Billing Code: 4160-90-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Interventions for Dyspnea in Patients with Advanced Cancer

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 *Interventions for Dyspnea in Patients with Advanced Cancer,* 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 Access to published and unpublished pertinent scientific information will improve the quality of this review.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* by 30 days after date of publication of this notice.

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 *Interventions for Dyspnea in Patients with Advanced Cancer*. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(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 *Interventions for Dyspnea in Patients with Advanced Cancer*, including those that describe adverse events. The entire research protocol is available online at:

https://effectivehealthcare.ahrq.gov/products/dyspnea-advanced-cancer/protocol

This is to notify the public that the EPC Program would find the following information on Interventions for Dyspnea in Patients with Advanced 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 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 four (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)

1. What are the comparative benefits of non-pharmacological interventions (either alone or in combination) for improving dyspnea in patients with advanced cancer?
2. What are the comparative benefits of pharmacological interventions (either alone or in combination) for improving dyspnea in patients with advanced cancer?

3. What are the comparative benefits of non-pharmacological, pharmacological, and multimodal interventions for improving dyspnea in patients with advanced cancer?
4. What are the harms of non-pharmacological and pharmacological interventions for improving dyspnea in patients with advanced cancer?

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

Population(s):

Patients (age ≥ 18 years of age) with advanced cancer (unlikely to be cured or unlikely to be controlled with treatment) and dyspnea.

Interventions:

Non-pharmacological interventions (KQ 1, 3, and 4)

Respiratory interventions:

a. Airflow/ cooling: fan therapy, water spray, changing the room environment (cooling the room/opening a window)
b. Compressed air
c. Supplemental oxygen therapy (for hypoxemic and non-hypoxemic patients)
d. Breathing gas: heliox
e. Noninvasive Positive-Pressure Ventilation (Bilevel positive airway pressure (BiPAP)/ Continuous positive airway pressure (CPAP))

Behavioral and psychoeducational interventions:

a. Cognitive-behavioral therapy (CBT)

b. Other behavioral interventions (may include components such as other psychosocial interventions, teaching problem-solving or coping and adaptation strategies, relaxation/distraction techniques, biofeedback, energy conservation)

Activity and rehabilitation interventions:

a. Walking aids/mobility aids
b. Exercise (healthcare professional-guided exercise, physical therapy, occupational therapy, aerobic exercise, non-aerobic exercise, isometric exercise, tai chi, qigong)
c. Respiratory training
d. Pulmonary rehabilitation
e. Chest wall vibration
f. Neuromuscular electrical stimulation (NMES)

Complementary and alternate medicine interventions:

a. Acupuncture
b. Acupressure
c. Reiki
d. Mindfulness
e. Yoga
f. Meditation
g. Music therapy

Combination of any of the above

Pharmacological interventions (drugs approved by the Food and Drug Administration (FDA) for any indication) (KQ 2, 3, and 4)**.**

Any routes of administration for all drug classes are included.

- **Bronchodilators**
    a. Beta-adrenergic receptor agonists: albuterol, arformoterol, formoterol, indaceterol, levalbuterol, olodaterol, terbutaline, vilanterol
    b. Antimuscarinics: aclidinium, atropine, glycopyrrolate, ipratropium, scopolamine, tiotropium, umeclidinium
    c. Methylxanthines: theophylline, aminophylline, caffeine
- **Nebulized saline**
- **Corticosteroids**: beclomethasone, betamethasone, budesonide, ciclesonide, dexamethasone, flunisolide, fluticasone, hydrocortisone, methylprednisolone, mometasone, prednisone
- **Diuretics**: amiloride, bumetanide, ethacrynic acid, furosemide, hydrochlorothiazide, indapinide, metolazone, spironolactone, torsemide, triamterine
- Lidocaine
- **Non-steroidal anti-inflammatory agents**: celecoxib, diclofenac, diflusinal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, salsalate, sulindac, tolmetin

- **Phenothiazines**: promethazine, prochlorperazine, chlorpromazine, thioridazine
- **Atypical antipsychotics:** aripiprazole, asenapine, brexpiprazole, cariprazine, clozapine, haloperidol, iloperidone, lurasidone, olanzapine, paliperidone, pimavanserin, quetiapine, risperidone, ziprasidone
- **Gamma-Aminobutyric acid (GABA) analog anticonvulsants**: gabapentin, pregabalin
- **Opioids**: buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tapentadol, tramadol
- **Anxiolytics**
    a. Benzodiazepines: alprazolam, clonazepam, diazepam, lorazepam, midazolam, oxazepam, temazepam
    b. Serotonin-norepinephrine reuptake inhibitors (SNRIs)/ Selective serotonin reuptake inhibitors (SSRIs): citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, levomilnacipran, milnacipran, paroxetine, sertraline, venlafaxine
    c. Other: bupropion, buspirone, mirtazapine
- **Combinations of any of the above**

Combinations of nonpharmacologic and pharmacologic or multimodal interventions

Comparators:

- KQ 1: Placebo, usual care, other non-pharmacological intervention or a combination of non-pharmacological interventions
- KQ 2: Placebo, usual care, other pharmacological intervention or dose or route, or a combination of pharmacological interventions
- KQ 3: Placebo, usual care, non-pharmacological interventions, pharmacologic interventions, or multimodal interventions (e.g., opioids versus respiratory training, or acupuncture versus morphine versus combination acupuncture and morphine)
- KQ 4: Any of the comparators for KQ 1, KQ 2, or KQ 3

Outcomes:

Patient- or caregiver-reported, or observational symptom-related outcomes (KQ1-3)

Caregiver-reported or observational symptom-related only if patients are unable to self-report

- Dyspnea as measured by a validated tool, which must include **patient- or caregiver-reported or observational symptom-related measures** of breathing difficulty or discomfort.
- Anxiety as measured by a validated tool. This tool must include **patient-or caregiver-reported** measures of anxiety.

- Functional status (measured by validated **patient- or caregiver-reported tool**)
- Health-related quality of life (general or disease-specific, measured by a validated patient- or caregiver-reported tool)

Clinical or utilization health outcomes (KQ1-4)

- Respiratory rate
- Oxygen or carbon dioxide/ bicarbonate levels
- Heart rate
- Blood pressure
- Objective measure of functional capacity, e.g., 6-minute walk test
- Level of sedation
- Utilization outcomes linked to dyspnea: hospitalizations, intensive care unit stays, emergency room visits

Patient-centered adverse effects of dyspnea treatments (KQ4)

- Central nervous system (cognitive changes, dizziness, drowsiness, fatigue, headache, respiratory depression)
- Gastrointestinal (constipation, nausea, vomiting)
- Pruritus
- Urinary retention, dry mouth
- Opioid use disorder
- Discomfort or distress from equipment, e.g., oxygen or masks
- Death

- Dropouts

Timing: Any duration of follow-up

Setting: Any setting

Study design: RCTs for all KQ

- For KQ1-3: RCTs, nonrandomized controlled trials, and observational studies with a concurrent comparison group, with at least 10 patients in each group
- For KQ 4: RCTs, nonrandomized controlled trials, observational studies with a concurrent comparison group, and prospective or retrospective cohort studies where the primary objective of the study is to evaluate harms from dyspnea treatments

Dated: October 28, 2019.

Virginia L. Mackay-Smith,

Associate Director,

Office of the Director, AHRQ.

[FR Doc. 2019-23871 Filed: 10/31/2019 8:45 am; Publication Date: 11/1/2019]