ICER

INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

Key Questions for Scoping Teleconference

General

1. What are the most important questions about the clinical effectiveness of radical prostatectomy and active surveillance whose answers drive or will drive the use of these strategies (e.g., survival, complications, quality of life considerations)?

2. What are the most important issues about the existing published data that our appraisal should take into consideration? Is there a specific time frame during which published data should be considered? Are there additional sources of data that should be included in our review?

3. As with our earlier appraisals of radiation treatment, we plan to focus on clinically-localized, low-risk disease, as characterized by D'Amico criteria (i.e., Gleason ≤6, PSA <10 ng/mL, stage T1-T2a). Are there additional considerations (e.g., age, life expectancy) regarding this population when considering active surveillance and radical prostatectomy?

4. Are there particular patient subgroups that we should evaluate separately in the assessment (e.g., patients less than 65 years of age)?

5. Are there any key considerations for costs that should or should not be included for these interventions? For example, in our previous appraisal of radiation treatment, we considered time in treatment and productivity loss. Are these constructs also appropriate for this appraisal?

Active surveillance

6. Given the lack of a universal protocol for active surveillance, we are assuming a protocol for the model's base case with the following components:
   a. Quarterly PSA testing
   b. Quarterly digital rectal exam for the first 2 years, followed by ongoing semi-annual exams
   c. Biopsy at 12 to 18 months and every 3 years thereafter

   Are there additional protocol variants we should consider?

7. Our appraisal will include rates of disease progression as well as development/worsening of urinary and sexual symptoms while on active surveillance; are there other key outcomes of importance to our review and modeling efforts?

8. We plan to model the likelihood of initiation of definitive treatment during active surveillance based on assumed rates of (a) disease progression; and (b) patient choice. Is this an appropriate approach?

Radical prostatectomy

9. We plan to consider both open and laparoscopic radical retropubic prostatectomy with bilateral nerve-sparing techniques; alternative analyses will consider robot-assisted laparoscopic surgery. Are there other surgical variants we should consider?

10. In addition to outcomes of interest for all prostate cancer management options (e.g., overall and progression-free survival, urinary and sexual complications), are there outcomes of specific interest in comparing types of radical prostatectomy? For example, blood loss and/or requirements for transfusion, operating room time, and length of stay in hospital?

Economic Model Description

We propose to develop a patient-level microsimulation model of prostate cancer treatment and its complications, progression, and death. The model will focus on patients with clinically-localized prostate cancer (as diagnosed by PSA) who are at low risk for biochemical recurrence and/or metastasis. Management options to be evaluated in the model will include:

- Active surveillance
- Radical prostatectomy (open and laparoscopic/robot-assisted)
- Permanent, low-dose-rate brachytherapy
- Intensity-modulated radiation therapy (photons)
- Proton beam therapy

Using a state transition (Markov) model, individual patient life histories will be simulated (i.e., Monte Carlo analysis) and aggregated to estimate cohort-level outcomes. Survival, side effects, and costs from each treatment as well as parameters governing unobservable steps in the progression of prostate cancer will be estimated via the literature and varied over a wide range to account for uncertainty. Patients on active surveillance may enter treatment at any time, due to either progression of their cancer or by choice. Patients who undergo radical prostatectomy or any of the radiation modalities may have their disease recur at any time following treatment.

Quality-adjusted life expectancy will be estimated based on data on mortality from prostate cancer and other causes as well as utility weights for various health states. Rates of urinary and sexual symptoms while on active surveillance, urinary, gastrointestinal, and/or sexual side effects following definitive treatment, and surgical complications (e.g., major hemorrhage, infection) will also be estimated. A range of assumptions regarding time courses for side effect resolution or continuation will be compared. Major categories of costs will include treatment/management costs, costs of complications and side effects, and patient time costs.