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

Scientific Information Request on Emerging Approaches to Diagnosis and Treatment of Non-Muscle-Invasive Bladder Cancer

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

ACTION: Request for Scientific Information 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 of Emerging Approaches to Diagnosis and Treatment of Non-Muscle-Invasive Bladder Cancer, which is currently being conducted by the Evidence-based Practice Centers for the AHRQ Effective Health Care Program. Access to published and unpublished pertinent scientific information will improve the quality of this review. AHRQ is conducting this systematic review pursuant to Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, and Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

DATES: Submission Deadline on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:
Online submissions:
http://effectivehealthcare.AHRQ.gov/index.cfm/submitscientific-information-packets/. Please select the study for which you are submitting information from the list to upload your documents.

E-mail submissions: SIPS@epc-src.org.

Print submissions:

Mailing Address:
Portland VA Research Foundation
Scientific Resource Center
ATTN: Scientific Information Packet Coordinator
PO Box 69539
Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):
Portland VA Research Foundation
Scientific Resource Center
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3710 SW U.S. Veterans Hospital Road
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FOR FURTHER INFORMATION CONTACT:

Ryan McKenna, Telephone: 503-220-8262 ext. 58653 or Email: SIPS@epc-src.org.

SUPPLEMENTARY INFORMATION:
The Agency for Healthcare Research and Quality has commissioned the Effective Health Care (EHC) Program Evidence-based Practice Centers to complete a review of the evidence for Emerging Approaches to Diagnosis and Treatment of Non-Muscle-Invasive Bladder Cancer.

The EHC 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 Emerging Approaches to Diagnosis and Treatment of Non-Muscle-Invasive Bladder Cancer, including those that describe adverse events. The entire research protocol, including the key questions, is also available online at: http://effectivehealthcare.AHRQ.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1941

This notice is to notify the public that the EHC Program would find the following information on Emerging Approaches to Diagnosis and Treatment of Non-Muscle-Invasive Bladder Cancer helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please indicate whether results are available on ClinicafTrials.gov along with the ClinicalTrials.gov trial number.
- For completed studies that do not have results on ClinicalTrials.gov, please provide 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 will be very beneficial to the EHC Program. The contents of all submissions will be made available to the public upon request. Materials submitted must be publicly available or can 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 EHC 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 EHC 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: http://effectivehealthcare.AHRO.gov/index.cfm/join-the-email-list1/.

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. The entire research protocol, is also available online at: http://effectivehealthcare.AHRO.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1941

The Key Questions

Key Question 1
What is the diagnostic accuracy of various urinary biomarkers compared with other urinary biomarkers or standard diagnostic methods (cystoscopy, cytology, and imaging) in 1) persons with signs or symptoms warranting evaluation for possible bladder cancer or 2) persons undergoing surveillance for previously treated bladder cancer?
- Does the diagnostic accuracy differ according to patient characteristics (e.g., age, sex, ethnicity), or according to the nature of the presenting signs or symptoms?

Key Question 2
For patients with non-muscle-invasive bladder cancer, does the use of a formal risk-adapted assessment approach to treatment decisions (e.g., Guidelines of the European Association of Urology or based on urinary biomarker tests) decrease mortality or improve other outcomes (e.g., recurrence, progression, need for cystectomy, quality of life) compared with treatment not guided by an assessed risk-adapted approach?

Key Question 3

For patients with non-muscle-invasive bladder cancer treated with transurethral resection of bladder tumor (TURBT), what is the effectiveness of various intravesical chemotherapeutic or immunotherapeutic agents for decreasing mortality or improving other outcomes (e.g., recurrence, progression, need for cystectomy, quality of life) compared with other agents, TURBT alone, or cystectomy?
- What is the comparative effectiveness of various chemotherapeutic or imnnunotherapeutic agents, as monotherapy or in combination?
- Does the comparative effectiveness differ according to tumor characteristics, such as histology, stage, grade, size, or molecular/genetic markers?
- Does the comparative effectiveness of various chemotherapeutic or immunotherapeutic agents differ according to dosing frequency, duration of treatment, and/or the timing of administration relative to TURBT?
- Does the comparative effectiveness differ according to patient characteristics, such as age, sex, ethnicity, performance status, or medical comorbidities?

Key Question 4

For patients with high risk non-muscle-invasive bladder cancer treated with TURBT, what is the effectiveness of external beam radiation therapy (either alone or with systemic chernotherapy/immunotherapy) for decreasing mortality or improving other outcomes compared with intravesical chemotherapy/immunotherapy alone or cystectomy?

Key Question 5

In surveillance of patients treated for non-muscle-invasive bladder cancer, what is the effectiveness of various urinary biomarkers to decrease mortality or improve other outcomes compared with other urinary biomarkers or standard diagnostic methods (cystoscopy, cytology, and imaging)?

- Does the comparative effectiveness differ according to tumor characteristics, such as histology, stage, grade, size, or molecular/genetic markers?
- Does the comparative effectiveness differ according to the treatment used (i.e., specific chemotherapeutic or immunotherapeutic agents and/or TURBT)?
- Does the comparative effectiveness differ according to the length of surveillance intervals?
- Does the comparative effectiveness differ according to patient characteristics, such as age, sex, or ethnicity?

Key Question 6
For initial diagnosis or surveillance of patients treated for non-muscle-invasive bladder cancer, what is the effectiveness of blue light or other methods of augmented cystoscopy compared with standard cystoscopy for recurrence rates, progression of bladder cancer, mortality, or other clinical outcomes?

Key Question 7
What are the comparative adverse effects of various tests for diagnosis and post-treatment surveillance of bladder cancer, including urinary biomarkers, cytology, and cystoscopy?

Key Question 8
What are the comparative adverse effects of various treatments for non-muscle-invasive bladder cancer, including intravesical chemotherapeutic or immunotherapeutic agents and TURBT?

- How do adverse effects of treatment vary by patient characteristics, such as age, sex, ethnicity, performance status, or medical connorbidities such as chronic kidney disease?

PICOTS (Population, Intervention, Comparator, Outcome, Timing, Setting)
Population(s)

- For KQ 1, 6, and 7: Adults with signs or symptoms of possible bladder cancer (e.g., gross or microscopic hematurla, irritative voiding symptoms)
- For KQ 2: Adults with non-muscle-invasive bladder cancer (stages Ta, Tis, or Ti)

- For KQ 3 and 8: Adults with non-muscle invasive bladder cancer treated with TURBT
- For KQ 4 and 8: Adults with high-risk non-muscle invasive bladder cancer treated with TURBT
- For KQs 1 and 5 through 7: Adults undergoing surveillance following treatment for non-muscle invasive bladder cancer

Interventions
- For KQ 1, 5, and 7: Urinary biomarkers\a\
- For KQ 2: Risk-adapted treatment approaches
- For KQ 3a, 3b, 3c, 3d, and 8: Intravesical chemotherapeutic or immunotherapeutic agents\b\
- For KQ 4: External beam radiation therapy, with or without systemic chemotherapy or immunotherapy
- For KQ 6: Blue light or other methods of augmented cystoscopy

\a\Restricted to tests that are approved for diagnosis of bladder cancer by the U.S. Food and Drug Administration (BTAstat® [BTA], Alere NMP228, BladderChek® [NMP22], UroVysion® [FISH] and ImmunoCytrm [immunocytology]) or available in the U.S. and classified as a Laboratory Developed Test by the FDA (CxBladderrm)

\b\Chemotherapeutic and immunotherapeutic agents of interest include: mitomycin; apaziquone; paclitaxel; gemcitabine; thiotepa; valrubicin; doxorubicin; bacillus Calnnette-Guerin (BCG); and interferon.

Comparators
- For KQ 1, 5, and 7: Other urinary biomarkers or standard diagnostic methods (cystoscopy, cytology, and imaging)
- For KQ 2: Treatment not guided by risk-adapted approach
- For KQ 3a, 3b, 3c, 3d, and 8: Other intravesical chemotherapeutic or innmunotherapeutic agent, different dose or duration of intravesical chemotherapy or immunotherapy, or transurethral resection of bladder tumor (TURBT) alone
- For KQ 4: Intravesical chemotherapeutic or immunotherapeutic agents or cystectomy

Outcomes
- For KQ 1 and 5: Diagnostic accuracy, using cystoscopy with biopsy as the reference standard
- For KQ 2, KQ 3, KQ 4, KQ 5: Mortality, disease-specific and all-cause
- For KQ 2, KQ 3, KQ 4, KQ 5: Need for cystectomy
- For KQ 2, KQ 3, KQ 4, KQ 5, KQ 6: Recurrence of cancer
- For KQ 2, KQ 3, KQ 4, KQ 5: Progression of cancer
- For KQ 2, KQ 3, KQ 4, KQ 5: Quality of life
- For KQ 7: Adverse effects of diagnostic testing (e.g., false-positives, labeling, anxiety, complications of cystoscopy)
- For KQ 8: Adverse effects of treatment (e.g., cystitis, urinary urgency, urinary frequency, incontinence, hematuria, pain, urosepsis, myelosuppression

Timing
Any duration of follow-up

Settings
- Inpatient settings
- Outpatient settings

Dated: August 26, 2014.

Richard Kronick,
AHRQ Director.

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