRARP			ORP		
Time (days)	**Able to perform intercourse probability**	**Able to perform intercourse time (days)**	**Time (days)**	**Able to perform intercourse probability**	**Able to perform intercourse time (days)**
11.922	0.001		11.922	0.000	
16.180	0.012	0.028	16.180	0.000	0.000
21.290	0.024	0.092	21.290	0.000	0.000
31.509	0.035	0.300	31.509	0.000	0.000
31.509	0.035	0.000	31.509	0.003	0.000
32.360	0.035	0.030	32.360	0.016	0.008
40.876	0.070	0.449	40.876	0.016	0.135
49.392	0.083	0.654	49.392	0.016	0.135
59.611	0.098	0.924	59.611	0.016	0.162
75.791	0.110	1.677	75.791	0.016	0.256
91.119	0.139	1.905	91.119	0.016	0.242
107.299	0.154	2.366	107.299	0.016	0.256
121.776	0.167	2.321	121.776	0.016	0.229
150.730	0.167	4.832	150.730	0.051	0.966
153.285	0.198	0.466	153.285	0.051	0.130
181.387	0.248	6.257	181.387	0.051	1.430
211.192	0.290	8.010	211.192	0.051	1.517
211.192	0.290	0.000	211.192	0.069	0.000
241.849	0.290	8.884	241.849	0.084	2.342
269.951	0.290	8.144	269.951	0.142	3.184
287.835	0.290	5.183	287.835	0.160	2.701
307.421	0.290	5.676	307.421	0.179	3.320
330.414	0.290	6.663	330.414	0.179	4.120
332.117	0.361	0.554	332.117	0.179	0.305
365.000	0.361	11.989	365.000	0.202	6.330
Able to perform intercourse (days)		77			28
Able to perform intercourse (years)		0.21			0.08
Unable to perform intercourse (years)		0.79			0.92
Utilities able to perform intercourse		0.956			0.956
Utilities unable to perform intercourse		0.898			0.898
QALYs able to perform intercourse		0.201			0.076
QALYs unable to perform intercourse		0.709			0.826
Total QALYs (first year, based on AUC)		0.910			0.902
Total QALYs discounted (first year, based on AUC)		0.867			0.859
Total QALYs discounted (first year, modelled)		0.870			0.860
Difference in QALYs based on AUC and modelled)		0.00			0.00
Total QALYs modelled		6.93			6.92
QALYs corrected		6.93			6.92

Abbreviations

AACR	Australian Association of Cancer Registries
ABS	Australian Bureau of Statistics
AHMAC	Australian Health Ministers' Advisory Council
AIHW	Australian Institute of Health and Welfare
ALOS	average length of stay
ANZAUS	Australian and New Zealand Association of Urological Surgeons
AR-DRG	Australian Refined Diagnosis Related Groups
AUA	American Urological Association
ARTG	Australian Register of Therapeutic Goods
AUC	area under the curve
BMI	body mass index
CI	confidence interval
CT	computed tomography
CUA	cost utility analysis
DoHA	Australian Government Department of Health and Ageing
DRE	digital rectal examination
DRG	diagnosis related group
DVT	deep vein thrombosis
EBL	estimated blood loss
EBRT	external beam radiation therapy
EPIC	Expanded Prostate Cancer Index Composite
EQ-5D	EuroQoL
FEM	fixed-effects method
Hb	haemoglobin

Abbreviations (continued)

HDR	high dose rate
HIC	Health Insurance Commission
HTA	health technology assessment
IMRT	intensity modulated radiation therapy
IPSS	international prostate symptom score
LDR	low dose rate
LOS	length of stay
LRARP	laparoscopic remotely assisted radical prostatectomy
KM	Kaplan-Meier
MBS	Medicare Benefits Schedule
MSAC	Medical Services Advisory Committee
M-TAG	Medical Technology Assessment Group
NHCDC	National Hospital Cost Data Collection
NHMRC	National Health and Medical Research Council
NHPA	National Health Priority Area
NHS	National Health Service
NR	not reported
NS	not significant
OECD	Organisation for Economic Co-operation and Development
ORP	open radical prostatectomy
PM	positive margin
PPP	purchasing power parities
PRBC	packed red blood cells
PSA	prostate specific antigen
PSADT	prostate specific antigen doubling time
QoL	quality of life

Abbreviations (continued)

QALY	quality-adjusted life years
RCT	randomised controlled trial
RD	risk difference
REM	random-effects method
RP	retropubic prostatectomy
RPBS	Repatriation Pharmaceutical Benefits Scheme
SD	standard deviation
SHIM	Sexual Health Inventory for Men
TGA	Therapeutic Goods Administration
TRUS	transrectal ultrasonography
TURP	transurethral resection of the prostate
UTI	urinary tract infection
VUI	Vattikuti Urology Institute

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