UPDATE ON NQF CARDIOVASCULAR MEASURES 2015
PUBLIC AND MEMBER COMMENT PERIOD

December 4, 2015

The National Minority Quality Forum's proposed trial eMeasure (#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" (Measure #2764) received more than 40 comments during the National Quality Forum's public and member comment period for their Cardiovascular Measures 2015 project that closed on November 23, 2015. The overwhelming majority of the comments voiced strong support for the September 9 decision of the NQF Cardiovascular Measures Standing Committee to approve NMQF's trial measure, and to enable Measure #2764 to advance to the next stage of voting and to complete required testing of validity and reliability.

Our sincere thanks to all who submitted comments in support of Measure #2764. The National Minority Quality Forum remains confident and resolute that Measure #2764 is clearly supported by available evidence, and represents an essential addition to the family of process measures that have been endorsed by NQF to improve the quality of care provided to patients who have been diagnosed with chronic heart failure.

We believe that it is of benefit to our stakeholders, however, to have an opportunity to review the negative comments that were posted on NQF's website, and our response to those comments. Attachment A is a matrix that contains the unedited negative comments as submitted to the National Quality Forum and shared with us by the National Quality Forum.

Attachment B is the National Minority Quality Forum's global response that addresses the salient points raised by the negative commenters. Our hope is that this information will reinforce your support for this measure, and enhance your understanding of the rationale for this measure.

The National Quality Forum has scheduled a Post-Comment Call of the Cardiovascular Measures Standing Committee for Monday, December 7, 2015 from 1 PM – 3 PM. **This is a public meeting.** If your schedule permits, we encourage you to dial-in and listen to the deliberations of the Committee. According to the agenda that has been posted, members of the public will have an opportunity to speak from 2:45 PM – 2:55 PM. The call agenda and materials can be viewed at this link. Register for the meeting at: http://nqf.commpartners.com/se/Rd/Rg.aspx?927162 .

If you have any questions about comments, the responses, or the next steps in this process, please contact Gretchen C. Wartman, Vice President for Policy and Program, at 202-223-7463 or gwartman@nmqf.org.

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Attachment A
Negative Public and Member Comments Submitted Regarding Measure #2764

Comment #/ Commenter	Comment as Submitted
#5456 Joseph P. Drozda, Jr., MD, FACC American College of Cardiology	On behalf of more than 49,000 members the American College of Cardiology appreciates the opportunity to comment on the Measure 2764 for Cardiovascular conditions: 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, stewarded by the National Minority Quality Forum. ACC is strongly supportive of ensuring the provision of evidence-based therapies to improve outcomes in all patients with heart failure, especially when those therapies address disparities in care that affect underrepresented minorities. However, we believe that there are fundamental issues with the proposed measure that undermine achievement of these important goals and may lead to important unintended consequences. This measure contradicts the recommendations of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. While the ACCF/AHA clinical practice guideline (CPG) strongly recommend hydralazine and nitrate therapy in African-American patients with symptomatic systolic heart failure despite other medical therapy, the CPG recommendation specifically permits use of either the fixed dose combination or separate administration of hydralazine and isosorbide dinitrate. The ACC/AHA guideline recommendation states: "The combination of hydralazine and isosorbide dinitrate is recommended to reduce morbidity and mortality for patients self-described as African Americans with NYHA class III–IV HFrEF receiving optimal therapy with ACE inhibitors and beta blockers, unless contraindicated). (Class I, Level of Evidence: A)" The CPG further notes that "If the fixed-dose combination is available, the initial dose should be 1 tablet containing 37.5 mg of hydralazine hydrochloride and 20 mg of isosorbide dinitrate 3 times daily. The dose can be increased to 2 tablets 3 times daily for a total daily dose of 225 mg of hydralazine hydrochloride and 120 mg of isosorbide dinitrate. When the 2 drugs are used separately, both pills should be administered at least 3 times daily. Initial low doses of the drugs given separately may be progressively increased to a goal similar to that achieved in the fixed-dose combination trial." Thus, the CPG explicitly notes that the fixed dose combination or the two component agents are considered equivalent. We appreciate that one of the purposes of this measure is to assess its feasibility as an e-measure. While in this context, it may be appealing to be more permissive with respect to the measure specifications, we believe that it is problematic to establish a measure—even for testing purposes—that by design penalizes providers for delivering care that is consistent with existing CPGs and may deny patient access to beneficial therapies. We ask that NQF to reconsider its decision and strongly encourage the NQF not to endorse this measure.
#5457 (#5456 continued) Joseph P. Drozda, Jr., MD, FACC American College of Cardiology	The American College of Cardiology appreciates the opportunity to comment on the National Quality Forum (NQF) - Measure for Cardiovascular conditions#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, stewarded by the National Minority Quality Forum. In the previous ACC comment we outlined how the proposed measure as it contradicts the recommendations of the 2013 ACCF/AHA Guideline for the Management of Heart Failure, this comment is to expand upon the clinical practice guideline (CPG) writing committee process and patient access availability to medication and pharmaceutical costs. The ACCF/AHA guideline writing committee had the option to limit this recommendation to only fixed dose combination hydralazine and isosorbide dinitrate therapy. However, the writing committee

Comment #/ Commenter	Comment as Submitted
	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. Note that the fixed-dose combination is proprietary and costs on average at locations of large national pharmacies, $137.15 for 60 tablets (according to goodrx.com) compared with $27.25 for 60 tablets of each of the individual components, which are available as generics. Although some patients may be able to obtain assistance from the manufacturer for the fixed-dose combination, such assistance is not guaranteed to all patients. We strongly believe that creating a performance measure that permits only the use of the fixed-dose combination of hydralazine and nitrates for African-American patients with systolic heart failure, would penalize providers who, in using generic agents, are providing guideline-concordant care. While this alone is adequate reason to deny endorsement to this measure, we also believe that by discouraging the use of a permissible approach a guideline-recommended therapy—particularly one that is substantially less expensive—the measure could have the paradoxical effect of denying this important therapy to many patients. ACC has concerns about the financial burden fixed-dose combination treatment would place on many patients increasing the likelihood of medical non-compliance, for this, we ask that NQF to reconsider its decision and revise the measure for future resubmission.
#5445 Dr. Mark Creager, President, American Heart Association/American Stroke Association; Submitted by Ms. Melanie Shahriary, RN, BSN	The AHA/ASA strongly supports the goal of having more self-identified black or African American HF patients treated with hydralazine/nitrates, however, we cannot support this measure as currently specified. We do not doubt that the developers share our goals of promoting evidence-based practice and addressing disparities in care, however, we are concerned that some features of the measure, as currently specified, as well as the challenges of acccurately collecting all the required data from electronic health records, are limitations that must be addressed before the measure receives full endorsement. Some of our specific concerns are detailed below. We believe the measure is based on a somewhat questionable assumption that providers have taken a dismissive approach to the evidence for this combination therapy. It also fails to fully acknowledge the complexity of addressing race in medical practice and the potential adverse consequences of prescribing a costly, TID medication with overt side effects. While we appreciate that the current application is for ""approval for trial use"" only, and that further testing will be required before considering it for full endorsement, we are conerned that there are problems with this measure than cannot be overcome by additional testing. In section 1b.1 of their application, the developers state: ""There is no substitute for the fixed-dose combination therapy."" It's true that the ACC/AHA Heart Failure guideline* gives the highest level recommendation (Class I, Level of Evidence A) to this therapy, however, not all guideline recommendations are appropriate for translation into performance measures. Among our most significant concerns about this measure is that the ACC/AHA guideline, which is cited in the application, does not specify the fixed-dose combination, which is currently available only as a brand-name proprietary formulation (BiDil), but this measure does. The requirement that only prescription of the fixed-dose combination fulfills the measure is of concern for a number of reasons: The observed differeces in formulations (brand vs. generic), though valid, are theoretical and not proven to be of clinical consequence. At least 2 of the 6 writing committee members who developed this measure have received consultant fees and/or honoraria from Arbor Pharmaceuticals, the company that produces Bidil.

Comment #/ Commenter	Comment as Submitted
	Insurance plans may be unlikely to pay for the more expensive fixed-dose combination unless the generic medications have been tried first. In addition, copays for the brand name formulation may be higher. This may result in unintended consequences, since patients may either not fill their prescriptions or physicians may avoid patients who can't afford or won't pay for the higher cost of the brand-name medication. [Please see comments continued in next comment.]"
#5446 (#5445 continued) Dr. Mark Creager, President, American Heart Association/American Stroke Association; Submitted by Ms. Melanie Shahriary, RN, BSN	AHA/ASA Comment continued: 4. This requirement also means that physiccians are unable to titrate the dose, which is especially critical for older patients, who may be unable to tolerate the fixed-dose combination. In addition, the measure as currently constructed, does not allow providers to exclude patiens from the measure for patient-specific reasons, such as refusal or intolerance, or for medical reasons other than the 5 specific contraindications identified in the measure. This seems contrary to the goal of more patient-centered, personalized care. We recognize the challenges of capturing unique, patient-centered reasons for failing to prescribe fixed-dose combination therapy in an EHR, however, this is critical, especially if the measure is attributed at the individual provider level. *Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T Januzzi JL, Johnso MR, Kasper EK ,Levy WC, Masoudi FA, McBride PE, McMurray JJV, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WHW, Tsai EJ, WIlkoff BL. 2013 ACCF/AHA guideline for the mangagement of heart failure: a report of the American COllege of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation.2013;128:e240-e327. **Source: https://www.cms.gov/openpayments/index.html"
#5448 Submitted by Mr. Adolph P. Falcon, MPP	The National Alliance for Hispanic Health (the Alliance) is deeply concerned that too many of the quality measures being promulgated by the NQF do not adequately reflect the need to tailor treatment protocols to individual patient populations and the science of precision medicine. You have an immediate opportunity to set a new course for your work. For this reason the Alliance offers our strongest support for measure #2764 that would promote the most effective course of treatment for eligible African Americans with heart failure (HF). The proposed quality measure of a fixed-dose “Combination of Hydralazine and Isosorbide Dinitrate Therapy for Self-identified Black or African American Patients with Heart Failure (HF) and LVEF <40% on ACEI or ARB and Beta-blocker Therapy” reflects the best science and peer reviewed literature on quality care for African American patients with heart failure. Furthermore, the proposed measure is recognized as standard of care by the American Heart Association and the first peer reviewed literature in support of this course of treatment appeared over a decade ago in the New England Journal of Medicine. Adopting this measure of care is long overdue. While quality measure #2764 speaks to the particular health needs of the African American community, it is critical that the National Quality Forum recognize in its standards the importance of guaranteeing every individual patient the very best care available and that quality measures reflect the diversity of people in this nation. In this case, it means making sure that African American patients with heart disease get access to the right drug for them. For this reason, the National Alliance for Hispanic Health offers its full support for proposed quality measure #2764.
# 5488 Paul Heidenreich	The American College of Cardiology and American Heart Assocation's Task Force on Performance Measures agrees with the concerns raised by the two partner organizations (ACC and AHA) in their

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Comment #/ Commenter	Comment as Submitted
Stanford University School of Medicine	comments. The measure is not consistent with the ACC/AHA Heart Failure Guidelines, and thus, is not appropriate for public reporting or pay for performance progams. We ask the NQF to reconsider its decision and strongly encourage the NQF not to endorse this measure as currently written.

Attachment B
GLOBAL RESPONSE TO NQF CARDIOVASCULAR MEASURES 2015
NEGATIVE PUBLIC AND MEMBER COMMENTS
Prepared December 4, 2015

The National Minority Quality Forum's proposed trial eMeasure (#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" (Measure #2764) is currently under consideration by the National Quality Forum for approval as a trial eMeasure that will be tested for validity and reliability as a process measure. Measure #2764 is based upon the African-American Heart Failure Trial (A-HeFT), which was completed over a decade ago; the subsequent approval by the Food and Drug Administration (FDA) of the fixed-dose combination with the specific label indication for self-identified Blacks/African-Americans; and almost 10 years of utilization and payment data that document low-levels of use of this highly-effective therapy.

The National Minority Quality Forum concurs with comment #5448, a positive comment in our view, which was submitted by the National Alliance for Hispanic Health. Measure #2764 is designed to address the gap in patient-centric performance measures that must be given priority in light of rapidly changing population demographics. Measure #2764, and the science that supports its specifications, will also open the door for the collection of data on provider experience and patient outcomes that will further the evolution of research and medical practice that is efficacious for all patients.

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.

The National Minority Quality Forum remains confident that those organizations and individuals who influence treatment guidelines and reimbursement policy are committed to improving the ability of the American health services financing and delivery system to meet the needs of the increasingly diverse American general population. We are challenged, therefore, to comprehend the continued resistance of certain sectors to embrace and promote the science, and to engage proactively to eliminate barriers to accessing this therapy by populations who experience avoidable morbidity and mortality associated with inadequate treatment, and by the physicians who are challenged daily in their efforts to provide high-quality, cost-beneficial services to their patient populations.

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.

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The National Minority Quality Forum believes that the National Quality Forum process of trial approval, endorsement and maintenance is designed to address quality measurement challenges through constructive and proactive engagement with the delivery system. NMQF has developed Measure #2764 to facilitate and advance this engagement. Failure to allow the process to move forward compromises the system through the lens of providers, patients and payers.

For the following reasons, therefore, the National Minority Quality Forum 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.

1. It is the National Minority Quality Forum's 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. Indeed, a negative commenter states that, "It's true that the ACCF/AHA Heart Failure guideline gives the highest level recommendation to the fixed-dose combination." Measure #2764 is based upon the adjudicated science that supports that recommendation and that documents the efficacy of the therapy Measure #2764 is designed to measure. Most importantly, it represents a value proposition and supports efforts to prevent unnecessary hospitalizations, to eliminate inequities in healthcare and health status, and to advance efforts to enhance precision in the design of treatment alternatives that are patient-centric.

2. The 2013 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. 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".

3. 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.

4. A comment stated that the 2013 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.

5. The 2013 ACCF/AHA guideline appears to use as evidence to support their determination of equivalence, evidence that supports only the fixed-dose combination. Therefore, 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. Indeed, 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.

6. 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.

7. Given that neither of the two component compounds is indicated for treatment of heart failure, the decision reached by the 2013 ACCF/AHA 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.

8. FDA has stated in writing that there is no generic for the therapy that FDA approved -- a fixed-dose single pill combination of two compounds that are only approved for treatment of chronic heart failure in that specific combination. Separately, neither is indicated for treatment of heart failure, and there is no science to support such an assertion. Promotion of such use can be construed as off-label use that puts providers, insurers and patients at risk.

Again, there is no generic of the fixed-dose combination, and there is no science to support the use of the two compounds that comprise the fixed-dose for the treatment of Stage III or Stage IV heart failure.

9. A comment notes that observed differences in formulations (brand vs generic), though valid, are theoretical and not proven to be of clinical consequence. This statement is of concern given that: (1) there is no generic to the brand; and (2) appears to take as evidence of potential equivalence the fact that there is no evidence to support the use of the two compounds separately.

10. Medicare does not reimburse for off-label use.

11. Concerns have been expressed that the challenges of accurately collecting all of the required data from electronic health records must be addressed before Measure #2764 receives full endorsement. The National Minority Quality Forum notes that the trial eMeasure program designed by the National Quality Forum is designed to address such a concern; and such is the objective of the validity and reliability testing protocol that is under development by the National Minority Quality Forum. Further, many of the critical data elements included in the specification of Measure #2764, including race, ethnicity and left-ventricular ejection fraction, are data elements that are mandated by the Joint Commission, by Meaningful Use criteria, or other EHR specifications. Their requirement is not limited to Measure #2764.

12. It has been suggested that Measure #2764, "...is based upon a somewhat questionable assumption that providers have taken a dismissive approach to the evidence for this combination therapy." The National Minority Quality Forum notes that Measure #2764 is based not upon assumptions, but upon data and evidence. The fact is that the fixed-dose combination of hydralazine hydrochloride and isosorbide dinitrate was approved by the FDA over a decade ago. The fact is that the number of eligible patients for whom the approved therapy is prescribed is significantly, indeed disturbingly, lower than the number of patients for whom that therapy is indicated. The fact is that eligible patients who do not receive the indicated therapy are at increased risk for hospitalization, avoidable morbidity, and premature mortality. These facts are sentinels that mandate an intervention by the policy and regulatory environment. Measure #2764 is a response to these facts.

13. Further, it has been suggested that Measure #2764 fails to fully acknowledge the complexity of addressing race in medical practice. This is an interesting statement, since the nature of this "complexity" is not specified. If the referenced "complexity" is in regard to the identification of race and ethnicity, we note that the science that undergirds Measure #2764 is based upon "self-identified" race. Since no peer-reviewed references are offered to support the comment regarding "complexity", this statement may, indeed, be an "assumption" that can be examined only through a testing process. We note again, however, that identification of race and ethnicity is mandated by the Joint Commission and by Meaningful Use. If this "complexity" exists, we submit that Measure #2764 is neither the beginning of this conversation, nor the end, particularly in light of the movement toward precision in

diagnoses and treatment that will require an even higher degree of specificity regarding patient characteristics.

14. A commenter suggests that Measure #2764 fails to fully acknowledge the potential adverse consequences of prescribing a costly, TID medication with overt side effects. It is not clear how the issue of overt side effects fits into this discussion. There is the potential for overt side effects for all major therapies. Measure #2764, as specified, does not compromise the ability or the responsibility of physicians to practice medicine based upon their best judgment, and exceptions to address the primary reasons for intolerances and side effects have been defined in the measure.

15. The issue of co-pays for a branded therapy also has been raised. The issue of cost and affordability was discussed during the September 9 meeting of the NQF Cardiovascular Measures committee. It was noted during that meeting that "costly" medications are linked to performance measures for cancer therapies and other "costly" diseases.

16. There were, during the September 9 meeting, assumptions articulated about the ability of the specified patient population to afford the medication, and the extent to which that potentially unaffordable cost would compromise the ability of the patient population to fill prescriptions written by physicians. The particular concern was whether the physician would get "dinged" if the prescription was written, but not filled. The answer was "No", the physician would not get "dinged" if the prescription was not filled. Further, developing performance measures based upon speculation about the potential behavior of insurance companies is, we submit, not appropriate for these discussions. Insurers should rely upon science to inform their coverage and payment decisions. The obverse should never be the case.

17. It is important to remind all stakeholders that performance measures endorsed by the National Quality Forum are voluntary measures. They are made available for care delivery systems and payers who elect to use them to advance the provision of quality care. The National Minority Quality Forum looks forward to working with the National Quality Forum as its processes evolve to embrace heterogeneity of disease presentation and treatment effect, and on the standardization of key components for all performance measures.

18. It has been suggested that Measure#2764 should include language regarding a patient's right to refuse the therapy. It is NMQF's understanding that all patients in the United States have the right to refuse any therapy recommended by clinicians. If NQF requires that patient refusal be included in measure specifications, NMQF has indicated will be pleased to make this non-substantive addition to Measure #2764.

If you have any questions about these responses, please contact Gretchen C. Wartman, Vice President for Policy and Program, at 202-223-7463 or gwartman@nmqf.org.