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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Use of Cardiac Resynchronization Therapy: A Systematic Review Update

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 *Use of Cardiac Resynchronization Therapy: A Systematic Review Update*, 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 Access to published and unpublished pertinent scientific information will improve the quality of this review.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 **[INSERT DATE 30 DAYS AFTER 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.):

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5600 Fishers Lane

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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 *Use of Cardiac Resynchronization Therapy: A Systematic Review Update*. 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 *Use of Cardiac Resynchronization Therapy: A Systematic Review Update*, including

those that describe adverse events. The entire research protocol is available online at: https://www.ahrq.gov/research/findings/ta/index.html

This is to notify the public that the EPC Program would find the following information on Use of Cardiac Resynchronization Therapy: A Systematic Review Update 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*, 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 EPC 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.

The Key Questions:

KQ1a: Is cardiac resynchronization therapy with defibrillator (CRT-D) effective in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with an LVEF≤35% and a QRS duration≥120ms?

KQ1b: Does the effectiveness of cardiac resynchronization therapy with defibrillator (CRT-D) vary by the following subgroups:

Age

Gender

Cardiomyopathy subtype

QRS morphology

Left ventricular ejection fraction

NYHA class

Atrial fibrillation

KQ2: What are the adverse effects or complications associated with CRT-D implantation?

KQ3a: Is cardiac resynchronization therapy in the absence of defibrillator capacity (CRT-P) effective in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with LVEF≤35% and a QRS duration≥120ms?

KQ3b: Does the effectiveness of cardiac resynchronization therapy in the absence of defibrillator capacity (CRT-P) vary by the following subgroups:

Age

Gender

Cardiomyopathy subtype

QRS morphology

Left ventricular ejection fraction

NYHA class

Atrial fibrillation

KQ4: What are the adverse effects or complications associated with CRT-P implantation?

KQ5: What is the effectiveness of CRT-D versus CRT-P in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with LVEF≤35% and a QRS duration≥120ms?

KQ6: What are the adverse effects or complications associated with CRT-D versus CRT-P implantation?

KQ7a: What is the effectiveness of alternative CRT techniques (adaptive CRT, multipoint pacing, His bundle pacing, quadripolar) versus conventional CRT techniques in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with an LVEF ≤35% and a QRS duration ≥120ms?

KQ7b: Does the effectiveness of alternative CRT techniques (adaptive CRT, multipoint pacing, His bundle pacing, quadripolar) vary by the following subgroups:

Age

Gender

Cardiomyopathy subtype

QRS morphology

Left ventricular ejection fraction

NYHA class

Atrial fibrillation

KQ8: What are the adverse effects or complications associated with alternative CRT techniques (adaptive CRT, multipoint pacing, His bundle pacing, quadripolar)?

KQ9: What is the effectiveness of His bundle pacing or CRT versus RV pacing in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with an LVEF between ≥36% to ≤50% and atrioventricular block?

KQ10: What are the adverse effects or complications associated with His bundle pacing or CRT versus RV pacing in reducing heart failure symptoms, improving myocardial function, reducing hospitalization and/or improving survival in patients with an LVEF between ≥36% to ≤50% and atrioventricular block?

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

Population(s)

KQ1 –KQ8: Subjects of age ≥ 18, with a left ventricular ejection fraction ≤35% and a QRS duration ≥120 ms.

KQ9 -10: Subjects of age ≥ 18, with an LVEF between ≥36% to ≤50% and atrioventricular block [We will use a recently published systematic review to address KQs 9-10]

Interventions

- nCardiac resynchronization therapy with a defibrillator (CRT-D)
- aCardiac resynchronization without a defibrillator (CRT-P)

- eAlternative cardiac resynchronization therapy alternative CRT techniques (adaptive CRT, multipoint pacing, His bundle pacing, quadripolar)

Comparators

- oCRT-D vs. implantable cardioverter defibrillator (ICD)
- ICRT-P vs. optimal medical therapy
- RCRT-D vs. CRT-P
- RAlternative CRT techniques versus conventional CRT techniques

Outcomes

KQ1a, 3a, 5, and 7a (effectiveness)

Clinical outcomes

- l6 minute hall walk distance
- Left ventricular end diastolic volume/volume index
- oLeft ventricular end systolic volume/volume index
- eLeft ventricular ejection fraction
- ePacker Score[17]

Quality of life

- uMinnesota Living with Heart Failure Inventory Score
- iKansas City Cardiomyopathy Score
- aSF-36

Health outcomes

- eHospitalizations for heart failure
- oAll- cause mortality

KQ2, KQ4, KQ6, and KQ8 (harms)

- QProcedure related complications
- rLength of hospital stay
- ePneumothorax
- nPocket hematoma
- oDevice Infection
- eCardiac perforation/ tamponade
- aLead dislodgement
- eVentricular arrhythmias
- eDeath (within a week)
- eInappropriate ICD shocks (CRT-D and alternative CRT-D techniques only)

KQ1b , KQ3b, 7b (subgroups)

- QAge
- gGender
- eCardiomyopathy subtype
- aQRS morphology
- RLeft ventricular ejection fraction
- eNYHA class
- sAtrial fibrillation

Timing

KQ1a, 3a, 5, and 7a, (effectiveness)

- QOutcomes from CRT-D, CRT-P, and alternative CRT techniques at 3-6 months, 1 year, and ≥2 year end-points

KQ2, 4, 6, and 8 (harms)

- QOutcomes from CRT-D, CRT-P, and alternative CRT techniques at any time point

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