TO: Cardiovascular Standing Committee

FR: NQF Staff

RE: Post-Comment Call to Discuss Public and Member Comments

DA: December 7, 2015

Background

In Phase 3 of this project, the 20-member Cardiovascular Standing Committee met during a 2-day in-person meeting to evaluate a total of 26 measures: 13 maintenance measures and 13 new measures against NQF's standard evaluation criteria. The Committee evaluated three new eMeasure versions of endorsed measures that were evaluated as separate measures from their registry-based counterparts. Sixteen measures were recommended for endorsement by the Committee and one eMeasure was recommended for Approval for Trial Use. The Committee did not reach consensus on two measures, six were not recommended for endorsement, and one measure recommendation was deferred to Cardiovascular 2016-2017 project. The *ad hoc* review of the revised specifications for the blood pressure control measure evaluated by the Committee has been deferred pending availability of new evidence. Healthcare Incentives Improvement Institute (HCI3) requested reconsideration of five measures that were not recommended by the Standing Committee. NQF staff will reconvene the Standing Committee for a future conference call to reconsider the five measures that were not recommended (#2740, #2749, #2747, #2748, and #2752) and the one measure where consensus was not reached for overall suitability (#2751).

Purpose of the Call

The Cardiovascular Standing Committee will meet via conference call on Monday, December 7, 2015 from 1:00-3:00pm ET. The purpose of this call is to:

- Review and discuss comments received during the post-evaluation public and member comment period that ended on November 23, 2015;
- Provide input on proposed responses to the post-evaluation comments; and
- Determine whether reconsideration of any measures or other courses of action is warranted.

Due to time constraints, during this call we will review comments by exception, in the case the Committee disagrees with the proposed responses.

Standing Committee Actions

1. Review this briefing memo and Draft Report.
2. Review and consider the full text of all comments received and the proposed responses to the post-evaluation comments (see Comment Table included with the call materials).
3. Be prepared to provide feedback and input on proposed post-evaluation comment responses.

Conference Call Information

Please use the following information to access the conference call line and webinar:

Speaker dial-in #: 1-(877) 298-1950
Web Link: http://nqf.commpartners.com/se/Rd/Mt.aspx?927162
Registration Link: http://nqf.commpartners.com/se/Rd/Rg.aspx?927162

Comments Received

NQF solicits comments on measures undergoing review in various ways and at various times throughout the evaluation process. First, NQF solicits comments on endorsed measures on an ongoing basis through the Quality Positioning System (QPS). Second, NQF solicits member and public comments prior to the evaluation of the measures via an online tool located on the project webpage. Third, NQF opens a 30-day comment period to both members and the public after measures have been evaluated by the full committee and once a report of the proceedings has been drafted.

Pre-evaluation comments

The pre-evaluation comment period was open from July 29, 2015 to August 12, 2015 for 25 of the 26 measures under review. Comments for an Implantable Cardioverter-Defibrillator (ICD) complications measure stewarded by the American College of Cardiology were not requested because measure submission materials could not be posted during this period. A total of 27 pre-evaluation comments were received for the remaining 25 measures, the majority of which pertained to, and were supportive of, the measure submitted for Trial Use Approval and stewarded by the National Minority Quality Forum. All pre-evaluation comments were provided to the Committee prior to their initial deliberations held during the workgroups calls.

Post-evaluation comments

The Draft Report went out for Public and Member comment October 23, 2015 to November 23, 2015. During this commenting period, NQF received 57 comments from eleven member organizations:

Consumers – 0	Professional – 12
Purchasers – 0	Health Plans – 25
Providers – 10	QMRI – 1
Supplier and Industry – 9	Public & Community Health - 0

In order to facilitate discussion, the majority of the post-evaluation comments have been categorized into major topic areas or themes. Where possible, NQF staff has proposed draft responses for the Committee to consider. Although all comments and proposed responses are subject to discussion, we will not necessarily discuss each comment and response on the post-comment call. Instead, we will spend the majority of the time considering the major topics and/or those measures with the most significant issues that arose from the comments. Note that the organization of the comments into major topic areas is not an attempt to limit Committee discussion.

We have included all of the comments that we received (both pre- and post-evaluation) in the Comment Table. This comment table contains the commenter's name, comment, associated measure, topic (if

applicable), and—for the post-evaluation comments—draft responses for the Committee's consideration. Please refer to this comment table to view and consider the individual comments received and the proposed responses to each.

Comments and their Disposition

Three major themes were identified in the post-evaluation comments, as follows:

1. Harmonization
2. Requests for changes
3. Preference of outcome measures

Theme 1 - Harmonization

Several comments received support the Committee's recommendations for harmonization of the measures identified as related or competing (*0669: Cardiac Imaging for Preoperative Risk Assessment for Non-Cardiac, Low Risk Surgery and 0670: Cardiac stress imaging not meeting appropriate use criteria: Preoperative evaluation in low risk surgery patients)*. Additional comments received recommend harmonization of three measures (*0081: Heart Failure (HF): Angiotensin-Converting Enzyme (ACE) Inhibitor or Angiotensin Receptor Blocker (ARB) Therapy for Left Ventricular Systolic Dysfunction (LVSD), 0083: Heart Failure (HF): Beta-Blocker Therapy for Left Ventricular Systolic Dysfunction (LVSD), and 0079: Left Ventricular Ejection Fraction Assessment (Outpatient Setting*).

> **Proposed Committee Response:** During the second post In-Person Meeting webinar on October 9, 2015 the Committee considered harmonization of measures within the Cardiovascular portfolio. The Committee encouraged the developers of two competing measures (#0669 and #0670) to harmonize the measure specifications. Harmonization of #0669 and #0670 should be completed prior to the measures' next annual update. The Committee also urged developers to work together in the future to further harmonize measures where possible. Additionally, the Committee will revisit the harmonization discussion of several measures during the next Cardiovascular measure endorsement project in 2016. Measures #0081, #0083, and #0079 were not identified as related or competing based on NQF criteria.
>
> **Action Item:** Does the Committee agree with the proposed response?

Theme 2 – Request for changes

A number of commenters suggested changes to several measures. The changes include adding additional exclusions and inclusion of additional pharmaceutical therapies.

> **Action Item:** The Committee should review the recommended changes and the developer responses, and then discuss during the call.

Theme 3 – Preference of outcome measures

For two measures (*0965: Discharge Medications (ACE/ARB and beta blockers) in Eligible ICD Implant Patients* and *2396: Carotid artery stenting: Evaluation of Vital Status and NIH Stroke Scale at Follow Up*) commenters noted a preference for outcome measures rather than the currently specified process measures.

> **Proposed Committee Response:** Generally, the Committee would prefer to recommend the endorsement of outcome measures rather than process or structural measures. However, measuring the process or structure may still be useful for quality improvement or other purposes; these measure types may still be useful where outcomes may be difficult to measure.
>
> **Action Item:** Does the Committee agree with the proposed response?

Measure Specific Comments

2764: Fixed-dose Combination of Hydralazine and Isosorbide Dinitrate Therapy for Self-identified Black or African American Patients with Heart Failure and LVEF <40% on ACEI or ARB and Beta-blocker Therapy

An overwhelming number of supportive comments were received for measure #2764. Three comments received referenced the 2013 ACC/AHA Heart Failure Guideline recommendations that encourage treatment of African-American heart failure patients with the isosorbide dinitrate and hydralazine hydrochloride combination therapy, but do not explicitly recommend the fixed-dose combination. The guidelines permit the use of the fixed-dose or separate therapies. The commenters' concern is that the measure could penalize providers who prescribe the separate therapies.

> **Developer Response:** The National Minority Quality Forum (NMQF) believes that Measure #2764 is consistent with the recommendations of the 2013 ACCF/AHA Guidelines for the Management of Heart Failure and the science that undergirds their recommendations; promotes clarity among physicians regarding evidence-based therapies for the treatment of Stage III & IV Heart Failure in the specified patient population; and facilitates the elimination of formulary management or economic barriers to this evidence-based therapy.
>
> ACC in their public comment takes the position that NMQF should include the two drugs administered separately, which is provided for in their clinical guidelines. They suggest that the two drugs used separately can constitute a generic of the fixed dose. They are, however, failing to clearly differentiate between off label use of an approved drug (branded or generic), and indicated use of an approved generic drug.
>
> By law an authorized generic drug has the approval of the Food and Drug Administration (FDA). To gain that approval, a generic drug must contain the same active ingredients as the innovator drug, be identical in strength, dose form, and route of administration, have the same use indications, be bioequivalent, meet the same batch requirements for identity, strength, purity, and quality, be manufactured under the same strict standards of FDA's good manufacturing

practice regulations required for innovator products. FDA has said there is no generic fixed dose. FDA monitors approved generics for safety.

The ACCF/AHA guidelines recommend off label use of isosorbide dinitrate (a generic of Isordil Titradose) and hydralazine hydrochloride (a generic of Apresoline Hydrochloride), two drugs with indications, labeling, dose and administration that are different from those of the fixed-dose approved by FDA. While the ACCF/AHA guideline writing committee may have the authority to use and recommend off label use of any medication, they should be fully transparent about the pros and cons of off-label prescribing versus using an approved medications, including level of evidence, problems of adherence, safety monitoring, possible liabilities, patient prognosis, and other relevant factors.

It is important to note that Medicare does not reimburse for off-label use.

As required by NQF guidance regarding the development of evidence-based performance measures, NMQF specified Measure #2764 based upon the strongest science/evidence, which supports the use of a combination of isosorbide dinitrate and hydralazine hydrochloride – evidence that is available only for the fixed-dose combination that was approved by the Food and Drug Administration (FDA) in 2005.

Based upon our review of the 2013 ACCF/AHA guidelines, the A-HeFT trial results, the 2010 Heart Failure Society of America guidelines, and other peer reviewed resources, NMQF determined that including language in Measure #2764 that would suggest the appropriateness of prescribing the two component compounds separately as equivalent to the fixed-dose combination approved by the FDA was not supported by available evidence, would be inconsistent with the high standards established by NQF for the development of performance measures to support the provision of quality care, and would be legally imprudent for the NMQF given the legal definitions of “generic” and “off-label use”.

It is our understanding that performance measures should be consistent with current evidence to ensure that appropriate, safe and high quality care is provided by physicians to their patients. The 2013 ACCF/AHA guideline appears to use as evidence to support their determination of equivalence, evidence that supports only the fixed-dose combination.

The National Minority Quality Forum supports efforts by NQF and its members to promote the development of performance measures that are consistent with scientific and clinical evidence, and result in improved outcomes of care while containing the growth of unnecessary expenditures. An essential component of accomplishing this objective is clarity and transparency in the development and application of these measures. As NMQF stated during the September 9 meeting of the Cardiovascular Measures Committee and in our application, recommendation of the use of the two component compounds as a “generic” is inconsistent with the statement by FDA that they have not approved a generic for the fixed-dose combination. A copy of the letter can be made available upon request.

In addition, given that neither of the two compounds is indicated for treatment of heart failure, the decision reached by the 2013 guideline writing committee constitutes a recommendation of off-label use that may be appropriate within the provider environment, but is not appropriate, we believe, for an NQF endorse performance measure. Therefore, the NMQF believes that

Measure #2764 does, indeed, represent the component of the 2013 ACCF/AHA guideline that is appropriate for a performance measure through the lenses of evidence, need, and importance.

Accordingly, NMQF asks the Cardiovascular Standing Committee to continue to recommend Measure #2764 so that testing of validity and reliability can proceed unimpeded, and this measure can advance to the endorsement phase of NQF deliberations.

The ACCF/AHA recommendation of the two separate compounds as equivalent appears to be based not upon strong evidence, but upon professional opinion and assumptions of affordability challenges inherent in the specified patient population. These concerns are not supported by any references or documentation, nor are they concerns that are de facto generalizable to all patients for whom the therapy in question is indicated.

The commenter states that the ACCF/AHA guideline writing committee had the option to limit the guideline recommendation to only the fixed-dose combination, yet explicitly decided to allow as equivalent the use of the individual components to ensure that patients have adequate flexibility in terms of drug availability or cost. The commenter offered no references to support the determination of equivalence by the writing committee, and no such references are evident in the 2013 ACCF/AHA Guideline for the Management of Heart Failure. The NMQF is not clear why the ACCF/AHA guideline writing committee believes it has the option to make science and evidence subservient to their stated concerns about affordability.

NMQF believes that drug availability and cost are issues that impede access to many therapies and devices, and hopes that the ACC's concern extends to all disease states, populations and therapies. NMQF, however, cannot support what appears to be the ACCF/AHA determination of equivalence or generic substitutability based upon no evidence for this particular therapy.

Further, the most important reason that patients are not receiving access to the approved fixed-dose combination is that it is not being prescribed.

We would also note that the fact that a therapy is currently proprietary does not, as we understand it, disqualify a therapy for inclusion in a performance measure.

The cost analysis of the evidence-based, FDA approved therapy compared to the individual components is misleading. The individual components are available as generics to reference/innovator drugs that were not indicated for treatment of heart failure. Neither separately nor taken together do the separate compounds meet the definition of a generic or an equivalent substitute for the FDA-approved fixed-dose combination.

The FDA is the approval body for branded and generic drugs. As noted on the FDA website, the FDA defines generics as drugs that have met the same rigid standards as the innovator drug. (http://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm) To gain FDA approval, a generic drug must:

- contain the same active ingredients as the innovator drug(inactive ingredients may vary)
- be identical in strength, dosage form, and route of administration
- have the same use indications
- be bioequivalent

• meet the same batch requirements for identity, strength, purity, and quality
• be manufactured under the same strict standards of FDA's good manufacturing practice regulations required for innovator products

The two component compounds of the fixed-dose combination do not meet this standard.

The National Minority Quality Forum is concerned about arbitrary and flexible definitions of the components of quality healthcare that may create confusion within both the provider and patient communities. The National Quality Forum is an environment that has the potential to eliminate much of this confusion. Measure #2764 is a step in the right direction.

Proposed Committee Response: The Committee considered the ACC/AHA Heart Failure Guidelines during the measure evaluation discussion and determined that a gap in appropriate treatment persists in the African-American subpopulation of heart failure patients warranting a need for this measure. Studies show a significant reduction in mortality of this specific subpopulation with the use of the fixed-dosed combination therapy.

Action Item: Does the Committee agree with the proposed response?

2712: Statin Use in Persons with Diabetes

Several measure specific comments were received for measure #2712. Two comments focus on tracking statin prescriptions in diabetic patients as not sufficient to assess whether the appropriate level of statins have been prescribed, thereby putting patients at risk of being undertreated. One comment notes that the list of medications does not include non-statin therapy as well as some FDA approved and well-recognized treatment options. The commenter asks the developer to include non-statins and other lipid-lowering drugs such as the new FDA approved PCSK-9 therapies to meet the measure requirements.

Developer Response: During the development of the measure, PQA considered whether the measure criteria could specify moderate to high intensity statin therapy. Since the measure is intended for use by Prescription Drug Plans and uses only prescription claims as a source of data, we are not able to identify individuals with side effects to statin therapy who require a lower intensity of statin therapy.

The measure is based on a specific section of the ACC/AHA guidelines, page 31: 4.5. Primary Prevention in Individuals with Diabetes: A high level of evidence supports the use of moderate-intensity statin therapy in persons with diabetes 40 to 75 years of age. Since the guideline only addresses the use of statin therapy for diabetics, the measure only includes those medications.

The new PCSK-9 medications are intended for adjunct therapy with a statin. Diabetic patients receiving combination therapy with both a statin and PCSK-9 medication will be compliant with the measure.

Each PQA measure is reviewed annually to determine if there is new evidence or new medications that affect the intent of the measure, and revisions to the measure would be considered, as appropriate

Proposed Committee Response: During the in-person meeting, the Committee discussed evaluating the intensity of statins prescribed as recommended in the ACC/AHA guidelines and including contraindications and/or intolerance to statin therapy as an exclusion. The developer noted that due to the limited data source, pharmacy claims, it is not possible to determine if patients received the appropriate level of statin intensity or if they have contraindications to statin therapy. Additionally, updates to the list of acceptable medications should be submitted by the developer to NQF during the annual update of the measure.

Action Item: Does the Committee agree with the proposed response?

Consensus Not Reached Measures

0965: Discharge Medications (ACE/ARB and beta blockers) in Eligible ICD Implant Patients (ACC)

Additional Information Provided by the Developer: Based on the discussion that took place at the NQF Standing Committee in-person meeting, ACC has made the following revisions to the measure submission:

- Frequency and distribution of the composite and individual components was provided by the developer to support NQF measure evaluation criterion 2d: Composite Construction. This additional information was reviewed by the Committee during the September 25, 2015 post in-person meeting call.

Decision	Information/Action Requested
Consensus Not Reached: Passed Evidence, Scientific Acceptability, Feasibility, and Usability; Consensus not reached for Composite Analysis	Frequency and distribution of composite and individual components requested. Issue: Based on the construction of the measure (all-or-none), the volume of the composite should be less than the lowest volume of the individual measures. Issue: The Committee questioned the accuracy of the data provided for the distribution of the composite measure and its medication components.

Action Item: Based on the consensus not reached outcome for the 2d criterion of the measure, does the Committee wish to re-vote on the overall suitability of the measure (and therefore potentially change the overall recommendation)?