



Effective Health Care

External Beam Radiotherapy (EBRT) and Androgen Deprivation Therapy (ADT) for Localized Prostate Cancer Nomination Summary Document

Results of Topic Selection Process & Next Steps

- The topic, *External Beam Radiotherapy (EBRT) and Androgen Deprivation Therapy (ADT) for Localized Prostate Cancer*, was found to be primarily addressed by the in process update of the 2008 AHRQ report titled *Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer*.
 - To view a description and status of the research protocol, please go to: <http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1434&pageaction=displayproduct#toc>
 - To sign up for notification when this and other EHC Program topics are posted, please go to: <http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/>
- Populations with prostate cancer at clinical stages T3b are not included in the in process AHRQ report. However, the evidence for EBRT and ADT in this population is limited
- The use of EBRT with or without ADT in patients after radical prostatectomy was found to be addressed by an evidence-base guideline released in 2013 by the American Urology Association (AUA) and the American Society for Radiation Oncology (ASTRO) titled *Adjuvant and Salvage Radiotherapy after Prostatectomy: AUA/ASTRO Guideline (2013)*.
 - Thompson I, Valicenti R, Albertsen P, Davis B, et al. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. *J Urol*. 2013 Aug; 190(2):441-9.
- Given that this in-progress report and the 2013 guideline cover the majority of the nomination and the evidence base for patients with T3b is limited, no further activity will be undertaken on this topic.

Topic Description

Nominator(s): Organization

Nomination Summary: The nominator is interested in the use of external beam radiotherapy (EBRT) alone or in combination with androgen deprivation therapy (ADT) specifically patients with low-, intermediate- and high-risk localized prostate cancer patients with no evidence of regional or distal metastases.

Staff-Generated PICO

Population(s): Men with localized prostate cancer (primary and recurrent)

Intervention(s): Androgen deprivation therapy (ADT), external beam radiotherapy

(EBRT)

Comparator(s): EBRT alone vs. EBRT plus ADT; length of ADT administration and different regimens / combinations of ADT

Outcome(s): Overall survival (e.g., mortality and disease-free survival), prevention of malignant spread, reduction of comorbidities, and quality of life

Key Questions from Nominator:

1. Among patients with localized low-risk prostate cancer (i.e., Prostate-specific antigen (PSA) <10 ng/ml and Gleason score <6 and <T2a), what is the comparative effectiveness of androgen deprivation therapy (ADT) plus external beam radiation therapy (EBRT) compared to EBRT alone?
 - a. If ADT improves outcomes, for how long should ADT be administered and what is the optimal ADT regimen?
2. Among patients with localized intermediate-risk prostate cancer (i.e., PSA 10-20 ng/ml or Gleason score 7 or T2b), what is the comparative effectiveness of ADT plus EBRT compared to EBRT alone?
 - a. If ADT improves outcomes, for how long should ADT be administered and what is the optimal ADT regimen?
3. Among patients with localized high-risk prostate cancer (i.e., PSA > 20 ng/ml or Gleason score 8-10 or > T2c), what is the comparative effectiveness of ADT plus EBRT compared to EBRT alone?
 - a. If ADT improves outcomes, for how long should ADT be administered and what is the optimal ADT regimen?
4. Among patients receiving salvage prostate bed radiotherapy for a biochemical recurrence of prostate cancer after radical prostatectomy, what is the comparative effectiveness of ADT plus definitive EBRT compared to EBRT alone?
 - a. If ADT improves outcomes, for how long should ADT be administered and what is the optimal ADT regimen?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)
- Localized prostate cancer consists of tumor growth that is confined to the prostate. Locally advanced tumors (i.e. high-risk) are tumors those that extend beyond the prostate gland but are not metastatic to distance sites. They often carry a poor prognosis: between 10% and 40% of patients die within 5 years after diagnosis.
- An in process review *Comparative effectiveness of therapies for clinically localized prostate cancer: an update of a 2008 comparative effectiveness review* will assess the effectiveness of EBRT and ADT in patients with prostate cancer at clinical stage T3a and below. In the update, the definition of “localized” prostate cancer has been expanded to include the T3a population based on a definition used by the National Comprehensive Cancer Network (NCCN). Since T3b and higher is not included in the definition used for the report, any studies that include disease stages higher than T3a were excluded. Key questions from this report include:

Key Question 1: What are the comparative risks and benefits of the following therapies for clinically localized prostate cancer?

- a. RP, including open (retropubic and perineal) and laparoscopic (with or without robotic assistance) approaches
- b. EBRT, including standard therapy and therapies designed to decrease exposure to normal tissues such as 3D-CRT, IMRT, proton beam therapy, and stereotactic body radiation therapy
- c. Interstitial BT
- d. Cryosurgery
- e. WW
- f. Active surveillance
- g. Hormonal (androgen deprivation) therapy as primary therapy, adjuvant, or neoadjuvant to other therapies
- h. HIFU

Key Question 2: How do specific patient characteristics (e.g., age, race/ethnicity, presence or absence of comorbid illness, preferences such as trade-off of treatment-related adverse effects vs. potential for disease progression) affect the outcomes of these therapies overall and differentially?

Key Question 3: How do provider/hospital characteristics affect outcomes of these therapies overall and differentially (e.g., geographic region, case volume, learning curve)?

Key Question 4: How do tumor characteristics (e.g., Gleason score, tumor volume, screen-detected vs. clinically detected tumors, and PSA levels) affect the outcomes of these therapies overall and differentially?

- Evidence for EBRT and ADT for the subgroup of patients with prostate cancer at stages T3b and above is limited. A scan of the literature identified a total of only nine studies.
- The use of EBRT with or without ADT after radical prostatectomy (see Key Question 4) was found to be addressed by titled an evidence-based guideline from AUA/ASTRO, titled *Adjuvant and Salvage Radiotherapy after Prostatectomy: AUA/ASTRO Guideline (2013)*. The systematic review examined evidence published from January 1990 through December 2012. A scan of the literature published since December 2012 does not change the recommendations or findings from this guideline.