

**Medicare Evidence Development &
Coverage Advisory Committee
(MEDCAC)
Health Outcomes in Heart Failure
Treatment Technology Studies
March 22, 2017**

Dr. Nancy Sweitzer | March 22, 2017



Employment: University of Arizona, Sarver Heart Center Director

Editor-In-Chief: Circulation: Heart Failure

Associate Editor: Circulation

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supports research, no salary support

Clinical Trial Leadership:

Novartis, modest, <\$10,000

Merck, modest, <\$10,000

Consultant for: Accorda Therapeutics, modest, < \$10,000, Medtronic, modest,
<\$10,000

Volunteer Activities:

Heart Failure Society of America Advocacy Committee

AHA: AHA has no conflicts to disclose



QUESTION 3 | Quality of Life Measures



- 3) How confident are you that quality of life measures [e.g., Kansas City Cardiomyopathy Questionnaire (KCCQ), Minnesota Living With Heart Failure Questionnaire (MLWHFQ):
 - a. Are adequate measures which reflect the patient experience;
 - b. Should be included as the standalone, meaningful primary health outcomes in research studies;
 - c. Should be included as a composite standalone, meaningful primary health outcomes in research studies?

a) Are adequate measures which reflect the patient experience: KCCQ

- Disease-specific QOL measures reflect the patient experience when they are well designed, as they capture what is meaningful to patients
- KCCQ has been extensively validated in multiple HF states, including both HFrEF and HFpEF, and covers the primary symptoms and impact of heart failure from patients' perspectives
 - It maintains validity even in the presence of significant comorbidity
 - A change of 5 points on the KCCQ is associated with changes in clinical status and physical functioning that are clinically significant
 - KCCQ has been shown to be more sensitive to clinical change than the MLHF questionnaire
 - The original version can be used, or a 12-item version to ease implementation and reduce burden on providers and patients

b) Should be included as the standalone, meaningful primary health outcomes in research studies?

- A meaningful primary health outcome must be clinically meaningful in its own right, and important to the patient. QOL outcomes meet this definition of meaningful outcomes, particularly when measured by a disease specific tool sensitive to the intervention being tested.
- It would thus absolutely be reasonable for disease-specific QOL measures to be standalone primary health outcomes in some research studies, providing safety and risks of the intervention are also known or assessed
- Symptoms and functional capacity have been standalone outcomes for therapies in other cardiovascular disease states with significant symptoms and limitations, like angina, peripheral vascular disease, and pulmonary hypertension

c) Should be included as composite standalone, meaningful primary health outcomes in research studies?

- Failure to include any measure of patient QOL could be seen as a failure to comprehensively study an intervention.
- This is particularly true with technology, as the response of different patients to technological interventions can be variable and unpredictable.
- It is critical that when included QOL measures not be part of composite endpoints, as they are qualitatively different from less subjective endpoints such as hospitalization or death.
- We are obligated to understand the impact of new technology on patients lives, not just on their disease manifestations and symptoms.
- We would strongly support a requirement for some assessment of impact on QOL as an adjunct to other endpoints in design of technology trials.

Discussion



- Please discuss whether additional patient-reported measurement [e.g., Short Form-36 (SF-36), EuroQol five dimensions questionnaire (EQ5D)] should be considered to capture burdens associated with the heart failure therapy under study.
- Please discuss the appropriate length of follow-up post-heart failure intervention for assessing patient-reported measurements.
- Please discuss the impact of unblinded study participants on patient-reported measurements and functional assessments.
- Please discuss how to best consider the impact of adverse events associated with heart failure technologies while balancing the potential for improvements to meaningful health outcomes.
- Please discuss how to balance the benefits and harms of therapies which may improve near-term patient-reported health outcome assessments or clinical measurements (e.g., 6 MWT or symptoms) but may decrease length of life.

Please discuss whether additional patient-reported measurement [e.g., Short Form-36 (SF-36), EuroQol five dimensions questionnaire (EQ5D)] should be considered to capture burdens associated with the heart failure therapy under study.

- There is little evidence that other questionnaires improve understanding of therapeutic burden associated with HF and HF therapies beyond what is found in KCCQ.
- Although there is a theoretical concern that collateral impact of treatment on QOL issues not directly related to HF may be missed, little data support this in HF populations since the HF condition tends to dominate QOL issues.
- Depending on the therapy, adjunctive surveys may be of interest to explore outcomes of interest in more detail: depression, social engagement, caregiver burden, mobility, etc, but these should be incorporated in addition to disease-specific measures on a case by case basis.

Please discuss the appropriate length of follow-up post-heart failure intervention for assessing patient-reported measurements.

- Often benefits in quality of life are realized quickly particularly if major surgical procedures are not necessary.
- QOL benefits appear to plateau for many therapies, as seen in resynchronization pacemakers and ventricular assist devices.
- Collecting additional QOL data after this plateau is not worthwhile, and may be contaminated by ongoing processes not impacted by the technology, diluting the efficacy signal.
- Ideally, early phase studies will provide clues to the pace of QOL improvement, but 6-12 months is reasonable for most technology interventions.

Please discuss the impact of unblinded study participants on patient-reported measurements and functional assessments.

- Lack of blinding is particularly problematic with technology based interventions because there is usually a belief in the technology among those willing to participate in such studies. This has been shown to potentially enhance the placebo effect significantly. Such placebo effects require a blinded study for evaluation.
- This has been seen repeatedly in HF trials, where significant improvement is predictably seen in the placebo arm.
- Approval of a technology-based therapy should require a blinded study unless absolutely impossible.

Please discuss how to best consider the impact of adverse events associated with heart failure technologies while balancing the potential for improvements to meaningful health outcomes.

- It is ideal, when interpreting results of research in which benefit is not unequivocal or universal, to understand the impact of the technology on domains of most interest to the patient.
- In HF patients, different patients have different goals, and these goals change as patients age, live with disease, and develop other limiting comorbidities.
- No decision is right for every heart failure patient. The ideally designed study will inform shared decision making by improving estimates of benefit and harm, while more clearly defining the type and severity of these outcomes. Such data can then be used by patients and providers in shared-decision making about pursuing additional therapies.

Please discuss how to balance the benefits and harms of therapies which may improve near-term patient-reported health outcome assessments or clinical measurements (e.g., 6 MWT or symptoms) but may decrease length of life.

- In a therapy in which benefits are clear, but harm is also present, the best course appears to develop tools, to the extent possible, to characterize risks for individual patients and allow informed and shared decision making.
- Providers do this routinely with anticoagulant therapy for atrial fibrillation, where there is a risk benefit equation for each patient. Similarly with decisions to use bare metal or drug eluting stents.
- At the end of a trial, we should have detailed information about benefit and harm that will enable discussions with patients.

Conclusion



Understanding the impact of new technologies on the patient experience, and quantifying the impact of the technology on disease manifestations most important to each individual are essential components of a well designed study.



A large, stylized graphic of a torch with a flame, rendered in a lighter shade of red than the background. The torch is positioned on the right side of the image, with the flame pointing upwards and to the left.

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