Comparative Effectiveness Review Disposition of Comments Report

Title: Therapies for Clinically Localized Prostate Cancer

Draft report available for public comment from June 01, 2020 to June 29, 2020.

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Comments to Draft Report

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each draft report is posted to the EHC Program Web site or AHRQ Web site for public comment for a 3-4-week period. Comments can be submitted via the Web site, mail or E-mail. At the conclusion of the public comment period, authors use the commentators' comments to revise the draft report.

Comments on draft reports and the authors' responses to the comments are posted for public viewing on the Web site approximately 3 months after the final report is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

This document includes the responses by the authors of the report to comments that were submitted for this draft report. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Summary of Peer Reviewer Comments and Author Response

This research review underwent peer review before the draft report was posted for public comment on the EHC website.

- In general the peer review and TEP comments were very supportive with the large majority rating the report excellent to very good. There were few concerns about methods or conclusions. Most responded that the report was well written, readable, rigorous, and relevant. The following are the main themes of concern: (1) limited evidence of comparative effectiveness; (2) little information on outcomes according to patient and tumor factors that are important in clinical decision making; (3) uncertainty as to how these findings would influence clinical practice and policy; (4) request for additional information as to whom the results pertain to and explanation of our rating of certainty of evidence; and (5) numerous areas of clarification/justification for inclusion/exclusion criteria and descriptor language.

  We responded and revised the report in several ways: (1) We highlighted key findings according to patient/tumor risk categories when available including in our abstract, evidence summary, and strength of evidence tables. (2) We acknowledged the limited information especially related to patient and tumor factors. We described findings when available, cautioned about over interpretation of subgroups findings, and encouraged future research to address. (3) We clarified how our report adds to current evidence base including new findings from prior reports, gaps in evidence and future research needs. We described policy and practice implications of our findings. We provided greater clarification including summary tables describing key findings from this report in comparison to findings from prior reports. (4) We highlighted in whom the results pertain regarding patient/tumor factors when available. (5) We provided summary comments in the review response document regarding our rationale and clarifying language for consistency, scientific accuracy, and to be responsive to reviewers.
- Peer reviewers requested that more information was provided about tumor risk category such as NCCN, D'Amico, CAPRA. The authors have revised the report to consistently include this information when available. It is now also clearly labelled what risk stratification system was used.
- The reviewers noted lack of clarity in the Introduction as the guideline recommended and practical application of active surveillance versus watchful waiting. These sentences have been reworded accordingly.
- The reviewers repeatedly emphasized the distinction between mostly PSA-based active monitoring (AM) in ProtecT versus active surveillance (AS) as it is used today. The authors have since introduced two separate terms (AM vs. AS) to emphasize this issue better.
- We have clarified that the results for EBRT plus ADT vs. EBRT that favor the former may only pertain to men with predominantly intermediate or high-risk disease.
- In several instances, reviewers requested additional information about study inclusion criteria and/or about baseline characteristics of those men actually enrolled; this has since been added.
- The authors have addressed a number of inconsistencies and/or minor errors that were kindly pointed out by the reviewers.

- The response to the reviewers addressed questions as to the value of this review, given that much of it relates to extended followup of existing trials, and also explained as to why some studies (based on design and quality) did not find consideration.
- An explanation was provided as to the wording used to characterize the effect size (in absolute terms) and the level of uncertainty according to GRADE.

Public Comments and Author Response

Commentator & Affiliation	Section	Comment	Response
Public Reviewer #1	General	I may have missed it, but I did not see any mention of moderate hypofractionation trials (e.g. RTOG 0415 and the CHHIP trials). I suppose they were excluded due to their inclusion in the previous AUA clinically localized prostate cancer guidelines? It just seems remiss when trials comparing RT to ultra-hypofractionation and SBRT are mentioned.	We thank the reviewer. These interventions were considered dose comparison studies across EBR, thus were ineligible and outside of the report's scope.