Billing Code: 4160-90-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Healthcare Research and Quality

# Supplemental Evidence and Data Request on Radiation Therapy for Brain Metastases: A Systematic Review

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions.

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Radiation Therapy for Brain Metastases: A Systematic Review,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before 30 days after the date of publication in the Federal Register.

ADDRESSES:
*E-mail submissions:* epc@ahrq.hhs.gov
*Print submissions*:
Mailing Address:
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality
ATTN: EPC SEADs Coordinator
5600 Fishers Lane
Mail Stop 06E53A

Rockville, MD 20857
Shipping Address (FedEx, UPS, etc.):
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality
ATTN: EPC SEADs Coordinator
5600 Fishers Lane
Mail Stop 06E77D
Rockville, MD 20857

FOR FURTHER INFORMATION CONTACT:
Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION:
The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for Radiation Therapy for Brain Metastases: A Systematic Review. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299b--37(a).

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Radiation Therapy for Brain Metastases: A Systematic Review*, including those that describe adverse events. The entire research protocol is available online at:
https://effectivehealthcare.ahrq.gov/products/radiation-brain-metastases/protocol

This is to notify the public that the EPC Program would find the following information on *Radiation Therapy for Brain Metastases: A Systematic Review* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

*The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.*

**Key Questions (KQ)**

**Key Question 1:** What is the effectiveness of whole brain radiation therapy (WBRT), alone or in combination with stereotactic radiosurgery (SRS) or systemic therapies, as initial treatment in patients with brain metastases on patient-relevant outcomes, such as overall survival and quality of life?

**KQ1a.** How does effectiveness vary by dose fractionation schedule and technique?

**KQ1b.** How does effectiveness differ by patient prognosis and primary tumor site?

**KQ1c.** How does effectiveness differ by the addition of systemic therapies?

**Key Question 2:** What is the effectiveness of SRS/fractionated stereotactic radiation as initial treatment in patients with brain metastases on patient-relevant outcomes, such as overall survival and quality of life?

**KQ2a.** How does effectiveness vary by dose fractionation schedule and technique?

**KQ2b.** How does effectiveness differ by patient prognosis and primary tumor site?

**KQ2c.** How does effectiveness differ by the addition of systemic therapies?

**Key Question 3:** What is the effectiveness (or comparative effectiveness) of postoperative SRS compared to WBRT, observation, or preoperative SRS in patients with brain metastases on patient-relevant outcomes, such as overall survival and quality of life?

**KQ3a.** How does effectiveness vary by dose fractionation schedule?

**Key Question 4:** What are the adverse effects (i.e., serious harms) of WBRT, SRS, and systemic therapies for patients with brain metastases (either alone or in combination)?

**KQ4a.** Do adverse effects vary by important patient characteristics (i.e., age, performance status, patient prognosis, disease status, primary tumor site) or dose fractionation schedule and technique?

**PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings)**

| PICOTS | Inclusion | Exclusion |
|---|---|---|
| **Population** | • Primary research studies that include a majority (50% or more) of adult patients with metastases in the brain resulting from non-small cell lung cancer, breast cancer, or melanoma | • Study samples comprising patients with cancer from other origins or primary brain tumors (e.g., glioblastomas) and pediatric samples |
| **Interventions** | • Studies evaluating radiation therapy, including WBRT and SRS alone or in combination, as initial or postoperative treatment, with or without systemic therapy (immunotherapy and chemotherapy)<br>• Studies have to report on effects of radiation therapy in the 1990s or later | • Studies without WBRT or SRS treatment arms<br>• Studies based exclusively on pre-1990 data |
| **Comparators** | • Studies comparing eligible interventions to other eligible interventions or other management approaches (no intervention; waitlist; delayed intervention [radiation to be given at a later time]; placebo; observation, watchful waiting, or surveillance; supportive care, palliative care, or steroid treatment; usual care; systemic | • Studies comparing only non-intervention features (e.g., comparing two patient subgroups) |

| PICOTS | Inclusion | Exclusion |
|---|---|---|
| | therapy, immunotherapy, or chemotherapy; WBRT; SRS; surgery; different dose fractionation schedules; different radiation therapy approaches; different intervention combinations) | |
| **Outcomes** | • Studies reporting on patient health outcomes, such as<br>○ overall survival, progression-free survival recurrence/cancer control (local tumor control, intracranial control / complete response, partial response, stable response of all metastases);<br>○ symptom burden, health status or health-related quality of life;<br>- functional status (physical, affective or neurocognition functions);<br>○ or adverse events, including acute and late toxicity (e.g., radiation necrosis, hair loss, or nausea)<br>• Patient health outcomes may include patient- and caregiver-reported outcomes as well as clinical, physician assessed, and hospital record outcomes and measures may include quantitative as well as qualitative reports and no restrictions will be imposed regarding the specific measurement, metric, aggregation method (e.g., mean, proportion), or timepoint. | • Studies reporting only on therapy acceptance, provider variables (e.g., provider knowledge), organizational measures (e.g., wait times), treatment utilization, or costs |
| **Timing** | • Studies will not be limited by the duration of the intervention or the length of follow up | • No exclusions apply |

| PICOTS | Inclusion | Exclusion |
|---|---|---|
| **Setting(s)** | • Inpatient and outpatient settings<br>• Studies may include national and international settings | • Studies in resource-limited settings such as developing countries will be reviewed for comparability with US settings |
| **Study design** | **All KQs**<br>• RCTs<br>• Studies with results published in clinicaltrial.gov will be included regardless of whether a journal publication is available<br>• English-language publications<br>**KQ4**<br>• Prospective experimental and observational studies (including non-randomized clinical trials and cohort studies comparing 2 or more intervention cohorts) of 200 patients or more or those that report a statistical power analysis for adverse events | • Studies without comparator (e.g., case studies)<br>• Evaluations reported only in abbreviated format (e.g., in a conference abstract) and that are not registered in a research registry<br>• Studies exclusively reported in non-English publications will be retained as a resource but will not be eligible for inclusion<br>• Systematic reviews will be retained for reference mining |

Dated: 29 January 2020.

Virginia L. Mackay-Smith,

Associate Director, Office of the Director, AHRQ.

[FR Doc. 2020-01996 Filed: 1/31/2020 8:45 am; Publication Date: 2/3/2020]