

SUMMARY OF KEY FINDINGS

- This review focuses on key considerations in the management of localized, low-risk prostate cancer; the evidence and clinical tradeoffs involved in the treatment of intermediate- or high-risk disease would differ substantially and are not addressed in these analyses. Primary management options for low-risk disease evaluated included active surveillance, open and robotic/laparoscopic radical prostatectomy, brachytherapy, intensity-modulated radiation therapy (IMRT), and proton beam therapy. All except proton beam therapy are listed by national guidelines as reasonable options for low-risk prostate cancer.
- There are no published reports of randomized controlled trials directly comparing these treatment options. Evidence from individual case series reports indicates comparable rates of disease recurrence as well as overall and cancer-specific mortality for all forms of surgery and radiation therapy.
- The evidence on the comparative effectiveness and harms of proton beam therapy is limited to relatively small, highly selective case series of short duration, making any judgments about its relative benefit or inferiority to other options premature. The uncertainty regarding proton beam therapy is accentuated because this technology involves delivery of a novel form of radiation, and there remain important questions about the full spectrum of possible effects.
- Robot-assisted laparoscopic prostatectomy represents a change in the method of delivery of an existing surgical treatment, traditional open prostatectomy. However, data on the comparative outcomes of robotic prostatectomy are also relatively short-term and arise from case series, limiting the certainty with which any judgment can be made on clinical benefits compared to open prostatectomy.
- Active surveillance is a relatively recent evolution of “watchful waiting,” and entails enhanced monitoring to retain the goal of curative treatment should clinical progression occur. Findings from older studies of watchful waiting suggest a modest survival benefit for surgery among younger men but equivalent disease-specific and overall survival outcomes for men aged >65 years. More recent studies of active surveillance are primarily case series with outcomes limited to 5-7 years. Approximately 30% of patients on active surveillance progress to or choose definitive treatment within 5 years, and disease-specific and overall survival rates within this time frame are comparable to those patients who opt for immediate radical prostatectomy.
- ICER’s economic model suggests that approximately 40% of patients aged 65 and older who begin active surveillance will die of other causes before their cancer progresses to require definitive treatment. The model findings also show that, even if a survival benefit of immediate surgery or other definitive treatment is assumed, the lower risk of complications and side effects associated with an active surveillance strategy produces more quality-adjusted life years for an entire population.

Therefore, despite the limitations in available data, ICER concludes that there can be high confidence that active surveillance is at least as effective, and likely more effective, than watchful waiting; and, that current evidence also allows high confidence in a judgment that for patients aged ≥ 65 the average net health benefit of active surveillance is comparable to immediate definitive treatment for patients with low-risk localized prostate cancer.

- For men younger than 65 and/or for patients who have a life expectancy greater than 20 years, the limitations in longer-term outcome data from active surveillance reduce the certainty to “moderate” that modern protocols for active surveillance produce mortality outcomes not substantially inferior to radical prostatectomy. However, the quality-of-life advantages of having many patients never require definitive treatment are maintained in this younger population.
- Comparison of the short-term complications and longer-term side effects of the different definitive therapies is challenging because of the lack of head-to-head trials, the role of clinician training and experience, and differences in the way patient outcomes have been measured in published studies. Nonetheless, the data do suggest some general distinctions. Radiation treatment has a higher rate of short- and long-term bowel side effects than surgery, and, among radiation options, IMRT has a higher rate than brachytherapy. Conversely, surgery has higher risks than radiation therapy of causing short-term (0-3 months) urinary incontinence and sexual dysfunction, with longer-term sexual dysfunction data very hard to interpret. The data on robotic-assisted prostatectomy are too preliminary to be able to make a judgment of any differences in clinical outcomes compared to traditional open prostatectomy.
- The management options for localized prostate cancer differ substantially in terms of the cost to third party payers. Using Medicare reimbursements as a basis, annual costs for active surveillance range from \$300-\$1,000 depending on whether re-biopsy is performed. Costs for definitive treatment range from ~\$10,000 for brachytherapy and radical prostatectomy to \$20,000 for IMRT and \$50,000 for proton beam therapy. Input to ICER from health plans and providers suggests that reimbursement rates are generally higher among private payers, and that the magnitude of differences between external beam therapies (IMRT and proton beam therapy) and other treatments is greater than that in Medicare.
- Findings from the ICER economic model suggest that, on a lifetime basis, quality-adjusted life expectancy for a 65 year-old man is highest for active surveillance and quite similar among the definitive treatment options. Model results indicate that, on average, the benefits of avoiding definitive treatment and its associated side effects from active surveillance translate into 1 year or more of increased quality-adjusted survival relative to immediate definitive treatment. Lifetime costs for active surveillance, brachytherapy, and surgery are similar (\$25-\$30K), while lifetime costs for IMRT and proton beam therapy are substantially higher (\$40-\$55K).