MEASURE WORKSHEET

This document summarizes the evaluation of the measure as it progresses through NQF's Consensus Development Process (CDP). The information submitted by measure developers/stewards is included after the Brief Measure Information, Preliminary Analysis, and Pre-meeting Public and Member Comments sections.

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Brief Measure Information

NQF #: 2764
Measure Title: 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 Steward: National Minority Quality Forum
Brief Description of Measure: Percentage of patients aged 18 years and older with a diagnosis of heart failure (HF) and a current or prior ejection fraction (EF) <40% who are self-identified Black or African Americans and receiving ACEI or ARB and Beta-blocker therapy who were prescribed a fixed-dose combination of hydralazine and isosorbide dinitrate seen for an office visit in the measurement period in the outpatient setting or at each hospital discharge
Developer Rationale: The African-American Heart Failure Trial (A-HeFT) first published in 2004 demonstrated that there is significant benefit for African American patients who receive the fixed-dose combination therapy of hydralazine and isosorbide dinitrate. A-HeFT built on the findings from the two Vasodilator-Heart Failure Trials (V-HeFT). A-HeFT, which was ended early due to the mortality rates in the placebo population, demonstrated a 43% reduction in mortality, a 33% decrease in initial hospitalizations, and a 50% improvement in patient-reported quality of life (Taylor, 2004; Sharma, 2014). These results clearly demonstrate that the fixed-dose combination therapy significantly improves patient morbidity, mortality and quality of life in this clinical cohort. There is no substitute for the fixed-dose combination therapy.

Even with this strong evidence of unprecedented efficacy and cost-effectiveness, research shows that more than 85% of African American patients are not receiving the quality of care that this therapy affords, constituting a significant gap in care quality (Dickson, 2015). The underuse of the fixed-dose combination of hydralazine plus isosorbide dinitrate in African Americans with severe heart failure is a health care and health quality disparity that exposes these patients to an elevated risk for mortality and hospitalization, and compromises efforts to contain the escalating system costs by preventing or reducing unnecessary hospitalizations and readmissions.

Based upon research on the mortality benefit of the fixed-dose combination (Fonarow, 2011), the National Minority Quality Forum estimates that 51,542 (27%) of the 189,891 African American Medicare beneficiaries who were being treated for heart failure and received their prescription drugs under Part D should have been treated with the fixed-dose combination; but only 2,377 (5%) had at least one prescription (30-day supply) of the therapy. Further, the National Minority Quality Forum estimates that between 2008 and 2010, only 3% of the eligible patient cohort in Medicare received the therapy. Given the documented number to treat to receive the mortality benefit (21), it can be estimated that from 2007 through 2010, 20,000 African American Medicare beneficiaries died as a result of the failure to receive quality care as defined by evidence-based guidelines.

Research continues to explore if the fixed-dose combination of hydralazine and isosorbide dinitrate is linked to a particular genetic polymorphism (NIH funded Genomic Response Analysis of Heart Failure Therapy in African Americans). While we anticipate that the evidence supporting this treatment will be refined over time, the proven benefits to this patient population is significant and there is a clear opportunity for improvement. Failure to do so constitutes a failure to provide quality and cost-effective care.

References:

Dickson VV, Knafl GJ, Wald J, Riegel B. Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure. J Am Heart Assoc. 2015;4:1-13.

Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161:1024-1030.
Sharma A, Colvin-Adams M, Yancy CW. Heart failure in African Americans: disparities can be overcome. Cleve Clin J Med. 2014;81:301-11.
Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004; 351:2049–57.

Numerator Statement: Patients prescribed a fixed-dose combination of hydralazine and isosorbide dinitrate seen for an office visit in the measurement period in the outpatient setting or at each hospital discharge

Denominator Statement: All patients aged 18 years and older with a diagnosis of heart failure with a current or prior EF <40% who are self-identified Black or African Americans and receiving ACEI or ARB and Beta-blocker therapy

Denominator Exclusions: Denominator exclusions include:

- Hypotension (severe or symptomatic)
- Severe lupus erythematosus
- Unstable angina
- Peripheral neuritis
- Patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors

Measure Type: Process
Data Source: Electronic Clinical Data : Electronic Health Record
Level of Analysis: Clinician : Group/Practice, Clinician : Individual
Is this an eMeasure? ☒ **Yes** ☐ **No** **If Yes, was it re-specified from a previously endorsed measure?** ☐ **Yes** ☒ **No**

Preliminary Analysis

To maintain NQF endorsement endorsed measures are evaluated periodically to ensure that the measures still meets the NQF endorsement criteria ("maintenance"). The emphasis for maintaining endorsement is focused on how effective the measure is for promoting improvements in quality. Endorsed measures should have some experience from the field to inform the evaluation. The emphasis for maintaining endorsement is noted for each criterion.

Criteria 1: Importance to Measure and Report

1a. Evidence

1a. Evidence. The evidence requirements for a *process or intermediate outcome* measure is that it is based on a systematic review (SR) and grading of the body of empirical evidence where the specific focus of the evidence matches what is being measured.

The Standing Committee is not discussing/voting Evidence criterion

Summary of Standing Committing's prior review in the Cardiovascular Phase 3 project:

The Committee expressed concern about the use of a fixed-dose combination of hydralazine and isosorbide dinitrate in this measure because the guidelines do not explicitly recommend a fixed-dose combination. The developer responded that the guideline recommendation is based on the African-American Heart Failure Trial (A-HeFT). A-HeFT examined the use of the fixed-dose combination therapy (BiDil) added to standard heart failure therapy in blacks with New York Association functional class III and IV heart failure. BiDil demonstrated a 43% reduction in mortality when compared with the placebo.

The developer provides the following evidence for this measure:

- **Systematic Review of the evidence specific to this measure?** ☒ **Yes** ☐ **No**
- **Quality, Quantity and Consistency of evidence provided?** ☒ **Yes** ☐ **No**

- **Evidence graded?** ☒ **Yes** ☐ **No**

Evidence Summary

- This process clinician and group level eMeasure calculates the percentage of patients aged 18 years and older with a diagnosis of heart failure (HF) and a current or prior ejection fraction (EF) <40% who are self-identified Black or African Americans and receiving ACEI or ARB and Beta-blocker therapy who were prescribed a fixed-dose combination of hydralazine and isosorbide dinitrate seen for an office visit in the measurement period in the outpatient setting or at each hospital discharge.
- The developer provides the 2013 ACCF/AHA guideline for the management of heart failure (**Class I; Level of Evidence: A**) with one recommendation for the combination of hydralazine and isosorbide dinitrate for patients self-described as African Americans (**Class I**) and the HFSA 2010 Comprehensive Heart Failure Practice Guideline (**Strength of Recommendation: Is Recommended**) with two recommendations: hydralazine and isosorbide dinitrate is recommended in addition to beta blockers and ACE inhibitors for African Americans with HF and reduced LVEF (**Strength of Evidence = A and B**) and hydralazine/isosorbide dinitrate is recommended for African American women with moderate to severe HF symptoms who are on background neurohormonal inhibition (**Strength of Evidence = B**).
- The evidence review supporting the hydralazine/isosorbide dinitrate recommendations was conducted through October 2011 and includes other references through April 2013 for the 2013 ACCF/AHA guideline. No information on the time period for the HFSA 2010 guideline was provided.
- QQC - 4 randomized controlled trials (RCTs) and 2 post hoc retrospective analyses supporting the 2013 ACCF/AHA guideline. No specific information on the number of studies included in the body of evidence for the HFSA 2010 Comprehensive Heart Failure Practice Guideline.
- Two additional analyses from A-HeFT were published after the publication of the 2013 ACCF/AHA Guideline for the Management of Heart Failure with the conclusion that "treatment with FDC-I/H was associated with a substantial reduction in the first and recurrent HF hospitalizations, and in total all-cause hospitalizations, reducing the total burden of costly and distressing hospitalizations."
- The developer provides a diagram that demonstrates how the use of a fixed-dose combination of hydralazine and isosorbide dinitrate in self-identified black or African American patients with HF and LVSD receiving ACEI/ARB and beta-blocker therapy is linked to patient outcomes.

Prior Committee Rating on Evidence: High-6; Moderate-10; Low-1

1b. Gap in Care/Opportunity for Improvement and 1b. Disparities

1b. Performance Gap. The performance gap requirements include demonstrating quality problems and opportunity for improvement.

The Standing Committee is not discussing/voting Performance Gap criterion

Summary of Standing Committing's prior review in the Cardiovascular Phase 3 project:

Given the data presented by the developer, the Committee agreed that there is opportunity for improvement. Because this is a newly-developed eMeasure the developers did not have overall performance data from the measure as specified but provided a summary of data from the literature that demonstrates the existence of a significant opportunity for improvement, especially when eligible patients receive the hydralazine/isosorbide dinitrate combination therapy in the ambulatory setting and at hospital discharge. According to one study cited by the developer, more than 85% of African-American patients are not receiving the hydralazine/isosorbide dinitrate combination therapy.

- The African-American Heart Failure Trial (A-HeFT), built on the findings from the two Vasodilator-Heart Failure Trials, demonstrated that there is significant benefit for African American patients who receive the fixed-dose combination therapy of hydralazine and isosorbide dinitrate. Specifically, the study demonstrated a 43% reduction in mortality, a 33% decrease in initial hospitalizations, and a 50% improvement in patient-reported quality of life.
- A 2015 research study determined that more than 85% of African American patients are not receiving the quality of care that this therapy affords, constituting a significant gap in care quality. Based upon research on the mortality benefit of the fixed-dose combination, the developer has estimated that 51,542 (27%) of the 189,891 African American Medicare beneficiaries who were being treated for heart failure and received their prescription drugs under Part D should have been treated with the fixed-dose combination; but only 2,377 (5%) had at least one prescription (30-day supply) of the therapy.
- The developer also estimates that only 3% of the eligible patient cohort in Medicare received the therapy between 2008-2010. Furthermore, the developer estimates that 20,000 African American Medicare beneficiaries died as a result of not receiving the fixed-dose therapy between 2007-2010.
- An observational analysis of data from the Get With the Guidelines-Heart Failure Registry showed that just over 22% of African American patients were discharged from the hospital with a prescription for the combination therapy. Rates increased from 16% to 24% over four years.
- Heart failure is more prevalent in African Americans than in whites; according to American Heart Association statistics, the annual incidence of heart failure in whites is approximately 6 per 1,000 person-years, while in African Americans it is 9.1 per 1,000 person years. Moreover, when hospitalized for heart failure, African Americans have a 45% greater risk of death or decline in functional status than whites. This measure is specifically for the African American population.

Prior Committee rating for opportunity for improvement: High-6; Moderate-10; Low-1

Criteria 2: Scientific Acceptability of Measure Properties

2a. Reliability

2a1. Reliability Specifications

2a1. Specifications requires the measure, as specified, to produce consistent (reliable) and credible (valid) results about the quality of care when implemented.

Data source(s): The developer listed Electronic Clinical Data from Electronic Health Records as the data source for this measure.

Specifications:

- The level of analysis is at the clinician-level.
- The numerator includes patients prescribed a fixed-dose combination of hydralazine and isosorbide dinitrate seen for an office visit in the measurement period in the outpatient setting or at each hospital discharge
- The denominator includes all patients aged 18 years and older with a diagnosis of heart failure with a current or prior EF <40% who are self-identified Black or African Americans and receiving ACEI or ARB and Beta-blocker therapy.
    - The following data elements are used to calculate the denominator:
        - Diagnosis of heart failure
        - Ejection Fraction <40% or diagnosis of left ventricular systolic dysfunction
        - Self-identified as Black or African American
        - ACEI or ARB therapy

        - Beta-blocker therapy
        - Office visit
        - Hospital Discharge
- The denominator exclusions included are:
    - hypotension (severe or symptomatic)
    - severe lupus erythematosus
    - unstable angina
    - peripheral neuritis
    - patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors
- The calculation algorithm and Value Sets are included.
- The eMeasure specifications and values sets meet all current NQF eMeasure technical requirements and are provided on Sharepoint for SC review.

Questions for the Committee:

- *Are all the data elements clearly defined?*
- *Do the measure specifications include the target population and accurately identify the numerator, denominator and exclusions?*
- *Is the calculation algorithm clear?*
- *Is it likely this measure can be consistently implemented?*

eMeasure Technical Advisor(s) review

Submitted measure is an HQMF compliant eMeasure	The submitted eMeasure specifications follow the industry accepted format for eMeasure (HL7 Health Quality Measures Format (HQMF)). **HQMF specifications** ☒ **Yes** ☐ **No**
Documentation of HQMF or QDM limitations	N/A – All components in the measure logic of the submitted eMeasure are represented using the HQMF and QDM; **OR** Submitted eMeasure contains components that cannot be represented due to limitations of HQMF or QDM and the submission explains the work around for these limitations; **OR** Submitted eMeasure contains components that cannot be represented due to limitations HQMF or QDM and the submission does NOT explain the work around for these limitations
Value Sets	The submitted eMeasure specifications uses existing value sets when possible and uses new value sets that have been vetted through the VSAC **OR** Some value sets used in the submitted eMeasure are not present in the NLM Value Set Authority Center but the measure developer has provided justification for using such value sets
Measure logic is unambiguous	Submission includes test results from a simulated data set demonstrating the measure logic can be interpreted precisely and unambiguously; **OR** Submission does not include test results from a simulated data set demonstrating the measure logic can be interpreted precisely and unambiguously; **OR** Submission includes test results from a simulated data set demonstrating the measure logic cannot be interpreted precisely and unambiguously.

Feasibility Testing	The submission contains a feasibility assessment that addresses data element feasibility and follow-up with measure developer indicates that the measure logic is feasible based on assessment by EHR vendors**; OR** The feasibility analysis submitted by the measure developer meets the requirements to be considered for eMeasure Trial Approval.

2a2. Reliability Testing Testing attachment

2a2. Reliability testing demonstrates if the measure data elements are repeatable, producing the same results a high proportion of the time when assessed in the same population in the same time period and/or that the measure score is precise enough to distinguish differences in performance across providers.

SUMMARY OF TESTING

Reliability testing level ☐ **Measure score** ☐ **Data element** ☒ **Both**

Reliability testing performed with the data source and level of analysis indicated for this measure ☒ **Yes** ☐ **No**

Method(s) of reliability testing

- The dataset included 2014 EHR data from a clinical registry (Dataset 1) and 2015 data from a network of federally-qualified and community health centers in the Midwest (Dataset 2) and an integrated inpatient and outpatient delivery system in the South (Dataset 3).
    - The developer noted that ejection fraction (EF) values from all three datasets were difficult to obtain given the ongoing challenges with collecting this data in discrete fields in EHRs. Per the developer, "because of this limited data, the testing provided in this document represents patients who are self-identified African American or black with a diagnosis of heart failure who were currently receiving ACE or ARB and beta-blocker therapy. Because a diagnosis of left ventricular systolic dysfunction (LVSD) or an EF <40% is a requirement for prescribing those two medications, if the EF or LVSD value was missing, we assumed that it was present if all of the other inclusion factors were met." – Ejection Fraction <40% or a diagnosis of left ventricular systolic dysfunction is one of the data elements required to calculate the denominator. NQF guidance states that testing should be done for all critical data elements.
- The following table shows the sample sizes for each of the datasets:

	Patients	Clinicians	Sites
Dataset 1	6,384	1,415	321
Dataset 2	145	Not available*	14
Dataset 3	3,018	825	10

*Dataset 2 did not provide information on the performing clinician.

- The developers used a beta-binomial model to assess the signal-to-noise ratio using **Dataset 1**. A reliability of 0.0 implies that all the variability in a measure is attributable to measurement error. A reliability of 1.0 implies that all the variability is attributable to real differences in performance. The higher the reliability score, the greater is the confidence with which one can distinguish the performance of one physician from another. This is an appropriate test for measure score reliability. A reliability of 0.70 is generally considered a minimum threshold for reliability.
- The developer also conducted inter-rater reliability testing on a subset of manually abstracted charts. For each set of manually abstracted charts, **30** of these charts were re-abstracted by a second nurse reviewer.
    - The developer calculated the k statistic for each of the elements where there was less than 100% agreement between the two abstractions.

Results of reliability testing

- Overall measure score reliability was **0.702** (0.184, 0.964) for all sites, regardless of the number of patients. Reliability at the minimum level of 20 quality reporting events was **0.858** (0.433, 0.990). ***[A minimum of patient quality reporting events is not included in the measure specifications]***
- Inter-rater reliability results:
  - The k statistics and confidence intervals for 30 patients from Dataset 2 and Dataset 3 are below:

	Inpatient encounter	Heart Failure Diagnosis	Fixed-dose therapy in the outpatient setting	Fixed-dose therapy in the inpatient setting
Dataset 2	0.867 (0.69, 1.00)	0.87 (0.62, 1.00)	100% Agreement	0.875 (0.708, 1.00)
Dataset 3	0.933 (0.803, 1.00)	100% Agreement	0.783 (0.374, 1.00)	0.866 (0.687, 1.00)

- There was 100% agreement on the remaining data elements:
  - Outpatient encounter
  - Sex
  - Race
  - Age
  - Ejection Fraction
  - ACE/ARB
  - Beta-Blocker
  - Severe or Symptomatic Hypotension
  - Severe Lupus Erythematosus
  - Unstable Angina
  - Peripheral Neuritis
  - PDE5
- It is unclear how 100% agreement was determined for the data element 'Ejection Fraction' because as noted above per the developer, "if the EF or LVSD value was missing, we assumed that it was present if all of the other inclusion factors were met."

Questions for the Committee:

- *Is the test sample adequate to generalize for widespread implementation?*
- *Does the Committee agree that it can be assumed that an ejection fraction <40% or a diagnosis of LVSD is present if all of the other inclusion factors were met?*
- *Do the results demonstrate sufficient reliability so that differences in the performance score can be identified?*

Guidance from the Reliability Algorithm: Specifications are precise, unambiguous, and complete (Box 1) → Empirical reliability testing conducted using statistical tests with the measure as specified (Box 2) → Reliability testing conducted with measure score (Box 4) →Signal to noise testing method appropriate (Box 5) → High/Moderate/Low certainty the measure score is reliable (Box 6) → Low certainty/confidence that performance measure scores are reliable due to inability to test all critical data elements required to calculate the denominator (Box 6c) → Other reliability testing reported (Box 7) → Reliability testing conducted with patient-level data elements used to construct the measure (Box 8) → Inter-rater reliability was not assessed separately for all of the critical data elements (minimum of numerator, denominator, exclusions) (Box 9) → Insufficient

Preliminary rating for reliability: ☐ **High** ☐ **Moderate** ☐ **Low** ☒ **Insufficient**

Rationale: Low certainty that performance measure scores are reliable because per the developer, "a diagnosis of left ventricular systolic dysfunction (LVSD) or an EF <40% is a requirement for prescribing those two medications, if the EF or LVSD

value was missing, we assumed that it was present if all of the other inclusion factors were met." Additionally, inter-rater reliability testing insufficient because the developer did not assess the reliability of ALL critical data elements (EF or LVSD <40%).

Note: "…a rating of insufficient means that either the information submitted is not adequate for a definitive answer or that the submission was incomplete or deficient in presenting existing evidence or information." (Committee Guidebook for the NQF Measure Endorsement Process. Version 3.0. Last updated: September 2016. p. 33)

2b. Validity

2b1. Validity: Specifications

2b1. Validity Specifications. This section should determine if the measure specifications are consistent with the evidence.

- The developer provided evidence that states that:
  - 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.
  - The combination of hydralazine and isosorbide dinitrate is recommended as part of standard therapy in addition to beta blockers and ACE inhibitors for African Americans with HF and reduced LVEF.
  - The combination of hydralazine/isosorbide dinitrate is recommended as standard therapy for African American women with moderate to severe HF symptoms who are on background neurohormonal inhibition.

Specifications consistent with evidence in 1a. ☐ **Yes** ☒ **Somewhat** ☐ **No**

Questions for the Committee:

- *Are the specifications consistent with the evidence?*

2b2. Validity testing

2b2. Validity Testing should demonstrate the measure data elements are correct and/or the measure score correctly reflects the quality of care provided, adequately identifying differences in quality.

SUMMARY OF TESTING

Validity testing level ☐ **Measure score** ☒ **Data element testing against a gold standard** ☐ **Both**

Validity testing method:

- The developer conducted data element validity testing by comparing each data element in the patient record to the EHR electronic report. Percent agreement was used to understand the extent of validity found.

Validity testing results:

- The developer provided the following testing results of the data elements:

Dataset 2: 98 patients

	% Agreement
Heart Failure	79
LVSD	63
ACE/ARB	100
Beta Blocker	99
Hypotension	100
Lupus Erythmatosus	100
Unstable Angina	100
Peripheral Neuritis	100

PDE5	100
Fixed Dose	99

Dataset 3: 100 patients

	% Agreement
Heart Failure	78
LVSD	59
ACE/ARB	89
Beta Blocker	78
Hypotension	99
Lupus Erythmatosus	100
Unstable Angina	99
Peripheral Neuritis	100
PDE5	98
Fixed Dose	100

- The developer provided only percentage agreement statistics; no additional results were provided (e.g., kappa scores, which indicate agreement over and above chance; sensitivity or specificity statistics). Per NQF guidance, assessing percent agreement of patient-level data elements only is insufficient.

Questions for the Committee:

- *Is the test sample adequate to generalize for widespread implementation?*
- *Do the results demonstrate sufficient validity so that conclusions about quality can be made?*
- *Do you agree that the score from this measure as specified is an indicator of quality?*

2b3-2b7. Threats to Validity

2b3. Exclusions:

- The developer was unable to complete statistical testing on the exclusions given the low rates. The developer stated they believe the total number of exclusions provided in Dataset 1 are overestimated given the lack of specificity on the severity of two of the exclusions (hypotension and lupus erythematosus). The developer noted that exclusion rates will likely decrease as the ability to capture the severity of diagnoses improves through implementation of the measure.
- Denominator exceptions include hypotension (severe or symptomatic), severe lupus erythematosus, unstable angina, peripheral neuritis, and patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors.

Questions for the Committee:

- *Are the exclusions consistent with the evidence?*
- *Are any patients or patient groups inappropriately excluded from the measure?*
- *Are the exceptions of sufficient frequency and variation across providers to be needed (and outweigh the data collection burden)?*

2b4. Risk adjustment: **Risk-adjustment method** ☒ **None** ☐ **Statistical model** ☐ **Stratification**

2b5. Meaningful difference *(can statistically significant and clinically/practically meaningful differences in performance measure scores can be identified)*:

- The developer was unable to perform statistical testing of differences due to small sample sizes. The developer provided the following descriptive statistics:

	Fixed Dose	Total Patients	Performance Score
Dataset 1:			
Sum	73	4692	1.6%
Min	0	437	0.0%
Avg	0.2	15.7	1.1%
Max	1	3	33.3%
Dataset 2:			
Sum	1	145	0.7%
Min	0	2	0.0%
Avg	0.1	10.4	0.4%
Max	1	20	5.0%
Dataset 3:			
Sum	0.0	1547	0.0%
Min	0.0	2	0.0%
Avg	0.0	171.9	0.0%
Max	0.0	1392	0.0%

- The developer noted that as the use of the measure becomes more widespread, they will be able to conduct additional testing of the meaningful differences that may exist.
- Per NQF guidance, measures with overall less-than-optimal performance may not demonstrate much variability across providers.

Question for the Committee:

o *Does this measure identify meaningful differences about quality among providers?*

2b6. Comparability of data sources/methods:

Not Applicable

2b7. Missing Data

- The developer did not provide a statistical analysis of the extent and distribution of missing data (or nonresponse).
- The developer stated that data element validity testing identified the extent and distribution of missing data between the report produced from the EHR and a manual abstraction of the patient record. 100% agreement was demonstrated for most data elements between the electronic report and visual inspection of the patient chart, with the exception of LVSD.

Guidance from the Validity Algorithm: Measure specifications somewhat consistent with evidence (Box 1) → All potential threats to validity that are relevant to the measure not empirically addressed (Box 2)→ Empirical validity testing conducted using the measure as specified (Box 3) →Validity testing conducted with patient-level data elements (Box 10) → Only percent agreement of critical data elements assessed (Box 11) → Insufficient

Preliminary rating for validity: ☐ **High** ☐ **Moderate** ☐ **Low** ☒ **Insufficient**

Rationale: Per NQF criteria, assessing percent agreement of patient-level data elements only is insufficient.

Note: "…a rating of insufficient means that either the information submitted is not adequate for a definitive answer or that the submission was incomplete or deficient in presenting existing evidence or information." (Committee Guidebook for the NQF Measure Endorsement Process. Version 3.0. Last updated: September 2016. p. 33)

Criterion 3. Feasibility

3. Feasibility is the extent to which the specifications including measure logic, require data that are readily available or could be captured without undue burden and can be implemented for performance measurement.

The Standing Committee is not discussing/voting Feasibility criterion

Summary of Standing Committing's prior review in the Cardiovascular Phase 3 project:

- *The developer provided an eMeasure Feasibility Scorecard of two EHRs (hospital and outpatient), testing all data elements required to calculate this measure. The Committee agreed that this measure is feasible for implementation with EHR systems.*
- *Some Committee members voiced concerns with the cost of the fixed-dose combination therapy, the availability of the medication in hospital formularies, and the burden of cost to the patients.*

- The eMeasure is specified for use with an EHR as the data source.
- The developers completed the assessment in a health system with two EHRs vendor products in the outpatient and inpatient settings and community health center with a different EHR product. All data elements for both EHRs scored 3s (except Ejection Fraction < 40%) meaning the data elements are routinely collected as part of routine care and require no additional data entry from the clinician for the quality measure and no EHR user interface changes. Ejection Fraction <40% scored 2 in data standards meaning data element is not routinely collected as part of routine care and additional time and effort over and above routine care is required, but perceived to have some benefit.
- Per the Writing Committee recommendation, the developer changed "Diagnosis of Worsening Ischemic Heart Disease* to "Unstable Angina" better identify applicable patients for fixed combination therapy. As unstable angina is seen as a subset of ischemic heart disease, the feasibility rating would not be impacted.
- The developer provides the measure specifications free of charge to provider end users.

Prior Committee rating for Feasibility: High-1; Moderate-14; Low-2

Criterion 4: Usability and Use

4. Usability and Use evaluate the extent to which audiences (e.g., consumers, purchasers, providers, policymakers) use or could use performance results for both accountability and performance improvement activities.

The Standing Committee is not discussing/voting Usability and Use criterion

Summary of Standing Committing's prior review in the Cardiovascular Phase 3 project:

- *The developer noted that a similar measure that does not require a fixed-dose is currently used in the American Heart Association's Get with the Guidelines.*
- *The developer provided plans for future accountability and quality improvement use.*

Current uses of the measure
Publicly reported? ☐ **Yes** ☒ **No**

Current use in an accountability program? ☐ **Yes** ☒ **No** ☐ **UNCLEAR**
OR
Planned use in an accountability program? ☒ **Yes** ☐ **No**

Accountability program details – ***updated information***

- The developers are dedicated to ensuring that this measure is implemented widely and submitted the measure for consideration by the Centers for Medicare & Medicaid Services (CMS) for consideration in the Merit-based Incentive Payment System (MIPS). This measure was also included on the Measures Under Consideration (MUC) list released by CMS in November 2016, but ultimately was not included.
- The measure is currently used in the Quality Improvement program Get with the Guidelines.

Improvement results – ***updated information***

- Overall, the testing of the measure demonstrated that there is poor performance on the measure and there is significant room for improvement. Specifically, the clinical registry demonstrated that 0% -1.1% of all eligible patients are currently receiving the FDA-approved fixed dose combination therapy across practices in the Southeast and in the South.

Potential harms:

- As the measure is newly developed, the developer states unintended consequences have yet to be identified.

Recent Feedback from MAP – ***updated information***

- This measure was recently submitted to the NQF's Measures Applications Partnership (MAP) for consideration in the Merit-Based Incentive Payment System (MIPS). MIPS is one of two tracks in the Quality Payment Program (QPP) policy designed to reform Medicare Part B payments. Individual clinicians self-select quality measures to submit to CMS. A clinician who participates in an Advanced Alternate Payment Model (Advanced APM) is excluded from MIPS.
    - The MAP noted that this measure could address both effective clinical care and potential disparities in heart failure as it would track use of a therapy that can reduce morbidity and mortality in patients who self-identify as African American. However, the MAP raised concerns that this measure is based on the use of a fixed-dose regimen, and American College of Cardiology/American Heart Association guidelines suggest that individual components of the combination therapy could be substituted. Ultimately, the Workgroup recommended that this measure be resubmitted to MAP for consideration in rulemaking after review of testing results by the NQF Cardiovascular Standing Committee.

Prior Committee rating for Usability & Use: High-2; Moderate-9; Low-6

Criterion 5: Related and Competing Measures

Currently endorsed 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)

Previously endorsed measures:

- 0162: ACEI or ARB for left ventricular systolic dysfunction - Heart Failure (HF) Patients (CMS)

- 0610: Heart Failure - Use of ACE Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB) Therapy (ActiveHealth Management)
- 0615: Heart Failure - Use of Beta Blocker Therapy (ActiveHealth Management)

- The developer reports that measure specifications for the target population and medication therapies for ACEI, ARB, and beta-blocker are completely harmonized with 0081 and 0083.

Pre-meeting public and member comments

Comment by: Dr. Steven R. Houser, PhD, FAHA
Organization: American Heart Association
Comment:
Dear Dr. George and Dr. Kottke:

On behalf of the American Heart Association (AHA), we appreciate the opportunity to provide input on NQF #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) as it undergoes off-cycle review for full endorsement.*

The AHA/ASA strongly supports the goal of having more self-identified black or African American heart failure patients treated with hydralazine/isosorbide dinitrate, however, we cannot support MUC16-74/NQF 2764 as currently specified. As we previously stated in our comments to NQF when the measure was undergoing review for trial use, we do not doubt that the developers share our goals of promoting evidence-based practice and addressing disparities in care. We are, however, very concerned that some aspects of the measure are inconsistent with the ACC/AHA clinical practice guidelines*. We also 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, three-times-a-day medication with overt side effects.

We have reviewed the testing data provided by the developer as part of their application for full endorsement. The testing data not only provides ample evidence of the challenges of accurately collecting all the data required for the measure from electronic health records, but also, we believe, fails to demonstrate that the measure meets the minimum criteria for scientific acceptability required by NQF for full endorsement. In addition, the testing approach is based upon certain assumptions that we believe are faulty. Our specific concerns with the measure and the testing provided by the developer are further detailed below.

In addition to the inconsistency with the guidelines noted above, the clinical trial evidence and guideline recommendations for this therapy were limited to patients with New York Heart Association (NYHA) functional Class III-IV, however, this criterion is not addressed in the measure. There is no exclusion for NYHA functional class I and II, for which there is not sufficient evidence of benefit. As such, it is likely that a large proportion of HF patients without current indications for hydralazine/isosorbide dinitrate combination therapy are included in the measure denominator. This may, in part, account for the remarkably poor performance rates on the measure seen in the testing process.

In section 1b.1 of their application for endorsement, the developers have stated that "there is no substitute for the fixed-dose combination therapy." Among our most significant concerns about this measure is that the ACC/AHA heart failure guideline, which is cited as a source in the application, does not specify the fixed-dose combination, which is currently available only as a brand-name proprietary formulation (BiDil®), but the measure does. The requirement that only prescription of the fixed-dose combination can fulfill the measure is of concern for several reasons:

1) The observed differences in formulations (brand vs. generic), though valid, are theoretical and not proven to be of clinical consequence.
2) A number of the workgroup members involved in developing this measure have received consultant fees and/or honoraria from Arbor Pharmaceuticals, the company that produces Bidil®**. These relationships are not disclosed in the application for endorsement. We would strongly encourage NQF to consider requiring that disclosures of relevant relationships such as this as part of all applications for endorsement moving forward.
3) 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.
4) This requirement also means that physicians 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 patients 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.

During the initial evaluation of the measure for approval for trial use, the standing committee and others expressed concerns regarding the restriction to only the brand name drug. This was also discussed by the MAP during their evaluation of the measure for use in federal programs. Given this concern and the fact that the overall performance rates for the fixed dose combination were extremely low (ranged from 0-1.6%) in the three datasets used for testing, it would be very helpful to have an analysis of what the rates would be if prescription of the individual components of the combination therapy were included. It is also questionable whether these results demonstrate that the measure can identify meaningful differences in performance across measured entities.

Finally, on p. 5 of the testing form the developer states: *We would note that ejection fraction (EF) values from all three datasets were difficult to obtain given the ongoing challenges with collecting this data in discrete fields in EHRs. Because of this limited data, the testing provided in this document represents patients who are self-identified African American or black with a diagnosis of heart failure who were currently receiving ACE or ARB and beta-blocker therapy. Because a diagnosis of left ventricular systolic dysfunction (LVSD) or an EF <40% is a requirement for prescribing those two medications, if the EF or LVSD value was missing, we assumed that it was present if all of the other inclusion factors were met.* We believe that this is a faulty assumption and that prescription of ACEI or ARB and beta-blocker is not a valid proxy for LVSD or an LVEF < 40%. This alone calls into question all of the testing results reported by the developer.

For all of the reasons outlined above, the AHA strongly opposes endorsement of this flawed measure or its use in any accountability, payment or public reporting program as it is currently specified.

We appreciate your consideration of these comments. If you have any questions, please feel free to contact Melanie Shahriary, Manager, Performance Measures, Quality and Health IT at melanie.shahriary@heart.org or 301-651-7548.

Sincerely,
Steven R. Houser, PhD, FAHA
President, American Heart Association
cc: Rose Marie Robertson, Gayle Whitman, Mark Schoeberl, Michele Bolles, Christine Rutan, Kathleen Shoemaker

Comment by: David S. Kountz, MD, MBA, FACP, Vice President, Academic Affairs
Organization: Jersey Shore University Medical Center, Co-Chief Academic Officer
Comment:
Dear Sir/Madam:

I am a general internist who is committed to reducing health disparities and premature morbidity and mortality in African Americans. I am past-president of International Society on Hypertension in Blacks, and like many of my colleagues, care deeply about advancing strategies that have proven benefits.

I am writing to add my voice to those of many highly respected minority health advocates who support the National Minority Quality Forum's (NMQF) Heart Failure Performance Measure, 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. The benefits of the "fixed-dose" for eligible African American patients with heart failure have already been evaluated and approved for trial use – based on science-based evidence — by NQF. Indeed, NQF's decision came after much careful consideration, stakeholder input and thoughtful debate. With adequate testing data in hand, NQF should now continue the march towards endorsement of this important performance measure. It is hard to imagine a scenario in which NQF could find a more egregious case of under-treatment of a minority patient population in which to engage.

I strongly believe that this proposed HF eMeasure can improve the care we provide to African American heart failure patients, and I urge your endorsement of eMeasure #2674.

Comment by: Beverly Oliver, MBA, MSN, FNP-BC, CHFN
Comment:
My name is Beverly Oliver, MBA, MSN, FNP-BC, CHFN. I have a Chronic Care Clinic that sees Heart Failure patients. My readmission rate for my clinic's Heart Failure patients within 30 days is less than 2%. The success of my clinic comes from education, frequent office visits and IV Lasix prn. One of the major successes is also from titration and use of Heart Failure medicines. I have used Bidil for over five years and have seen a marked reduction in hospitalization, increase in EF and improvement in my patients' quality of life.

I wish to reiterate my strong support for NQF endorsement, as well as the eventual CMS adoption, of this important quality measure.

After the NQF approved proposed Quality Measure #16-74 for trial use early last year, the only remaining obstacle to full endorsement should be determining the feasibility of the measure. On this count, I have read that the NMQF has provided sufficient data to validate that the eMeasure would lead to a benefit

for the identified population. That same research showed that the measure would be complementary to current electronic health record (EHR) reporting systems and would not disturb clinical practices.

An endorsement from the NQF represents a vital means of ensuring that this life-saving treatment reaches more patients. I urge you to fully support eMeasure #2764 and to recognize the growing importance of developing quality measures aimed at eradicating the health disparities we continue to face as a nation.

Comment by: Traci Ferguson; Submitted by Ms. Kiersten Adams
Organization: WellCare Health Plans, Inc.
Comment:
WellCare Health Plans, Inc. fully supports NQF quality measure #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."" The benefits of combining Hydralazine and Isosorbide Dinitrate have been published in various peer-reviewed sources, including the New England Journal of Medicine. Additionally, this approach is supported by both the American College of Cardiology and the American Heart Association.

The required testing demonstrated that the measure as specified can be implemented in electronic health record system (EHRs) and will produce results that are reliable and valid. No indications of unintended consequences were identified; therefore, no modifications to the measure are warranted. We encourage NQF to move forward with adoption and use of this measure, as it meets all criteria for endorsement.

As one of the country's largest health care companies dedicated solely to serving public program beneficiaries, we see the effects that disparities can have on health outcomes. Adoption of his measure will ensure that eligible African American patients with symptomatic heart failure receive the proposed course of treatment. WellCare believes that endorsement of this quality measure submitted by the National Minority Quality forum will increase the utilization of this evidence- based standard of care, thus saving thousands of lives each year.

Comment by: Roxanne Yaghoubi
Organization: Healthcare Leadership Council (HLC)
Comment:
The Healthcare Leadership Council (HLC) is writing to express its support for the National Minority Quality Forum's (NMQF) heart failure performance eMeasure, #2764.

HLC, a coalition of chief executives from all disciplines within American healthcare, is the exclusive forum for the nation's healthcare leaders to jointly develop policies, plans, and programs to achieve their vision of a 21st century system that makes affordable, high-quality care accessible to all Americans. Members of HLC – hospitals, academic health centers, health plans, pharmaceutical companies, medical device manufacturers, biotech firms, health product distributors, pharmacies, and information technology companies – envision a quality-driven system that fosters innovation. HLC members advocate measures to increase the quality and efficiency of American healthcare by emphasizing wellness and prevention, care coordination, and the use of evidence-based medicine, while utilizing consumer choice and competition to elevate value.

HLC strongly believes that F-ISDN/HYN accomplishes these goals. In African Americans with heart failure, this therapy is proven to reduce mortality by 43% and first-time hospitalizations for heart failure by 38%,

while improving quality of life. However, patients are not receiving this life-saving therapy. NMQF's testing showed that only 1.1% of all eligible patients were receiving the therapy across more than 300 practices in the Southeast. Less than 1% of all eligible patients were prescribed the medication in the test sample's federally qualified and community health centers, and 0% of eligible patients received the medication at an integrated delivery system in the South. This lack of access is causing the deaths of thousands of African Americans every year.

When NQF reviews this testing data during its Cardiovascular Standing Committee Meeting on February 2, HLC strongly urges you to support the heart failure performance measure. This measure would fill a significant gap in the provision of quality care and there are no significant obstacles to its implementation.

Thank you for the opportunity to comment on this important issue. HLC feels there is tremendous potential for the healthcare industry as a whole to encourage robust collaboration and quality improvement in order to achieve our shared goal of improving the value of healthcare delivery for all.

Comment by: Kenneth Burnham, MD, Director Comprehensive Heart Failure Care Center
Organization: Cardiology Associates, Mobile, AL
Comment:
As a heart failure cardiologist treating a significant number of African American patients with systolic heart failure I wholeheartedly endorse the National Minority Quality Forum's heart failure performance measure: Fixed-dose Combination of Hydralazine and Isosorbide Dinitrate for Self-Identified Black or African American Patients with Heart Failure and LVEF <40% on ACEI or ARB and Beta-blocker Therapy.

Our current guidelines make this a Class I recommendation with a relative risk reduction in mortality of 43%, RRR in hospitalization of 33%, with a NNT (over 36 months) of only 7. Yet, the reality is that many patients have never been prescibed this therapy. Many others are on hydralazine and perhaps a few on isosorbide, but many of our patients are able to figure out that the headache comes from the nitrate and stop taking it. So the importance of fixed-dose combination - which is what was trialed in AHEFT, is not only helpful, but I believe criticial. Our own FDA (in its orange book) agreed that there was no generic substitute or component mixing strategy that has been proven to be a therapeutic switch for the fixed-dose combination.

As you are well aware, and endorsement from the National Quality Forum has led to physician behavior changes that have positively affected the care of patients. Your consideration and endorsement of this measure in African American patients is particularly important in influencing positive change in guideline directed therapy in this patient group who suffers disproportionately from HF and have a therapy that is so underutilized.

Thank you,
Kenneth M. Burnham, MD
Director Comprehensive Heart Failure Care Center, Cardiology Associates, Mobile, AL

Comment by: David Maron
Comment:
I wish to express my strong, continuing support for eMeasure #2764, a proposed heart failure performance measure entitled "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." The measure's steward is the National Minority Quality Forum (NMQF).

I am a cardiologist at an academic medical center and co-direct our inpatient general cardiology service. I treat African American patients with heart failure.

The benefits of fixed-dose combination hydralazine and isosorbide dinitrate for African American patients with heart failure are well documented. The landmark trial by Taylor et al. in NEJM 2004 led to a Class IA recommendation in the ACC/AHA guidelines for the management of heart failure in African American patients. Unfortunately, use of this treatment is less than 10% in African American patients with heart failure. I support this quality measure for the management of eligible patients with HF in order to drive greater awareness and utilization of this life saving treatment.

In approving this measure for trial use last year, the NQF has already spoken to its scientific merit. I therefore urge you to look favorably upon the testing data that has been presented to you by the measure's steward which demonstrates electronic health record compatibility and the absence of any indication of unintended negative consequences of promoting the measure.

I hope, therefore, that the Committee will endorse this important measure.

Comment by: Ms. Elizabeth O. Ofili MD, MPH, FACC, Morehouse School of Medicine Director and Senior Associate Dean of Clinical Research Center & Clinical and Translational Research
Organization: Morehouse School of Medicine
Comment:
I am Elizabeth Ofili, MD, MPH, FACC. I am the Morehouse School of Medicine Director and Senior Associate Dean of Clinical Research Center & Clinical and Translational Research. I am writing in support of Measure #2764, Fixed Dose Combination of Hydralazine and Isosorbide Dinitrate Therapy for Self-Ventricular Ejection Fraction (LVEF) <40% on ACEI or ARB and Beta-blocker Therapy.

I ask the Cardiovascular Standing Committee to approve the testing data, attest to the scientific acceptability of the measure, and advance Measure 2764 to endorsement. This request is justified by the strong scientifc evidence that undergirds the measure, the documented need for the measure, the unmet need for this therapy among the specified patient cohort, and the outcomes of the testing of the measure in EHR systems.

Every year thousands of heart failure patients are hospitalized or die due to failure to treat with the fixed-dose combination, the therapy that was approved by the Food and Drug Administration more than a decade ago. Morehouse School of Medicine, therefore, was honored to partner with Grady Hospital as one of three testing sites for Measure #2764. The testing data from our site, as well as those from the other testing sites, confirmed the validity and reliability of the measure in electronic health records systems, and the room for improvement of provider performance on the process specific in the measure.

Challenges reported with the availability of ejection fraction values to determine left ventricular systolic dysfunction are a function of failure of providers to report this data element in fields that are available in the EHRs. This provider behavior must be changed to enable improvements in quality of care and improved patient outcomes for patients with heart failure, regardless of the stage of the disease or the patient's race, ethnicity, gender, sex, or geographic location.

The testing results demonstrate that Measure #2764, as specified, will produce results that are reliable and valid. No modifications to the measure specifications are indicated by testing or evidence.

In closing, as a health services researcher, a practicing cardiologists, and a leader in academic medicine with a commitment to improvement in the precision and quality of the care provided by all cardiologists, I have been gratified by the work that has been done to improve the care processes for this underserved patient cohort. I invite the American College of Cardiology to collaborate with Morehouse School of Medicine, the National Minority Quality Forum, and the Association of Black Cardiologists in our collective efforts to advance health equilty and evidence-based treatment of heart failure in African American patients.

Thank you.

Comment by: Gary Puckrein; Submitted by Ms. Gretchen Clark Wartman
Organization: National Minority Quality Forum
Comment:
The National Minority Quality Forum (NMQF) is pleased to submit this Cardiovascular Standing Committee Pre-Meeting Public Comment regarding the testing of the scientific acceptability of NQF Measure #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).

The Testing Attachment for this eMeasure is the only component of our application for endorsement that has not yet been reviewed. All other components were reviewed and approved by the Cardiovascular Standing Committee, the Consensus Standards Approval Committee, and the Executive Committee of the NQF Board of Directors.

At each stage of the deliberations, Measure #2764 was the subject of important substantive discussion. Committee members, members of the public, and NQF members were accorded opportunities during the meetings and during the public comment periods to articulate their perspectives, pro and con. The NQF Consensus Development Process factored in all input, and reached the conclusion three times that Measure #2764, as specified, would be a positive addition to the family of NQF-endorsed measures, would accrue to the benefit of the specified patient population, and warranted approval.

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 Measure #2764 to advance and to complete required testing of validity and reliability.

Measure #2764 represents a value proposition that 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. The National Minority Quality Forum appreciates this opportunity to submit this comment through this public forum to clarify critical, and in our view essential and forward-looking aspects of Measure #2764.

It is the National Minority Quality Forum's understanding that performance measures must be consistent with current evidence to ensure that appropriate, safe and high quality care is provided by physicians to their patients. During one of the earlier public comment periods, a commenter stated 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 peer-reviewed research and science that supports that are directly linked to the measure specifications.

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”.

Recommendation of the use of the two component compounds as a “generic” to the fixed-dose combination is inconsistent with the FDA’s statement that they have not approved a generic for the fixed-dose combination. A copy of that FDA letter can be made available upon request.

The NQF Executive Committee, Consensus Standards Approval Committee and Cardiovascular Standing Committee concurred with that position. For those who are interested in more detail on these discussions, click here to listen to the audio of the February 2016 meeting of the NQF Executive Committee.

It is important to note that the FDA approved hydralazine alone or as an adjunct for hypertension. Isosorbide dinitrate is indicated for the prevention of angina pectoris due to coronary artery disease. Individually, the FDA approved neither hydralazine nor isosorbide dinitrate for the treatment of chronic heart failure. Therefore, prescribing of these medications for treatment of heart failure is off-label use. Off-label use involves prescribing medications for indications or using dosages or dosage forms that have not been approved by the FDA. FDA advises, “Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects”.

Of note, product labeling for the FDA heart failure-approved fixed-dose combination adequately addresses tolerability issues with a dosing alternative stating: “Dosage may be decreased to as little as one-half tablet three times a day if intolerable side effects occur. Efforts should be made to titrate up as soon as side effects subside.” No such simplified dosing information is available for component compound labeling.

The lack of utilization of guideline recommended therapy has been extensively documented within the American Heart Association’s Get-With-the-Guidelines registry database and published in the journal of the American Heart Association stating that use was, ‘unacceptably low considering the conclusive trial evidence demonstrating substantial reductions in all-cause mortality and hospitalizations with H-ISDN use.’[1],2 We submit that confusion regarding off-label prescribing has served to perpetuate this under-utilization and disparity of care. [[1]Golwala H., Thadani U., Liang L. Use of Hydralazine-Isosorbide Dinitrate Combination in African American and Other Race/Ethnic Group Patients With Heart Failure and Reduced Left Ventricular Ejection Fraction Journal of the American Heart Association. 2013;2:e000214; https://doi.org/10.1161/JAHA.113.000214 ; 2Yancy CW, Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, McBride ML, Mehra MR, O’Connor CM, Reynolds D, Walsh MN.Adherence

to guideline-recommended adjunctive heart failure therapiesamong outpatient cardiology practices (findings from IMPROVE HF). Am JCardiol. 2010;105:255–260.]

While the ACCF/AHA guidelines can include recommendations of off label use of hydralazine and isosorbide dinitrate as an alternative to the fixed dose, there are laws and regulations regarding off label use to which providers must adhere, and of which patients must be made aware. Medicare Part D, for example, coversdrugs prescribed for off-label use only if the drugs are identified as safe and effective for that use in one of three officially recognized drug compendia. Not one of these compendia is readily accessible to the public; some are available only by expensive subscription; and none of these compendia recommend hydralazine and isosorbide dinitrate for the treatment of heart failure in blacks. The Veterans Administration and commercial insurers also have regulations regarding off label use of medications.

It has been suggested several times by some commenters 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 for treatment of heart failure 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 evidence-based sentinels of poor quality care that mandate an intervention by the policy and regulatory environment. Measure #2764 is a response to this evidence.

It has been suggested that Measure #2764 "…fails to fully acknowledge the complexity of addressing race in medical practice." 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. Further, the identification of race and ethnicity is mandated by the Joint Commission and by Meaningful Use.

No peer-reviewed references are offered to support the comment regarding "complexity"; however, we do refer all interested in these issues to the 2002 Institute of Medicine report, Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Measure #2764 is neither the beginning nor the end of the discourse regarding challenges within health services research, delivery and financing to address biodiversity. Measure #2764 does inform advancement of the conversation, and adds a metric to incentivize and measure a component of quality care for a particular patient cohort. It must not be further delayed.

The inclusions and exclusions of Measure #2764 warrant some exploration. This performance measure is defined in the same manner as other performance measures that have been endorsed for treatment of heart failure. It is, by definition, specified for patients with at least New York Heart Association (NYHA) Class III heart failure. Because of the well-defined denominator, there is no need to exclude patients diagnosed with NYHA class I & II, for which, as a commenter notes, "there is not sufficient evidence of benefit."

Currently, a diagnosis of left ventricular systolic dysfunction (LVSD) or an EF <40% is a part of the guideline recommendations for prescribing ACE/ARB and Beta-blocker therapies, and this measure is directly aligned with existing NQF-endorsed measures on those therapies for patients with heart failure. The ability to collect and report EF values continues to be a challenge for providers and has historically

been a challenge for all electronic measures requiring an ejection fraction (EF) value. As noted in our testing results, because of these difficulties in obtaining an EF value, we used the following proxy: If the EF or LVSD value was missing, the presence of LVSD or an EF <40% was assumed if all of the other inclusion factors including ACE/ARB and Beta-blocker were met. We opted to trust the provider's clinical knowledge and judgement. Specifically, if a patient with a diagnosis of heart failure was prescribed both ACE or ARB and a beta-blocker, then given the guideline recommendations, the provider did so because the patient also had LVSD or an EF <40%. As a result, including those patients prescribed those two therapies regardless of the presence of LVSD or an EF <40% in our testing would not compromise the validity of the measure and testing results.

The failure of providers to record ejection fraction in the fields that are available in medical records is a quality of care issue that is 100% a function of provider behavior, behavior that potentially compromises diagnosis, prescribing and patient management. It is a quality of care issue that can be addressed through provider education or through another process measure. It cannot and must not be used to compromise access to this effective therapy.

It must be noted that an ejection fraction value is a key component of at least 13 other NQF-endorsed performance measures, including:

- ACEI or ARB for left ventricular systolic dysfunction- Acute Myocardial Infarction (AMI) Patients (NQF #0137)
- Beta-Blocker Therapy (i.e., Bisoprolol, Carvedilol, or Sustained-Release Metoprolol Succinate) for LVSD Prescribed at Discharge (NQF #2438)
- Coronary Artery Disease (CAD): Angiotensin-Converting Enzyme (ACE) Inhibitor or Angiotensin Receptor Blocker (ARB) Therapy - Diabetes or Left Ventricular Systolic Dysfunction (LVEF < 40%) (NQF #0066)
- Coronary Artery Disease (CAD): Beta-Blocker Therapy-Prior Myocardial Infarction (MI) or Left Ventricular Systolic Dysfunction (LVEF <40%) (NQF #0070)
- Coronary Artery Disease (CAD): Beta-Blocker Therapy-Prior Myocardial Infarction (MI) or Left Ventricular Systolic Dysfunction (LVEF <40%) (NQF #2906)
- Coronary Artery Disease (CAD): Beta-Blocker Therapy-Prior Myocardial Infarction (MI) or Left Ventricular Systolic Dysfunction (LVEF <40%) (NQF #3049)
- Heart Failure (HF): Angiotensin-Converting Enzyme (ACE) Inhibitor or Angiotensin Receptor Blocker (ARB) Therapy for Left Ventricular Systolic Dysfunction (LVSD) (NQF #0081)
- Heart Failure (HF): Angiotensin-Converting Enzyme (ACE) Inhibitor or Angiotensin Receptor Blocker (ARB) Therapy for Left Ventricular Systolic Dysfunction (LVSD) (NQF #2907)
- Heart Failure (HF): Angiotensin-Converting Enzyme (ACE) Inhibitor or Angiotensin Receptor Blocker (ARB) Therapy for Left Ventricular Systolic Dysfunction (LVSD) (NQF #3050)
- Heart Failure (HF): Beta-Blocker Therapy for Left Ventricular Systolic Dysfunction (LVSD)
- Heart Failure (HF): Beta-Blocker Therapy for Left Ventricular Systolic Dysfunction (LVSD) (NQF #2908)
- Heart Failure (HF): Beta-Blocker Therapy for Left Ventricular Systolic Dysfunction (LVSD) (NQF #3051)

The National Minority Quality Forum believes that the testing results for Measure #2764, as specified, indicate that poor performance is not a result of the denominator specifications, but demonstrate that patients are not receiving this approved therapy.

Speculative concerns have been expressed 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 access and to fill prescriptions written by physicians. These concerns are not supported by any references or documentation, may be based upon stereotypes, and are not concerns that are de facto generalizable to all patients for whom the therapy in question is indicated. Further, these expressed concerns about affordability are hinged upon a false belief that there is a legal and efficacious "generic" or substitute for the FDA-approved fixed-dose combination. That is not the case.

It must be noted that developing performance measures based upon speculation about the potential behavior of insurance companies is, we submit, not appropriate for discussions of evidence-based components of quality care. Insurers should rely upon science to inform their coverage and payment decisions. The inverse should never be the case.

Concerns have been expressed 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.

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 that we will be pleased to make this non-substantive addition to Measure #2764.

Comment by: Mr. Adolph Falcon
Organization: National Alliance for Hispanic Health
Comment:
The National Alliance for Hispanic Health (the Alliance) strongly supports the Heart Failure Performance Measure, 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. The Alliance is the premier science-based and community-driven organization that focuses on improving the health and well-being of Hispanics and works with others to secure health for all.

The Alliance continues to remain concerned that too many of the National Quality Forum's (NQF's) quality measures follow a one-size-fits-all pattern that does not account for differences in patient populations. Accounting for differences, including race, ethnicity, and gender are cricital to good science and good medicine that reflects advances in personalized medicine. The treatment of African-Americans with heart failure is a prime example.

Medical studies, such as the 2014 A-HeFT study (Taylor AL, Ziesche S, Yancy C, et al. N Engl J Med. 2004;351 (20):2049-2057) have demonstrated thebenefits of a fixed-dose treatment, as proposed by eMeasure #2764. The 2014 A-HeFT study demonstrated that there are differences in the prevalence and causation of congestive heart failure including, on average, finding that self-identified African Americans have a less active renin–angiotensin system and a lower bioavailability of nitric oxide than those self-identified as white. The proposed eMeasure #2764 quality measure would reflect this finding of a population-based difference in heart failure and help address the fact that fewer than ten percent of eligible patients are given the appropriate treatment for heart failure. (Gregg C. Fonarow, Clyde W. Yancy,

Adrian F. Hernandez, Eric D. Peterson, John A. Spertus, and Paul A. Heidenreich, "Potential impact of optimal implementation of evidence-based heart failure therapies on mortality", American Heart Journal, June 2011, Volume 161, Number 6, pp. 1025-1026).

Furthermore, in its submission to NQF, we are encouraged that data from the National Minority Quality Fourm (NMQF) show that current electronic health record (EHR) recording systems could be used in coordination with the new eMeasure without disrupting clinical practices. Ensuring that prescribers will be able to identify patients and provide the treatment to appropriate HF patients will lead to improved care for the targeted population. The NQF has an opportunity to chart a new path towards the promise of precision medicine and better health care in adopting the heart failure eMeasure #2764. The Alliance fully supports endorsement of the measure and hopes that the NQF will act to ensure that every patient is guaranteed the best possible care available.

Comment by: David N. Smith, MD

Comment:

I am writing to express my support for the National Minority Quality Forum's (NMQF) Heart Failure Performance Measure, 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.

The benefits of the "fixed-dose" for African American patients with heart failure are clear, "efficacious and increase survival among black patients with advanced heart failure."

Despite its proven benefits, only 1.1% of eligible patients currently receive the FDA-approved fixed dose therapy with 1% in a federally qualified and community health center sample. This is an opportunity to thwart thousands of lives lost with reduced mortality and hospitalization from HF.

Were we to eliminate the discussion of race and focus purely on benefit, there would be no question of the fixed dose combination's virtue. If we cover the discussion to question dosing, then we must reconsider all previous studies and current medical training that purports any combination regimen in treatment of heart failure - much to the reprimand, professional and financial, of all providers on quality measures. If a question of whether a generic combination separated in components delivers the same outcomes as the combination supported by pivotal trials is allowed to delay, if not deter, treatment to indicated patients, we would have to defend why this concern never stopped other drug classes. We must answer why we would extrapolate ARNI therapy with ENTRESTO (also with varying doses of fixed dose combinations) to nonwhite patients including females under 65 from ethnic groups (other than white or Asian) outside of the U.S. Would such restraint and criticism apply to life-saving therapy if the discussion was in cancer patients. Finally, if the underpinning of the discussion lies in the study's evidence in African Americans and thus concern of a "racial drug", then we must recall the benefit was originally defined in non-African Americans in multiple studies and, as such, an impediment to use here serves only to withhold care in one group and ignore a potentially augmented approach in another group.

It is my firm belief that this proposed HF eMeasure can strengthen the nation's commitment to providing high quality care to all its citizens. I can no longer justify telling my patients to try a medicine we think may work for you while simultaneously fighting to get them something that we know works on both population and practical metrics. I strongly urge the NQF's endorsement of eMeasure #2674.

Comment by: Mr. Richard Allen Williams, MD, President of the National Medical Association (NMA), Founder of the Association of Black Cardiologists
Organization: National Medical Association (NMA)
Comment:
I am Richard Allen Williams, MD, President of the National Medical Association (NMA), Founder of the Association of Black Cardiologists. I am submitting this public comment in support of Measure #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.

In specific, I am writing to request that the Cardiovascular Standing Committee approve the testing data and support the advancement of Measure #2764 to endorsement. The measure is based upon a foundation of strong scientific evidence that has already been accepted by NQF as part and parcel of its trial use approval. Additionally, there is a clear and unmistakeable need for the measure.

The NMA represents the interests of more than 50,000 African American physicians and the patients they serve. Our support for Measure #2764 is consistent with our role as the nation's leading force for parity and justice in medicine and the elimination of disparities in health care. Unfortunately, more than 10 years after FDA approved the fixed-dose combination of isosorbide dinitrate and hydralazine, only seven percent of eligible African American HF patients are estimated to receive this life saving treatment, leading to thousands of deaths each year that could have been avoided.

Endorsements of Measure #2764 by the Committee will send a strong message to providers, patients and policymakers alike that, when science and value are established and in sync, the National Quality Forum, the Centers for Medicare and Medicaid Services, and the nation's healthcare providers will take the lead in creating a health services delivery sysem that is responsive to the needs of all Americans.

Thank you for your consideration.

Comment by: Phillip B. Duncan, MD, FACC
Organization: Cardia Health Management Network
Comment:
I have been in the private practice of cardiology for over 30 years. In that time I have cared for thousands of patients with heart failure and that has become a particular focus of my practice. My patient population is diverse but approximately 60% African American.

It has been encouraging to see a number of new therapies become available to improve outcomes for my heart failure patients. With each of these clinically proven therapies we have worked tirelessly to apply the appropriate therapy to the appropriate patients. Fixed dose I/H has been found to be effective in the treatment of self-described African American patients with NYHA Class III-IV systolic heart failure. I have used this drug with excellent outcomes in my patient population.

I find it uncosionable to deny the best available clinically indicated therapy to any group of individuals. That is why I strongly support this quality measure.

Sincerely,
Phillip B Duncan, MD, FACC

Comment by: Cassandra McCullough; Submitted by Ms. Camille Bonta, MHS

Organization: Association of Black Cardiologists
Comment:
The Association of Black Cardiologists (ABC) continues to express its strong support of quality measure (MUC16-74) — Fixed-dose Combination of Hydralazine and Isosorbide Dinitrate Therapy for Self-identified Black or African American Patients with Heart Failure (fixed dose) and advocate for its use in the Medicare program.

We commend the National Qualify Forum (NQF) for its examination of how quality measurement can be used to address disparities in cardiovascular disease. The fixed dose measure, while a process measure, can be used as a proxy to achieve the outcome of reducing health disparities in the African American cardiovascular patient population. We recognize that the Measure Applications Partnership (MAP) Clinician Workgroup has recommended that measure MUC16-074 be resubmitted for consideration after review of testing results by the NQF Cardiovascular Standing Committee. We ask the NQF Cardiovascular Standing Committee to accept the testing results.

Indeed, testing data showed that:

- only 1.1 percent of all eligible patients are currently receiving the FDA-approved fixed dose combination therapy across 303 practices in the Southeast;
- less than 1percent of eligible patients were prescribed the medication in the federally qualified and community health center sample; and
- 0% of eligible patients were prescribed the medication in the integrated delivery system in the South that was measured.

The merit of the measure (Fixed-dose Combination of Hydralazine and Isosorbide Dinitrate Therapy for Self-identified Black or African American Patients with Heart Failure), and the Association of Black Cardiologist's (ABC) support of it, is supported by results of the A-HeFT study, published in 2004 by the New England Journal of Medicine (NEJM) which examined whether a fixed dose of both isosorbide dinitrate and hydralazine provides additional benefit in blacks with advanced heart failure. This study demonstrated a significant 43 percent improvement in survival among black patients with advanced heart failure given isosorbide dinitrate plus hydralazine compared to a placebo group. Additionally, the rate of first hospitalizations for heart failure was reduced by 33 percent, as compared with that in the placebo group, and quality-of-life scores also improved compared to the placebo group. In fact, the A-HeFT trial was halted early due to a significantly higher mortality rate in the placebo group than in the group given the fixed-dose combination isosorbide dinitrate plus hydralazine.

It should be noted that individual components of the combination therapy has been suggested to be adequately representative of the fixed-dose regimen. However, there is no FDA approved generic equivalent for the fixed-dose combination that led to the results of the A-HeFT.

African Americans are at increased risk of heart failure and experience worse outcomes post-heart failure development.(1) Yet, studies show that African American with heart failure are not receiving guideline-recommended H-ISDN therapy when indicated.(2)

There is a clear opportunity to close the disparity gap and improve outcomes for African American heart failure patients. While not a complete solution, this measure will at least drive better adherence to quality of care. We therefore strongly request NQF's support for the measure.

Founded in 1974, the Association of Black Cardiologists (ABC) is a nonprofit organization with an international membership 1,700 comprised of health professionals, lay members of the community

(Community Health Advocates), corporate members, and institutional members. At the ABC, there is no issue more central to our cause than ensuring that all Americans are given the foremost care to combat, treat, and overcome cardiovascular disease. This includes the recognition that cardiovascular disease occurs disproportionately in African Americans.

Comment by: Modele Ogunniyi
Comment:

I support the eMeasure #2764, the National Minority Quality Forum's (NMQF) proposed Heart Failure Performance Measure entitled "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.

As a cardiologist, who manages predominantly African American patients with heart failure,the results of the A-HEFT trial have demonstrated the importance of this quality measure in eligible patients. The NMQF has also provided supporting documentation.

I hope, therefore, that the Committee will endorse this important eMeasure.

NATIONAL QUALITY FORUM—Evidence (subcriterion 1a)

Measure Number (*if previously endorsed*)**:** Click here to enter NQF number

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

IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here: Click here to enter composite measure #/ title

Date of Submission: Click here to enter a date

Instructions

- *For composite performance measures:*
  - *A separate evidence form is required for each component measure unless several components were studied together.*
  - *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*
- Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed.
- If you are unable to check a box, please highlight or shade the box for your response.
- Maximum of 10 pages (*incudes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.***
- Contact NQF staff regarding questions. Check for resources at Submitting Standards webpage.

Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF's evaluation criteria.

1a. Evidence to Support the Measure Focus

The measure focus is evidence-based, demonstrated as follows:

- Health outcome: [3] a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior.
- Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [4] that the measured intermediate clinical outcome leads to a desired health outcome.
- Process: [5] a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [4] that the measured process leads to a desired health outcome.
- Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [4] that the measured structure leads to a desired health outcome.
- Efficiency: [6] evidence not required for the resource use component.

Notes

3. Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.

4. The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) grading definitions and methods, or Grading of Recommendations, Assessment, Development and Evaluation (GRADE) guidelines.

Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.

6. Measures of efficiency combine the concepts of resource use and quality (see NQF's Measurement Framework: Evaluating Efficiency Across Episodes of Care; AQA Principles of Efficiency Measures).

5.

1a.1.This is a measure of: (*should be consistent with type of measure entered in De.1*) Outcome

- ☐ Health outcome: Click here to name the health outcome
- ☐ Patient-reported outcome (PRO): Click here to name the PRO
  PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors
- ☐ Intermediate clinical outcome (*e.g., lab value*): Click here to name the intermediate outcome
- ☒ Process: Fixed-dose combination therapy of hydralazine and isosorbide dinitrate therapy for self-identified Black or African American patients with HF, LVSD and on ACEI or ARB and beta-blocker therapy
- ☐ Structure: Click here to name the structure
- ☐ Other: Click here to name what is being measured

HEALTH OUTCOME/PRO PERFORMANCE MEASURE *If not a health outcome or PRO, skip to*

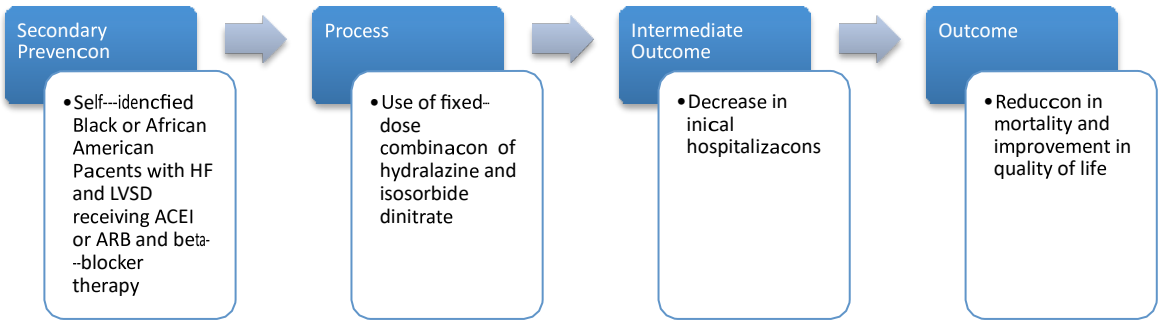
1a.2. Briefly state or diagram the path between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.

1a.2.1. State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (*i.e., influence on outcome/PRO*).

Note: For health outcome/PRO performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.

INTERMEDIATE OUTCOME, PROCESS, OR STRUCTURE PERFORMANCE MEASURE

1a.3. Briefly state or diagram the path between structure, process, intermediate outcome, and health outcomes. Include all the steps between the measure focus and the health outcome.



The African-American Heart Failure Trial (A-HeFT) first published in 2004 demonstrated that there is significant benefit for African American patients who receive a fixed-dose combination therapy of hydralazine and isosorbide dinitrate. This trial built on the findings from the two Vasodilator-Heart Failure Trials (V-HeFT). A-HeFT, which was ended early due to the mortality rates in the placebo population, demonstrated a 43% reduction in mortality, 33% decrease in initial hospitalizations, and a 50% improvement in patient-reported quality of life (Taylor, 2004, Sharma, 2014). These results clearly demonstrate that the fixed-dose combination therapy significantly improves patient morbidity, mortality and quality of life in this clinical cohort. There is no substitute for the fixed-dose combination therapy.

References:

Sharma A, Colvin-Adams M, Yancy CW. Heart failure in African Americans: disparities can be overcome. Cleve Clin J Med. 2014;81:301-11.

Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004; 351:2049–57.

1a.3.1. What is the source of the systematic review of the body of evidence that supports the performance measure?

☒ Clinical Practice Guideline recommendation – ***complete sections 1a.4, and 1a.7***

☐ US Preventive Services Task Force Recommendation – ***complete sections 1a.5 and 1a.7***
☐ Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections 1a.6 and 1a.7***
☐ Other – ***complete section 1a.8***

Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.

1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION

1a.4.1. Guideline citation (*including date*) and **URL for guideline** (*if available online*):

Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson 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 management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147–239.

http://content.onlinejacc.org/article.aspx?articleid=1695825

Lindenfeld J, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, Klapholz M, Moser DK, Rogers JG, Starling RC, Stevenson WG, Tang WHW, Teerlink JR, Walsh MN. Executive Summary: HFSA

2010 Comprehensive Heart Failure Practice Guideline. J Card Fail 2010;16:475-539. http://www.hfsa.org/hfsa-wp/wp/heart-failure-guidelines-2/.

1a.4.2. Identify guideline recommendation number and/or page number and quote verbatim, the specific guideline recommendation.

2013 ACCF/AHA Guideline for the Management of Heart Failure (e179)

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**)

HFSA 2010 Comprehensive Heart Failure Practice Guideline

p. e80-81:

A combination of hydralazine and isosorbide dinitrate is recommended as part of standard therapy in addition to beta blockers and ACE inhibitors for African Americans with HF and reduced LVEF.

- NYHA III or IV HF (**Strength of Evidence = A**)
- NYHA II HF (**Strength of Evidence = B**)

p. e171:

The combination of hydralazine/isosorbide dinitrate is recommended as standard therapy for African American women with moderate to severe HF symptoms who are on background neurohormonal inhibition. (**Strength of Evidence = B**)

1a.4.3. Grade assigned to the quoted recommendation with definition of the grade:

2013 ACCF/AHA Guideline for the Management of Heart Failure

Class of Recommendation: Class I

Definitions:

Class of Recommendation (COR) is an estimate of the size of the treatment effect considering risks versus benefits in addition to evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm.

Class I: Procedure/Treatment should be performed/administered

HFSA 2010 Comprehensive Heart Failure Practice Guideline

Strength of Recommendation: Is recommended

Definition: The phrase ''is recommended'' should be taken to mean that the recommended therapy or management process should be followed as often as possible in individual patients. Exceptions are carefully delineated.

1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system. (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

2013 ACCF/AHA Guideline for the Management of Heart Failure

Class of Recommendation (COR) is an estimate of the size of the treatment effect considering risks versus benefits in addition to evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm.
Class I: Procedure/Treatment should be performed/administered Class IIa: It is reasonable to perform procedure/administer treatment Class IIb: Procedure/Treatment may be considered
Class III: No benefit (Not helpful or No proven benefit)
Class III: Harm (Excess cost w/o benefit or Harmful to patients)

HFSA 2010 Comprehensive Heart Failure Practice Guideline

Strength of Recommendation:
The HFSA guideline employs the categorization for strength of recommendation outlined in Table 1.3. There are several degrees of favorable recommendations and a single category for therapies felt to be not effective. The phrase ''is recommended'' should be taken to mean that the recommended therapy or management process should be followed as often as possible in individual patients. Exceptions are carefully delineated. ''Should be considered'' means that a majority of patients should receive the intervention, with some discretion involving individual patients. ''May be considered'' means that individualization of therapy is indicated (Table 1.3). When the available evidence is considered to be insufficient or too premature, or consensus fails, issues are labeled un- resolved and included as appropriate at the end of the relevant section.

Is recommended: Part of routine care; exceptions to therapy should be minimized
Should be considered: Majority of patients should receive the intervention; some discretion in application to individual patients should be allowed
May be considered: Individualization of therapy is indicated
Is not recommended: Therapeutic intervention should not be used

1a.4.5. Citation and URL for methodology for grading recommendations (*if different from 1a.4.1*)**:**

ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. Cardiosource.com. 2010. Available at:
http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and
http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf

Lindenfeld J, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, Klapholz M, Moser DK, Rogers JG, Starling RC, Stevenson WG, Tang WHW, Teerlink JR, Walsh MN. Executive Summary: HFSA 2010 Comprehensive Heart Failure Practice Guideline. J Card Fail 2010;16:475–539. http://www.hfsa.org/hfsa-wp/wp/heart-failure-guidelines-2/.

1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?

☒ Yes → ***complete section*** ____

☐ No → ***report on another systematic review of the evidence in sections____and____; if another review does not exist, provide what is known from the guideline review of evidence in ____***

1a.5. UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

1a.5.1. Recommendation citation (*including date*) and **URL for recommendation** (*if available online*):

1a.5.2. Identify recommendation number and/or page number and quote verbatim, the specific recommendation.

1a.5.3. Grade assigned to the quoted recommendation with definition of the grade:

1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system. (*Note: the grading system for the evidence should be reported in section 1a.7.*)

1a.5.5. Citation and URL for methodology for grading recommendations (*if different from 1a.5.1*)**:**

Complete section ____

1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE

1a.6.1. Citation (*including date*) and **URL** (*if available online*):

1a.6.2. Citation and URL for methodology for evidence review and grading (*if different from 1a.6.1*)**:**

Complete section ____

1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE SUPPORTING THE MEASURE

If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.

1a.7.1. What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?

2013 ACCF/AHA Guideline for the Management of Heart Failure

This guideline covers multiple management issues for the adult patient with Heart Failure (HF) including the guideline-directed medical therapy (GDMT) such as the combination of hydralazine and isosorbide dinitrate for African

American patients receiving ACE/ARB therapy.

HFSA 2010 Comprehensive Heart Failure Practice Guideline

The guideline developed by HFSA in 2010 addresses prevention, evaluation, disease management and therapies (pharmacologic and device) and end of life management.

1a.7.2. Grade assigned for the quality of the quoted evidence with definition of the grade:

2013 ACCF/AHA Guideline for the Management of Heart Failure

An overall grade for the quality of evidence was not assigned. Rather, the quality of a study (or set of studies) supporting a recommendation was graded on an estimate of the certainty or precision of the treatment effect.

The recommendation to support this measure is Level of Evidence of A: Data derived from multiple randomized clinical trials or meta- analyses. References used to determine level of evidence must be provided and cited with the recommendation.

HFSA 2010 Comprehensive Heart Failure Practice Guideline

The recommendations from this guideline in support of the measure are Strength of Evidence:

- A: Randomized, Controlled, Clinical Trials; May be assigned based on results of a single methodologically rigorous trial and
- B: Cohort and Case-Control Studies Post hoc, subgroup analysis, and meta-analysis; Prospective observational studies or registries

1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.

2013 ACCF/AHA Guideline for the Management of Heart Failure

Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. Level of Evidence

of A: Data derived from multiple randomized clinical trials or meta- analyses.

Level of Evidence B: Data derived from a single randomized trial, or nonrandomized studies. References used to determine level of evidence must be provided and cited with the recommendation.

Level of Evidence C: Consensus opinion of experts, case studies, or standard of care. HFSA 2010

Comprehensive Heart Failure Practice Guideline

Strength of evidence is determined both by the type of evidence available and the assessment of validity, applicability, and certainty of a specific type of evidence. Following the lead of previous guidelines, strength of evidence in this guideline is heavily dependent on the source or type of evidence used. The HFSA guideline process has used three grades (A, B, or C) to characterize the type of evidence available to support specific recommendations.

Strength of Evidence A: Randomized, Controlled, Clinical Trials; May be assigned based on results of a single methodologically rigorous trial and

Strength of evidence B: Cohort and Case-Control Studies Post hoc, subgroup analysis, and meta-analysis; Prospective observational studies or registries

Strength of Evidence C: Expert Opinion; Observational studies-epidemiologic findings; Safety reporting from large-scale use in practice

1a.7.4. What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range: An extensive evidence review was conducted through October 2011 and includes selected other references through April 2013 for the 2013 ACCF/AHA Guideline for the Management of Heart Failure. No information on the time period was provided for the HFSA 2010 Comprehensive Heart Failure Practice Guideline.

QUANTITY AND QUALITY OF BODY OF EVIDENCE

1a.7.5. How many and what type of study designs are included in the body of evidence? (*e.g., 3 randomized controlled trials and 1 observational study*)

2013 ACCF/AHA Guideline for the Management of Heart Failure

The body of evidence supporting the recommendations on guideline-directed medical therapy includes: 4 randomized controlled trials (RCTs)
2 post hoc retrospective analyses

HFSA 2010 Comprehensive Heart Failure Practice Guideline

Specific information on the number of studies included in the body of evidence not provided.

1a.7.6. What is the overall quality of evidence <u>across studies</u> in the body of evidence? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

2013 ACCF/AHA Guideline for the Management of Heart Failure

The recommendation for this medication therapy is rated as Level of Evidence A, meaning that the data was derived from multiple RCTs or meta-analyses. Additional information on the overall quality of evidence across the RCTs is not

provided.

HFSA 2010 Comprehensive Heart Failure Practice Guideline

The recommendations for hydralazine and isosorbide dinitrate therapy are rated as Strength of Evidence A and B, meaning that the data was derived from RCTs, cohort and Case-Control Studies Post hoc, subgroup analysis, meta-analysis or prospective observational studies or registries. Additional information on the overall quality of evidence is not provided.

ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE

1a.7.7. What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161:1024–1030.e3. In 2011, Fonarow and colleagues complete a post hoc retrospective analysis to identify current gaps in care for patients with HF and reduced LVEF and to quantify the potential benefits of specific evidence based therapies. Review of RCT data for combination of hydralazine and isosorbide dinitrate showed that a patient's relative risk for death was reduced by 43% and the number needed to treat for mortality (standardized to 12 months) was 21. If this combination was prescribed to all of the patients for which it was appropriate, then 9.8% or 6,655 lives could be saved each year.

2013 ACCF/AHA Guideline for the Management of Heart Failure p. e179:

In a large-scale trial that compared the vasodilator combination with placebo, the use of hydralazine and isosorbide dinitrate reduced mortality but not hospitalizations in patients with HF treated with digoxin and diuretics but not an ACE inhibitor or beta blocker. However, in 2 other trials that compared the vasodilator combination with an ACE inhibitor, the ACE inhibitor produced more favorable effects on survival. A post hoc retrospective analysis of these vasodilator trials demonstrated particular efficacy of isosorbide dinitrate and hydralazine in the African American cohort. In a subsequent trial, which was limited to patients self-described as African American, the addition of a fixed-dose combination of hydralazine and isosorbide dinitrate to standard therapy with an ACE inhibitor or ARB, a beta blocker, and an aldosterone antagonist offered significant benefit.

The combination of hydralazine and isosorbide dinitrate is recommended for African Americans with HFrEF who remain symptomatic despite concomitant use of ACE inhibitors, beta blockers, and aldosterone antagonists. Whether this benefit is evident in non–African Americans with HFrEF remains to be investigated. The combination of hydralazine and isosorbide dinitrate should not be used for the treatment of HFrEF in patients who have no prior use of standard neurohumoral antagonist therapy and should not be substituted for ACE inhibitor or ARB therapy in patients who are tolerating therapy without difficulty. Despite the lack of data with the vasodilator combination in patients who are intolerant of ACE inhibitors or ARBs, the combined use of hydralazine and isosorbide dinitrate may be considered as a therapeutic option in such patients.

p. e81:
The Vasodilator Heart Failure Trial (V-HeFT) was the first major randomized HF trial and was conducted in Veterans Administration hospitals throughout the US. Patients who remained symptomatic with mild to severe symptoms of HF despite treatment with diuretics and digoxin were randomized to a combination of hydralazine and isosorbide dinitrate or prazosin or placebo. The combination of hydralazine and isosorbide dinitrate was associated with a reduction in all-cause mortality compared to both placebo and prazosin that was of borderline statistical significance (P = .053). In V-HeFT II, the combination of hydralazine and isosorbide dinitrate was compared with enalapril in a population similar to V-HeFT I. All- cause mortality was 28% lower with enalapril than with the hydralazine isosorbide dinitrate combination. However, quality of life and peak exercise capacity as measured by peak oxygen consumption were better with hydralazine-isosorbide dinitrate.

The African-American Heart Failure Trial (A-HeFT) enrolled 1050 self-identified African-American patients who had NYHA class III or IV HF with dilated ventricles and reduced LVEF. In this placebo-controlled, blinded, and randomized trial, subjects were randomly assigned to receive a fixed combination of isosorbide dinitrate plus hydralazine or placebo in addition to standard therapy for HF.

The primary end point was a composite score made up of weighted values for death from any cause, a first hospitalization for HF, and change in the quality of life. The study was terminated early because of a significantly higher mortality rate in the placebo group than in the group given the fixed combination of isosorbide dinitrate plus hydralazine (10.2% vs 6.2%, P = .02). The mean primary composite score was significantly better in the group given isosorbide dinitrate plus hydralazine than in the placebo group, as were its individual components: 43% reduction in the rate of death from any cause, 33% relative reduction in the rate of first hospitalization for HF, and an improvement in the quality of life. These results taken together constitute a strong recommendation for the addition of the fixed combination of isosorbide dinitrate/hydralazine to the standard medical regimen for HF in African Americans. Data cannot exclude a benefit of the isosorbide dinitrate/hydralazine combination in non-African Americans when added to the standard medical regimen for HF.

p. e171:

The A-HeFT (African-American Heart Failure Trial) confirmed the benefit of hydralazine/isosorbide dinitrate in black HF patients. Importantly, 40% of the A-HeFT cohort were women. An analysis of outcomes by gender in A-HeFT showed that fixed-dose combined hydralazine/ isosorbide dinitrate improved HF outcomes in both men and women. There were no gender differences between men and women in the benefit of hydralazine/isosorbide dinitrate on the primary composite score, time to first HF hospitalization, and event-free survival.

1a.7.8. What harms were studied and how do they affect the net benefit (benefits over harms)?

2013 ACCF/AHA Guideline for the Management of Heart Failure p. e179:

Adherence to this combination has generally been poor because of the large number of tablets required, frequency of administration, and the high incidence of adverse reactions. Frequent adverse effects include headache, dizziness, and gastrointestinal complaints. Nevertheless, the benefit of these drugs can be substantial and warrant a slower titration of the drugs to enhance tolerance of the therapy.

HFSA 2010 Comprehensive Heart Failure Practice Guideline Potential harms were not

addressed in this review of the evidence.

UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE

1a.7.9. If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review.

Two additional analyses from A-HeFT were published after the publication of the 2013 ACCF/AHA Guideline for the Management of Heart Failure.

Note: Text below for description and results is verbatim from the article abstract.

Anand IS, Win S, Rector TS, Cohn JN, Taylor AL. Effect of fixed-dose combination of isosorbide dinitrate and hydralazine on all hospitalizations and on 30-day readmission rates in patients with heart failure: results from the African-American Heart Failure Trial. Circ Heart Fail. 2014;7:759-65. doi: 10.1161/CIRCHEARTFAILURE.114.001360. Epub 2014 Jun 26.

Background: Fixed-dose combination of isosorbide dinitrate and hydralazine (FDC-I/H) reduced mortality by 43% and death or first hospitalization for heart failure (HF) by 37% in the African-American Heart Failure Trial (A-HeFT). Reduction in mortality makes it difficult to determine the effect on hospitalizations unless the analysis adjusts for death as a competing risk.

Methods and Results: In A-HeFT, 1050 self-identified black patients with moderate to severe HF were randomized to FDC-I/H or placebo. The effects of FDC-I/H on first and all hospitalizations and 30-day readmission rates were analyzed. Deaths as competing risks were adjusted using Fine-Gray regression and joint models of hospitalizations and mortality. There were 558 all-cause and 251 HF hospitalizations in placebo compared with 435 and 173 hospitalizations in the FDC-I/H group. Adjusting for deaths as a competing risk, the effect of FDC-I/H on the first hospitalization for HF, expressed in hazard ratio (95% confidence interval), was 0.61 (0.47-0.80; P<0.001) and 0.88 (0.72-1.06; P=0.18) on the first all-cause hospitalization. The effect of FDC-I/H on all recurrent hospitalizations for HF was 0.66 (0.52-0.83; P=0.0005), similar to the effect on the first hospitalizations for HF, whereas the effect on all hospitalizations for any cause was 0.75 (0.63-0.91; P=0.003). The 30-day all-cause readmission rate after the first hospitalization for HF was 23.6% (29 of 123) in placebo versus 14.8% (12 of 81) in the FDC-I/H group, but the effect (0.59; 0.30-1.16; P=0.12) in this small subgroup was not significant.

Conclusions: Treatment with FDC-I/H was associated with a substantial reduction in the first and recurrent HF hospitalizations, and in total all-cause hospitalizations, reducing the total burden of costly and distressing hospitalizations.

McNamara DM, Taylor AL, Tam SW, Worcel M, Yancy CW, Hanley-Yanez K, Cohn JN, Feldman AM. G-protein beta-3 subunit genotype predicts enhanced benefit of fixed-dose isosorbide dinitrate and hydralazine: results of A-HeFT. JACC Heart Fail. 2014;2:551-7. doi: 10.1016/j.jchf.2014.04.016. Epub 2014 Oct 8.

Objectives: The purpose of this study was to evaluate the influence of the guanine nucleotide-binding proteins (G-proteins), beta-3 subunit (GNB3) genotype on the effectiveness of a fixed-dose combination of isosorbide dinitrate

and hydralazine (FDC I/H) in A-HeFT (African American Heart Failure Trial).

Background: GNB3 plays a role in alpha2-adrenergic signaling. A polymorphism (C825T) exists, and the T allele is linked to enhanced alpha-adrenergic tone and is more prevalent in African Americans.

Methods: A total of 350 subjects enrolled in the genetic substudy (GRAHF [Genetic Risk Assessment of Heart Failure in African Americans]) were genotyped for the C825T polymorphism. The impact of FDC I/H on a composite score (CS) that incorporated death, hospital stay for heart failure, and change in quality of life (QoL) and on event-free survival were assessed in GNB3 genotype subsets.

Results: The GRAHF cohort was 60% male, 25% ischemic, 97% New York Heart Association functional class III, age 57 ± 13 years, with a mean qualifying left ventricular ejection fraction of 0.24 ± 0.06. For GNB3 genotype, 184 subjects were TT (53%), 137 (39%) CT, and 29 (8%) were CC. In GNB3 TT subjects,FDC I/H improved the CS (FDC I/H = 0.50 ± 1.6; placebo = -0.11 ± 1.8, p = 0.02), QoL (FDC I/H = 0.69 ± 1.4;
placebo = 0.24 ± 1.5, p = 0.04), and event-free survival (hazard ratio: 0.51, p = 0.047), but not in subjects with the C allele (for CS, FDC I/H = -0.05 ± 1.7; placebo = -0.09 ± 1.7, p = 0.87; for QoL, FDC I/H = 0.28 ± 1.5; placebo = 0.14 ± 1.5, p = 0.56; and for event-free survival, p = 0.35).

Conclusions: The GNB3 TT genotype was associated with greater therapeutic effect of FDC I/H in A-HeFT. The role of the GNB3 genotype for targeting therapy with FDC I/H deserves further study.

Impact on conclusions of systematic review: While additional research on whether use of hydralazine and isosorbide dinitrate is linked to a genetic polymorphism may refine the clinical recommendations, findings in these publications further support the current recommendations and level of evidence ratings for the use of combination therapy in African American patients.

1a.8 OTHER SOURCE OF EVIDENCE

If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.

1a.8.1 What process was used to identify the evidence?

1a.8.2. Provide the citation and summary for each piece of evidence.

1. Evidence, Performance Gap, Priority – Importance to Measure and Report

Extent to which the specific measure focus is evidence-based, important to making significant gains in healthcare quality, and improving health outcomes for a specific high-priority (high-impact) aspect of healthcare where there is variation in or overall less-than-optimal performance. ***Measures must be judged to meet all subcriteria to pass this criterion and be evaluated against the remaining criteria.***

1a. Evidence to Support the Measure Focus – See attached Evidence Submission Form
NMQF_HF_Fixed_Dose_Therapy_evidence_form_final.pdf

1b. Performance Gap

Demonstration of quality problems and opportunity for improvement, i.e., data demonstrating:

- considerable variation, or overall less-than-optimal performance, in the quality of care across providers; and/or
- disparities in care across population groups.

1b.1. Briefly explain the rationale for this measure *(e.g., the benefits or improvements in quality envisioned by use of this measure)*

The African-American Heart Failure Trial (A-HeFT) first published in 2004 demonstrated that there is significant benefit for African American patients who receive the fixed-dose combination therapy of hydralazine and isosorbide dinitrate. A-HeFT built on the findings from the two Vasodilator-Heart Failure Trials (V-HeFT). A-HeFT, which was ended early due to the mortality rates in the placebo population, demonstrated a 43% reduction in mortality, a 33% decrease in initial hospitalizations, and a 50% improvement in patient-reported quality of life (Taylor, 2004; Sharma, 2014). These results clearly demonstrate that the fixed-dose combination therapy significantly improves patient morbidity, mortality and quality of life in this clinical cohort. There is no substitute for the fixed-dose combination therapy.

Even with this strong evidence of unprecedented efficacy and cost-effectiveness, research shows that more than 85% of African American patients are not receiving the quality of care that this therapy affords, constituting a significant gap in care quality (Dickson, 2015). The underuse of the fixed-dose combination of hydralazine plus isosorbide dinitrate in African Americans with severe heart failure is a health care and health quality disparity that exposes these patients to an elevated risk for mortality and hospitalization, and compromises efforts to contain the escalating system costs by preventing or reducing unnecessary hospitalizations and readmissions.

Based upon research on the mortality benefit of the fixed-dose combination (Fonarow, 2011), the National Minority Quality Forum estimates that 51,542 (27%) of the 189,891 African American Medicare beneficiaries who were being treated for heart failure and received their prescription drugs under Part D should have been treated with the fixed-dose combination; but only 2,377 (5%) had at least one prescription (30-day supply) of the therapy. Further, the National Minority Quality Forum estimates that between 2008 and 2010, only 3% of the eligible patient cohort in Medicare received the therapy. Given the documented number to treat to receive the mortality benefit (21), it can be estimated that from 2007 through 2010, 20,000 African American Medicare beneficiaries died as a result of the failure to receive quality care as defined by evidence-based guidelines.

Research continues to explore if the fixed-dose combination of hydralazine and isosorbide dinitrate is linked to a particular genetic polymorphism (NIH funded Genomic Response Analysis of Heart Failure Therapy in African Americans). While we anticipate that the evidence supporting this treatment will be refined over time, the proven benefits to this patient population is significant and there is a clear opportunity for improvement. Failure to do so constitutes a failure to provide quality and cost-effective care.

References:

Dickson VV, Knafl GJ, Wald J, Riegel B. Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure. J Am Heart Assoc. 2015;4:1-13.
Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161:1024-1030.
Sharma A, Colvin-Adams M, Yancy CW. Heart failure in African Americans: disparities can be overcome. Cleve Clin J Med. 2014;81:301-11.
Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004; 351:2049–57.

1b.2. Provide performance scores on the measure as specified (current and over time) at the specified level of analysis. *(This is required for endorsement maintenance. Include mean, std dev, min, max, interquartile range, scores by decile. Describe the data source including number of measured entities; number of patients; dates of data; if a sample, characteristics of the entities included). This information also will be used to address the subcriterion on improvement (4b.1) under Usability and Use.*
NMQF partnered with three organizations to test this measure.

Dataset 1:
A clinical registry that contains data from approximately 30 different electronic health records systems (EHRs), covering over 500 sites or practices throughout the southeast, and representing in excess of 3 million patients. We received an extract of their EHR that includes all patients meeting the denominator criteria for the measure. We used calendar year 2014 for this dataset. The dataset included 6,384 patients with 1,415 clinicians across 321 sites.

Dataset 2:
A network of federally-qualified and community health centers in the Midwest. We received an extract of their EHR (GE Centricity) that included all patients meeting the denominator criteria for the measure. In addition, we manually reviewed 98 randomly selected charts for patients in this EHR subset of patients. We used calendar year 2015 for this dataset. The dataset included 145 patients across 14 sites.

Dataset 3:
An integrated inpatient and outpatient delivery system in the South. We received an extract from their EHR (Epic) of all patients meeting the denominator criteria for the measure. In addition, we used a simple random sample of 100 patients identified in the EHR for a manual abstraction of the patient chart data for the elements required for the measure. We used calendar year 2015 for this dataset. The dataset included 3,018 patients with 825 clinicians across 10 sites.

Dataset 1:
Sum 1.6%
Min 0.0%
Avg 1.1%
Max 33.3%

Dataset 2:
Sum 0.7%
Min 0.0%
Avg 0.4%
Max 5.0%

Dataset 3:
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

1b.3. If no or limited performance data on the measure as specified is reported in 1b2, then provide a summary of data from the literature that indicates opportunity for improvement or overall less than optimal performance on the specific focus of measurement.
Several analyses on whether eligible patients are receiving the hydralazine and isosorbide dinitrate combination therapy as supported by current evidence have been published. All demonstrate the existence of a significant opportunity for improvement both in the ambulatory setting and at the time of discharge from a hospital.

- A secondary analysis of data identified that more than 85% of African American patients were not receiving the combination therapy (Dickson, 2015).
- An observational analysis of data from the Get With the Guidelines-Heart Failure Registry showed that just over 22% of African American patients were discharged from the hospital with a prescription for the combination therapy. Rates did increase from 16% to 24% over four years (Golwala, 2013).

- A post hoc retrospective analysis conducted by Fonarow and colleagues using data from IMPROVE HF and Get with the Guidelines registry identified that only 7.3% of African American patients received the recommended combination therapy of hydralazine and isosorbide dinitrate (Fonarow, 2011).
- Rates are similarly low in the outpatient setting with the IMPROVE-HF, a prospective cohort study, showing that only 7.3% of patients received hydralazine and isosorbide dinitrate (Yancy, 2010).
- Only 4.5% of African American patients with HF and LVSD included in the OPTIMIZE-HF registry received the combination therapy (Yancy, 2008).

References:

Dickson VV, Knafl GJ, Wald J, Riegel B. Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure. J Am Heart Assoc. 2015;4:1-13.
Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161:1024-1030.
Golwala HB, et al. Use of hydralazine-isosorbide dinitrate combination in African American and other race/ethnic group patients with heart failure and reduced left ventricular ejection fraction. J Am Heart Assoc. 2013;2:e000214. doi: 10.1161/JAHA.113.000214.
Yancy CW, Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, McBride ML, Mehra MR, O´Connor CM, Reynolds D, Walsh MN. Adherence to guideline-recommended adjunctive heart failure therapies among outpatient cardiology practices (findings from IMPROVE HF). Am J Cardiol. 2010;105:255–260.
Yancy CW, Abraham WT, Albert NM, Clare R, Stough WG, Gheorghiade M, Greenberg BH, O´Connor CM, She L, Sun JL, Young JB, Fonarow GC. Quality of care of and outcomes for African Americans hospitalized with heart failure: findings from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol. 2008;51:1675–1684.

1b.4. **Provide disparities data from the measure as specified (current and over time) by population group, e.g., by race/ethnicity, gender, age, insurance status, socioeconomic status, and/or disability.** *(This is required for endorsement maintenance. Describe the data source including number of measured entities; number of patients; dates of data; if a sample, characteristics of the entities include.) This information also will be used to address the subcriterion on improvement (4b.1) under Usability and Use.*
NMQF partnered with three organizations to test this measure.

Dataset 1:
A clinical registry that contains data from approximately 30 different electronic health records systems (EHRs), covering over 500 sites or practices throughout the southeast, and representing in excess of 3 million patients. We received an extract of their EHR that includes all patients meeting the denominator criteria for the measure. We used calendar year 2014 for this dataset. The dataset included 6,384 patients with 1,415 clinicians across 321 sites.

Dataset 2:
A network of federally-qualified and community health centers in the Midwest. We received an extract of their EHR (GE Centricity) that included all patients meeting the denominator criteria for the measure. In addition, we manually reviewed 98 randomly selected charts for patients in this EHR subset of patients. We used calendar year 2015 for this dataset. The dataset included 145 patients across 14 sites.

Dataset 3:
An integrated inpatient and outpatient delivery system in the South. We received an extract from their EHR (Epic) of all patients meeting the denominator criteria for the measure. In addition, we used a simple random sample of 100 patients identified in the EHR for a manual abstraction of the patient chart data for the elements required for the measure. We used calendar year 2015 for this dataset. The dataset included 3,018 patients with 825 clinicians across 10 sites.

Since this measure specifically focuses on patients who self-identify as African American or Black, data is only provided by age and gender.

Dataset 1:

Female 18-45
Sum 3.0%
Min 0.0%
Avg 1.0%
Max 50.0%

Female 45-65
Sum 1.8%
Min 0.0%
Avg 2.6%
Max 100.0%

Female 65+
Sum 1.3%
Min 0.0%
Avg 0.3%
Max 33.3%

Male 18-45
Sum 1.3%
Min 0.0%
Avg 1.7%
Max 100.0%

Male 45-65
Sum 1.4%
Min 0.0%
Avg 1.4%
Max 50.0%

Male 65+
Sum 1.5%
Min 0.0%
Avg 1.3%
Max 100.0%

Dataset 2:

Female 18-45
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Female 45-65
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Female 65+
Sum 0.0%
Min 0.0%
Avg 0.0%

Max 0.0%

Male 18-45
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Male 45-65
Sum 2.0%
Min 0.0%
Avg 1.1%
Max 11.1%

Male 65+
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Dataset 3:

Female 18-45
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Female 45-65
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Female 65+
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Male 18-45
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Male 45-65
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

Male 65+
Sum 0.0%

Min 0.0%
Avg 0.0%
Max 0.0%

1b.5. If no or limited data on disparities from the measure as specified is reported in 1b4, then provide a summary of data from the literature that addresses disparities in care on the specific focus of measurement. Include citations.

Heart failure is a major public health burden in the United States that disproportionately affects African Americans, who have not experienced the same benefit from treatment as white patients have. More than 5 million people = 20 years of age in the United States have heart failure, with 550,000 new cases of heart failure diagnosed each year. In the US, heart failure affects about 3% of the African American populations; whereas this rate is about 2% in the general population (Ferdinand, 2014). According to the American Heart Association heart disease and stroke statistics 2014 update, annual rates per 1,000 population of new heart failure events are 16.9 and 25.5 for Black men aged 65-74 and 75-84, respectively; and 14.2 and 25.5 for Black women aged 65-74 and 75-84, respectively (Go, 2014).

Heart failure is more prevalent in African Americans than in whites, occurs earlier, imposes higher rates of death and morbidity, and has a more malignant course. Much of the disparity can be assigned to modifiable risk factors such as uncontrolled hypertension and on suboptimal health care. Therefore, when African Americans are treated according to guidelines, discrepant outcomes can be minimized (Sharma, 2014). According to American Heart Association statistics, the annual incidence of heart failure in whites is approximately 6 per 1,000 person-years, while in African Americans it is 9.1 per 1,000 person years. In the Atherosclerosis Risk in Communities Study, the incidence of new heart failure as 1.0 per 1,000 person-years in Chinese Americans, 2.4 in whites, 3.5 in Hispanics, and 4.6 in African Americans. Moreover, when hospitalized for heart failure, African Americans have a 45% greater risk of death or decline in functional status than whites. In the Women's Health Initiative — a 15-year study initiated by the National Institutes of Health in 1991 — African American women had higher rates of heart failure than white women, possibly linked to higher rates of diabetes (Sharma, 2014).

This measure specifically targets Black or African American patients with heart failure and left ventricular systolic dysfunction where a specific therapy is supported by evidence-based guidelines. For this reason, the data provided here are identical to 1b.3.

Several published analyses on whether eligible patients are receiving the hydralazine and isosorbide dinitrate combination therapy as supported by current evidence are highlighted below. All demonstrate the existence of a significant opportunity for improvement both in the ambulatory setting and at the time of discharge from a hospital.

- A secondary analysis of data identified that more than 85% of African American patients were not receiving the combination therapy (Dickson, 2015).
- An observational analysis of data from the Get With the Guidelines-Heart Failure Registry showed that just over 22% of African American patients were discharged from the hospital with a prescription for the combination therapy. Rates did increase from 16% to 24% over four years (Golwala, 2013).
- A post hoc retrospective analysis conducted by Fonarow and colleagues using data from IMPROVE HF and Get with the Guidelines registry identified that only 7.3% of African American patients received the recommended combination therapy of hydralazine and isosorbide dinitrate (Fonarow, 2011).
- Rates are similarly low in the outpatient setting with the IMPROVE-HF, a prospective cohort study, showing that only 7.3% of patients received hydralazine and isosorbide dinitrate (Yancy, 2010).
- Only 4.5% of African American patients with HF and LVSD included in the OPTIMIZE-HF registry received the combination therapy (Yancy, 2008).

References:

Dickson VV, Knafl GJ, Wald J, Riegel B. Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure. J Am Heart Assoc. 2015; 4:1-13.
Ferdinand K. Customizing therapy for African Americans with Heart Failure: Improving Outcomes and Reducing Readmissions. A CME-certified Grand Rounds Activity. Rockpoint 2014.
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Go AS, et al. Heart Disease and Stroke Statistics—2014 Update: A Report From the American Heart Association Statistics committee and Stroke Statistics Subcommittee. Circulation. 2014;129:e28–e292.
Sharma A, Colvin-Adams M, Yancy CW. Heart failure in African Americans: Disparities can be overcome. Cleveland Clinic Journal of Medicine. 2014; 81:301-311.
Yancy CW, Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, McBride ML, Mehra MR, O´Connor CM, Reynolds D, Walsh MN. Adherence to guideline-recommended adjunctive heart failure therapies among outpatient cardiology practices (findings from IMPROVE HF). Am J Cardiol. 2010;105:255–260.
Yancy CW, Abraham WT, Albert NM, Clare R, Stough WG, Gheorghiade M, Greenberg BH, O´Connor CM, She L, Sun JL, Young JB, Fonarow GC. Quality of care of and outcomes for African Americans hospitalized with heart failure: findings from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol. 2008;51:1675–1684.

1c. High Priority (previously referred to as High Impact)

The measure addresses:

- a specific national health goal/priority identified by DHHS or the National Priorities Partnership convened by NQF; OR
- a demonstrated high-priority (high-impact) aspect of healthcare (e.g., affects large numbers of patients and/or has a substantial impact for a smaller population; leading cause of morbidity/mortality; high resource use (current and/or future); severity of illness; and severity of patient/societal consequences of poor quality).

1c.1. **Demonstrated high priority aspect of healthcare**

A leading cause of morbidity/mortality, Patient/societal consequences of poor quality, Severity of illness

1c.2. **If Other:**

1c.3. **Provide epidemiologic or resource use data that demonstrates the measure addresses a high priority aspect of healthcare. List citations in 1c.4.**

This measure specifically relates to the National Quality Strategy (NQS) priority area of Effective Clinical Care: Promoting the most effective prevention and treatment practices for the leading causes of mortality, starting with cardiovascular disease.

Heart failure is a major public health burden in the United States that disproportionately affects African Americans, who have not experienced the same benefit from treatment as white patients have.

- More than 5 million people = 20 years of age in the United States have heart failure, with 550,000 new cases of heart failure diagnosed each year (Ferdinand, 2014).
- In the US, heart failure affects about 3% of the African American populations; whereas, this rate is about 2% in the general population (Ferdinand, 2014).
- According to the American Heart Association (AHA) heart disease and stroke statistics 2014 update, annual rates per 1,000 population of new heart failure events are 16.9 and 25.5 for Black men aged 65-74 and 75-84, respectively; and 14.2 and 25.5 for Black women aged 65-74 and 75-84, respectively (Go, 2014).

Heart failure is more prevalent in African Americans than in whites, occurs earlier, imposes higher rates of death and morbidity, and has a more malignant course. Much of the disparity can be assigned to modifiable risk factors such as uncontrolled hypertension and on suboptimal health care. Therefore, when African Americans are treated according to guidelines, discrepant outcomes can be minimized (Sharma, 2014).

- According to AHA statistics, the annual incidence of heart failure in whites is approximately 6 per 1,000 person-years, while in African Americans it is 9.1 per 1,000 person years.
- In the Atherosclerosis Risk in Communities Study, the incidence of new heart failure as 1.0 per 1,000 person-years in Chinese Americans, 2.4 in whites, 3.5 in Hispanics, and 4.6 in African Americans. Moreover, when hospitalized for heart failure, African Americans have a 45% greater risk of death or decline in functional status than whites.
- In the Women's Health Initiative — a 15-year study initiated by the National Institutes of Health in 1991 — African American women had higher rates of heart failure than white women, possibly linked to higher rates of diabetes (Sharma, 2014).

The African-American Heart Failure Trial (A-HeFT) first published in 2004 demonstrated that there is significant benefit for African American patients who receive the fixed-dose combination therapy of hydralazine and isosorbide dinitrate. A-HeFT built on the findings from the two Vasodilator-Heart Failure Trials (V-HeFT). A-HeFT, which was ended early due to the mortality rates in the placebo population, demonstrated a 43% reduction in mortality, a 33% decrease in initial hospitalizations, and a 50% improvement in patient-reported quality of life (Taylor, 2004; Sharma, 2014). These results clearly demonstrate that the fixed-dose combination therapy significantly improves patient morbidity, mortality and quality of life in this clinical cohort. There is no substitute for the fixed-dose combination therapy.

Based upon research on the mortality benefit of the fixed-dose combination (Fonarow, 2011), the National Minority Quality Forum estimates that 51,542 (27%) of the 189,891 African American Medicare beneficiaries who were being treated for heart failure and received their prescription drugs under Part D should have been treated with the fixed-dose combination; but only 2,377 (5%) had at least one prescription (30-day supply) of the therapy. Further, the National Minority Quality Forum estimates that between 2008 and 2010, only 3% of the eligible patient cohort in Medicare received the therapy. Given the documented number to treat to receive the mortality benefit (21), it can be estimated that from 2007 through 2010, 20,000 African American Medicare beneficiaries died as a result of the failure to receive quality care as defined by evidence-based guidelines.

1c.4. **Citations for data demonstrating high priority provided in 1a.3**
References:

Ferdinand K. Customizing therapy for African Americans with Heart Failure: Improving Outcomes and Reducing Readmissions. A CME-certified Grand Rounds Activity. Rockpoint 2014.
Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161:1024-1030.
Go AS, et al. Heart Disease and Stroke Statistics—2014 Update: A Report From the American Heart Association Statistics committee and Stroke Statistics Subcommittee. Circulation. 2014;129:e28–e292.
Sharma A, Colvin-Adams M, Yancy CW. Heart failure in African Americans: Disparities can be overcome. Cleveland Clinic Journal of Medicine. 2014; 81:301-311.
Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004; 351:2049–57.

1c.5. **If a PRO-PM (e.g. HRQoL/functional status, symptom/burden, experience with care, health-related behaviors), provide evidence that the target population values the measured PRO and finds it meaningful.** *(Describe how and from whom their input was obtained.)*
Not applicable

2. Reliability and Validity—Scientific Acceptability of Measure Properties

Extent to which the measure, as specified, produces consistent (reliable) and credible (valid) results about the quality of care when implemented. ***Measures must be judged to meet the subcriteria for both reliability and validity to pass this criterion and be evaluated against the remaining criteria.***

2a.1. Specifications The measure is well defined and precisely specified so it can be implemented consistently within and across organizations and allows for comparability. eMeasures should be specified in the Health Quality Measures Format (HQMF) and the Quality Data Model (QDM).

De.5. **Subject/Topic Area** *(check all the areas that apply):*
Cardiovascular : Congestive Heart Failure

De.6. **Cross Cutting Areas** *(check all the areas that apply):*
«crosscutting_area»

S.1. **Measure-specific Web Page** *(Provide a URL link to a web page specific for this measure that contains current detailed specifications including code lists, risk model details, and supplemental materials. Do not enter a URL linking to a home page or to general information.)*
http://heartfailurequalityimprovementinitiative.com/performance-measures/

S.2a. **If this is an eMeasure**, HQMF specifications must be attached. Attach the zipped output from the eMeasure authoring tool (MAT) - if the MAT was not used, contact staff. (Use the specification fields in this online form for the plain-language description of the specifications)
This is an eMeasure **Attachment:** NMQF_fixed_dose_thrpy_Bonnie_test_data-636166310861108000.zip,3.28.16_nmqf_fixed_dose_thrpy_032916.zip

S.2b. **Data Dictionary, Code Table, or Value Sets** *(and risk model codes and coefficients when applicable) must be attached. (Excel or csv file in the suggested format preferred - if not, contact staff)*
Attachment **Attachment:** nmqf_fixed_dose_thrpy_value_sets_032916.xls

S.3. **For endorsement maintenance**, please briefly describe any changes to the measure specifications since last endorsement date and explain the reasons.
Not applicable

S.4. **Numerator Statement** *(Brief, narrative description of the measure focus or what is being measured about the target population, i.e., cases from the target population with the target process, condition, event, or outcome)*
IF an OUTCOME MEASURE, state the outcome being measured. Calculation of the risk-adjusted outcome should be described in the calculation algorithm.
Patients prescribed a fixed-dose combination of hydralazine and isosorbide dinitrate seen for an office visit in the measurement period in the outpatient setting or at each hospital discharge

S.5. **Time Period for Data** *(What is the time period in which data will be aggregated for the measure, e.g., 12 mo, 3 years, look back to August for flu vaccination? Note if there are different time periods for the numerator and denominator.)*
Measurement period (12 months)

S.6. **Numerator Details** *(All information required to identify and calculate the cases from the target population with the target process, condition, event, or outcome such as definitions, specific data collection items/responses, code/value sets – Note: lists of individual codes with descriptors that exceed 1 page should be provided in an Excel or csv file in required format at S.2b)*
IF an OUTCOME MEASURE, describe how the observed outcome is identified/counted. Calculation of the risk-adjusted outcome should be described in the calculation algorithm.
The following data element is used to calculate the numerator:
1. Fixed-dose combination of hydralazine and isosorbide dinitrate prescription

Logic for calculating the numerator is included in the eMeasure specification.

Value sets used:
Fixed dose combination of hydralazine and isosorbide dinitrate (2.16.840.1.113762.1.4.1124.15)

S.7. **Denominator Statement** *(Brief, narrative description of the target population being measured)*
All patients aged 18 years and older with a diagnosis of heart failure with a current or prior EF <40% who are self-identified Black or African Americans and receiving ACEI or ARB and Beta-blocker therapy

S.8. **Target Population Category** *(Check all the populations for which the measure is specified and tested if any):*
Elderly, Populations at Risk

S.9. **Denominator Details** *(All information required to identify and calculate the target population/denominator such as definitions, specific data collection items/responses , code/value sets – Note: lists of individual codes with descriptors that exceed 1 page should be provided in an Excel or csv file in required format at S.2b)*
The following data elements are used to calculate the denominator:

1. Diagnosis of heart failure
2. Ejection Fraction <40% or diagnosis of left ventricular systolic dysfunction
3. Self-identified as Black or African American
4. ACEI or ARB therapy
5. Beta-blocker therapy
6. Office visit
7. Hospital Discharge

Logic for calculating the denominator is included in the eMeasure specification.

Value sets used:
Heart Failure (2.16.840.1.113883.3.526.2.23, 2.16.840.1.113883.3.526.2.24, 2.16.840.1.113883.3.526.2.25, 2.16.840.1.113883.3.526.3.376)
Left Ventricular Systolic Dysfunction (2.16.840.1.113883.3.526.2.859, 2.16.840.1.113883.3.526.3.1091)
Moderate or Severe LVSD (2.16.840.1.113883.3.526.2.861, 2.16.840.1.113883.3.526.3.1090)
Ejection Fraction (2.16.840.1.113883.3.526.2.1238, 2.16.840.1.113883.3.526.3.1134)
Moderate or Severe (2.16.840.1.113883.3.526.3.1092)
Care Services in Long-Term Residential Facility (2.16.840.1.113883.3.464.1003.101.11.1070, 2.16.840.1.113883.3.464.1003.101.12.1014)
Self identified as Black or African American (2.16.840.1.113762.1.4.1124.1)
Discharge Services - Hospital Inpatient (2.16.840.1.113883.3.464.1003.101.11.1035, 2.16.840.1.113883.3.464.1003.101.12.1007)
Face-to-Face Interaction (2.16.840.1.113883.3.464.1003.101.11.1216, 2.16.840.1.113883.3.464.1003.101.12.1048)
Home Healthcare Services (2.16.840.1.113883.3.464.1003.101.11.1080, 2.16.840.1.113883.3.464.1003.101.12.1016)
Nursing Facility Visit (2.16.840.1.113883.3.464.1003.101.11.1060, 2.16.840.1.113883.3.464.1003.101.12.1012)
Office Visit (2.16.840.1.113883.3.464.1003.101.11.1005, 2.16.840.1.113883.3.464.1003.101.12.1001)
Outpatient Consultation (2.16.840.1.113883.3.464.1003.101.11.1040, 2.16.840.1.113883.3.464.1003.101.12.1008)
Patient provider interaction (2.16.840.1.113883.3.526.2.1049, 2.16.840.1.113883.3.526.3.1012)
ACE Inhibitor or ARB (2.16.840.1.113883.3.526.2.39, 2.16.840.1.113883.3.526.3.1139)
Beta Blocker Therapy for LVSD (2.16.840.1.113883.3.526.2.133, 2.16.840.1.113883.3.526.3.1174)

S.10. **Denominator Exclusions** *(Brief narrative description of exclusions from the target population)*
Denominator exclusions include:
- Hypotension (severe or symptomatic)
- Severe lupus erythematosus
- Unstable angina
- Peripheral neuritis
- Patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors

S.11. **Denominator Exclusion Details** *(All information required to identify and calculate exclusions from the denominator such as definitions, specific data collection items/responses, code/value sets – Note: lists of individual codes with descriptors that exceed 1 page should be provided in an Excel or csv file in required format at S.2b)*
The following data elements are used to calculate the denominator exclusions:
1. Hypotension (severe or symptomatic)
2. Severe lupus erythematosus
3. Unstable angina
4. Peripheral neuritis
5. Patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors

Logic for calculating the denominator exclusions are included in the eMeasure specification.

Value sets used:
Hypotension (2.16.840.1.113883.3.526.2.175, 2.16.840.1.113883.3.526.2.180, 2.16.840.1.113883.3.526.2.185, 2.16.840.1.113883.3.526.3.370)

Lupus erythematosus (2.16.840.1.113762.1.4.1124.9, 2.16.840.1.113762.1.4.1124.10, 2.16.840.1.113762.1.4.1124.11, 2.16.840.1.113762.1.4.1124.12)
Unstable angina (2.16.840.1.113762.1.4.1124.16, 2.16.840.1.113762.1.4.1124.17, 2.16.840.1.113762.1.4.1124.18)
Peripheral neuritis (2.16.840.1.113762.1.4.1124.4, 2.16.840.1.113762.1.4.1124.5, 2.16.840.1.113762.1.4.1124.6, 2.16.840.1.113762.1.4.1124.7)
Patient actively taking Phosphodiesterase Type 5 (PDE5) Inhibitors (2.16.840.1.113762.1.4.1124.14)
Severe (2.16.840.1.113762.1.4.1124.19)
Symptomatic (2.16.840.1.113762.1.4.1124.20)

S.12. **Stratification Details/Variables** *(All information required to stratify the measure results including the stratification variables, definitions, specific data collection items/responses, code/value sets – Note: lists of individual codes with descriptors that exceed 1 page should be provided in an Excel or csv file in required format with at S.2b)*
Not applicable

S.13. **Risk Adjustment Type** (Select type. Provide specifications for risk stratification in S.12 and for statistical model in S.14-15)
No risk adjustment or risk stratification
If other:

S.14. **Identify the statistical risk model method and variables** *(Name the statistical method - e.g., logistic regression and list all the risk factor variables. Note - risk model development and testing should be addressed with measure testing under Scientific Acceptability)*
Not applicable

S.15. **Detailed risk model specifications** *(must be in attached data dictionary/code list Excel or csv file. Also indicate if available at measure-specific URL identified in S.1.)*
Note: Risk model details (including coefficients, equations, codes with descriptors, definitions), should be provided on a separate worksheet in the suggested format in the Excel or csv file with data dictionary/code lists at S.2b.

S.15a. **Detailed risk model specifications** (*if not provided in excel or csv file at S.2b*)
Not applicable

S.16. **Type of score:**
Rate/proportion
If other:

S.17. **Interpretation of Score** *(Classifies interpretation of score according to whether better quality is associated with a higher score, a lower score, a score falling within a defined interval, or a passing score)*
Better quality = Higher score

S.18. **Calculation Algorithm/Measure Logic** *(Describe the calculation of the measure score as an ordered sequence of steps including identifying the target population; exclusions; cases meeting the target process, condition, event, or outcome; aggregating data; risk adjustment; etc.)*
The measure logic is provided in the eMeasure specification.

Performance is calculated as:

1. Identify the initial patient population for the measure.
2. From those patients in the initial patient population, identify those that meet the denominator criteria.
3. From the patients who qualify for the denominator, identify those who meet the numerator criteria.
4. Identify those patients who did not meet the numerator criteria and determine whether an appropriate exclusion is documented.
5. Remove those patients with an exclusion from the denominator.
6. Calculation: Numerator/Denominator-Denominator Exclusions

S.19. **Calculation Algorithm/Measure Logic Diagram URL or Attachment** *(You also may provide a diagram of the Calculation Algorithm/Measure Logic described above at measure-specific Web page URL identified in S.1 OR in attached appendix at A.1)*
No diagram provided

S.20. **Sampling** *(If measure is based on a sample, provide instructions for obtaining the sample and guidance on minimum sample size.)*
IF a PRO-PM, identify whether (and how) proxy responses are allowed.
Not applicable

S.21. **Survey/Patient-reported data** *(If measure is based on a survey, provide instructions for conducting the survey and guidance on minimum response rate.)*
IF a PRO-PM, specify calculation of response rates to be reported with performance measure results.
Not applicable

S.22. **Missing data** (specify how missing data are handled, e.g., imputation, delete case.)
Required for Composites and PRO-PMs.
This measure is specified with specific criteria, data elements and value sets. If a patient record does not include one or more of these components for the initial patient population or denominator, then patients are not considered eligible for the measure and not included.

If data to determine whether a patient should be considered for the numerator or exclusions is missing, then the numerator or exclusions not considered to be met and the provider will not get credit for meeting performance for that patient.

S.23. **Data Source** *(Check ONLY the sources for which the measure is SPECIFIED AND TESTED).*
If other, please describe in S.24.
Electronic Health Record (Only), Registry

S.24. **Data Source or Collection Instrument** *(Identify the specific data source/data collection instrument e.g. name of database, clinical registry, collection instrument, etc.)*
IF a PRO-PM, identify the specific PROM(s); and standard methods, modes, and languages of administration.
Not applicable

S.25. **Data Source or Collection Instrument** *(available at measure-specific Web page URL identified in S.1 OR in attached appendix at A.1)*
No data collection instrument provided

S.26. **Level of Analysis** *(Check ONLY the levels of analysis for which the measure is SPECIFIED AND TESTED)*
Clinician : Group/Practice, Clinician : Individual

S.27. **Care Setting** *(Check ONLY the settings for which the measure is SPECIFIED AND TESTED)*
Clinician Office/Clinic, Hospital
If other:

S.28. **COMPOSITE Performance Measure** - Additional Specifications *(Use this section as needed for aggregation and weighting rules, or calculation of individual performance measures if not individually endorsed.)*
Not applicable

2a. Reliability – See attached Measure Testing Submission Form
2b. Validity – See attached Measure Testing Submission Form
Measure_2764_Testing_Attachment_NMQF_submission_to_NQF_09-16-2016_final.pdf

Measure Number (*if previously endorsed*)**:** 2764

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

Date of Submission: 9/16/2016

Type of Measure:

☐ Composite – ***STOP – use composite testing form***	☐ Outcome (*including PRO-PM*)
☐ Cost/resource	☒ Process
☐ Efficiency	☐ Structure

Instructions

- Measures must be tested for all the data sources and levels of analyses that are specified. ***If there is more than one set of data specifications or more than one level of analysis, contact NQF staff*** about how to present all the testing information in one form.
- **For all measures, sections 1, 2a2, 2b2, 2b3, and 2b5 must be completed.**
- **For outcome and resource use measures**, section **2b4** also must be completed.
- If specified for **multiple data sources/sets of specificaitons** (e.g., claims and EHRs), section **2b6** also must be completed.
- Respond to all questions as instructed with answers immediately following the question. All information on testing to demonstrate meeting the subcriteria for reliability (2a2) and validity (2b2-2b6) must be in this form. An appendix for *supplemental* materials may be submitted, but there is no guarantee it will be reviewed.
- If you are unable to check a box, please highlight or shade the box for your response.
- Maximum of 20 pages (*incuding questions/instructions;* minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.***
- Contact NQF staff regarding questions. Check for resources at Submitting Standards webpage.
- For information on the most updated guidance on how to address sociodemographic variables and testing in

Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the testing results for this measure meet NQF's evaluation criteria for testing.

2a2. Reliability testing [10] demonstrates the measure data elements are repeatable, producing the same results a high proportion of the time when assessed in the same population in the same time period and/or that the measure score is precise. For **PRO-PMs and composite performance measures**, reliability should be demonstrated for the computed performance score.

2b2. Validity testing [11] demonstrates that the measure data elements are correct and/or the measure score correctly reflects the quality of care provided, adequately identifying differences in quality. For **PRO-PMs and composite performance measures**, validity should be demonstrated for the computed performance score.

2b3. Exclusions are supported by the clinical evidence; otherwise, they are supported by evidence of sufficient

Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the testing results for this measure meet NQF's evaluation criteria for testing.

2a2. Reliability testing [10] demonstrates the measure data elements are repeatable, producing the same results a high proportion of the time when assessed in the same population in the same time period and/or that the measure score is precise. For **PRO-PMs and composite performance measures**, reliability should be demonstrated for the computed performance score.

2b2. Validity testing [11] demonstrates that the measure data elements are correct and/or the measure score correctly reflects the quality of care provided, adequately identifying differences in quality. For **PRO-PMs and composite performance measures**, validity should be demonstrated for the computed performance score.

2b3. Exclusions are supported by the clinical evidence; otherwise, they are supported by evidence of sufficient

exclusion impacts performance on the measure; in such cases, the measure must be specified so that the information about patient preference and the effect on the measure is transparent (e.g., numerator category computed separately, denominator exclusion category computed separately).[13]

2b4. For outcome measures and other measures when indicated (e.g., resource use):

- **an evidence-based risk-adjustment strategy** (e.g., risk models, risk stratification) is specified; is based on patient factors (including clinical and sociodemographic factors) that influence the measured outcome and are present at start of care; [14,15] and has demonstrated adequate discrimination and calibration

OR

- rationale/data support no risk adjustment/ stratification.

2b5. Data analysis of computed measure scores demonstrates that methods for scoring and analysis of the specified measure allow for **identification of statistically significant and practically/clinically meaningful** [16] **differences in performance**;

OR

there is evidence of overall less-than-optimal performance.

2b6. If multiple data sources/methods are specified, there is demonstration they produce comparable results.

2b7. For **eMeasures, composites, and PRO-PMs** (or other measures susceptible to missing data), analyses identify the extent and distribution of missing data (or nonresponse) and demonstrate that performance results are not biased due to systematic missing data (or differences between responders and nonresponders) and how the specified handling of missing data minimizes bias.

Notes

10. Reliability testing applies to both the data elements and computed measure score. Examples of reliability testing for data elements include, but are not limited to: inter-rater/abstractor or intra-rater/abstractor studies; internal consistency for multi-item scales; test-retest for survey items. Reliability testing of the measure score addresses precision of measurement (e.g., signal-to-noise).

11. Validity testing applies to both the data elements and computed measure score. Validity testing of data elements typically analyzes agreement with another authoritative source of the same information. Examples of validity testing of the measure score include, but are not limited to: testing hypotheses that the measures scores indicate quality of care, e.g., measure scores are different for groups known to have differences in quality assessed by another valid quality measure or method; correlation of measure scores with another valid indicator of quality for the specific topic; or relationship to conceptually related measures (e.g., scores on process measures to scores on outcome measures). Face validity of the measure score as a quality indicator may be adequate if accomplished through a systematic and transparent process, by identified experts, and explicitly addresses whether performance scores resulting from the measure as specified can be used to distinguish good from poor quality.

12. Examples of evidence that an exclusion distorts measure results include, but are not limited to: frequency of occurrence, variability of exclusions across providers, and sensitivity analyses with and without the exclusion.

13. Patient preference is not a clinical exception to eligibility and can be influenced by provider interventions.

14. Risk factors that influence outcomes should not be specified as exclusions

15. With large enough sample sizes, small differences that are statistically significant may or may not be practically or clinically meaningful. The substantive question may be, for example, whether a statistically significant difference of one percentage point in the percentage of patients who received smoking cessation counseling (e.g., 74 percent v. 75 percent) is clinically meaningful; or whether a statistically significant difference of $25 in cost for an episode of care (e.g., $5,000 v. $5,025) is practically meaningful. Measures with overall less-than-optimal performance may not demonstrate much variability across providers.

1. DATA/SAMPLE USED FOR ALL TESTING OF THIS MEASURE

Often the same data are used for all aspects of measure testing. In an effort to eliminate duplication, the first five questions apply to all measure testing. If there are differences by aspect of testing,(e.g., reliability vs. validity) be sure to indicate the specific differences in question 1.7.

1.1. What type of data was used for testing? (*Check all the sources of data identified in the measure specifications and data used for testing the measure. Testing must be provided for all the sources of data specified and intended for measure implementation.* ***If different data sources are used for the numerator and denominator, indicate N [numerator] or D [denominator] after the checkbox.***)

Measure Specified to Use Data From: (*must be consistent with data sources entered in S.23*)	**Measure Tested with Data From:**
☐ abstracted from paper record	☐ abstracted from paper record
☐ administrative claims	☐ administrative claims
☐ clinical database/registry	☒ clinical database/registry [measure score level]
☒ abstracted from electronic health record	☒ abstracted from electronic health record
☒ eMeasure (HQMF) implemented in EHRs	☒ eMeasure (HQMF) implemented in EHRs
☐ other: Click here to describe	☐ other: Click here to describe

1.2. If an existing dataset was used, identify the specific dataset (*the dataset used for testing must be consistent with the measure specifications for target population and healthcare entities being measured; e.g., Medicare Part A claims, Medicaid claims, other commercial insurance, nursing home MDS, home health OASIS, clinical registry*).

NMQF partnered with three organizations to collect data to test this measure.

Dataset 1:
A clinical registry that contains data from approximately 30 different electronic health records systems (EHRs), covering over 500 sites or practices throughout the southeast, and representing in excess of 3 million patients. We received an extract of their EHR that includes all patients meeting the denominator criteria for the measure.

Dataset 2:
A network of federally-qualified and community health centers in the Midwest. We received an extract of their EHR (GE Centricity) that included all patients meeting the denominator criteria for the measure. In addition, we manually reviewed 98 randomly selected charts for patients in this EHR subset of patients.

Dataset 3:
An integrated inpatient and outpatient delivery system in the South. We received an extract from their EHR (Epic) of all patients meeting the denominator criteria for the measure. In addition, we used a simple random sample of 100 patients identified in the EHR for a manual abstraction of the patient chart data for the elements required for the measure.

1.3. What are the dates of the data used in testing?

We used 12 months of performance data at a minimum to be consistent with the measure specifications to identify the patient population for each dataset.

Dataset 1: We used encounters occurring in calendar year 2014. For Dataset 1, we also used data from the prior four years to capture exclusions and confirmation of ejection fraction results (to confirm LVSD).

Datasets 2 and 3:
Data was manually abstracted and compared to electronically extracted data. We elected to use calendar year 2015 data to attempt to take advantage of advances in EHR capture of the required data elements for this measure. We also used a historical look-back period for exclusions and confirmation of ejection fraction results.

1.4. What levels of analysis were tested? (*testing must be provided for all the levels specified and intended for measure implementation, e.g., individual clinician, hospital, health plan*)

Measure Specified to Measure Performance of: (*must be consistent with levels entered in item S.26*)	**Measure Tested at Level of:**
☒ individual clinician	☒ individual clinician
☒ group/practice	☒ group/practice
☐ hospital/facility/agency	☐ hospital/facility/agency
☐ health plan	☐ health plan
☐ other: Click here to describe	☐ other: Click here to describe

1.5. How many and which measured entities were included in the testing and analysis (by level of analysis and data source)? (*identify the number and descriptive characteristics of measured entities included in the analysis (e.g., size, location, type); if a sample was used, describe how entities were selected for inclusion in the sample*)

The data from the three datasets identified in Section 1.2 provided fields that identified patients receiving care from the same site or practice. We interpreted the Sites to represent single practices, and there were varying numbers of identified clinicians within each Site. For our work, a site was considered the element of analysis when looking at the variation across entities. The following table shows the number of patients, clinicians and sites/practices identified for each dataset.

	Patients	Clinicians	Sites
Dataset 1	6,384	1,415	321
Dataset 2	145	Not available*	14
Dataset 3	3,018	825	10

* Dataset 2 did not provide information on the performing clinician.

1.6. How many and which patients were included in the testing and analysis (by level of analysis and data source)? (*identify the number and descriptive characteristics of patients included in the analysis (e.g., age, sex, race, diagnosis); if a sample was used, describe how patients were selected for inclusion in the sample*)

The following table shows the number of patients, clinicians and sites/practices identified for each dataset.

	Patients	Clinicians	Sites
Dataset 1	6,384	1,415	321
Dataset 2	145	Not available*	14
Dataset 3	3,018	825	10

* Dataset 2 did not provide information on the performing clinician.

Patients were included in the dataset based on the following criteria:

- At least 18 years of age
- Self-identified as Black or African American
- Encounter during measurement period
  - (≥ 2) Care Services in Long-Term Residential Facility, Home Healthcare Services, Nursing Facility Visit, Office Visit, Outpatient Consultation, Patient Provider Interaction;
    OR
  - Discharge Services – Hospital Inpatient
- Active diagnosis of heart failure

Each dataset, at a minimum, contained coding to identify a patient's status with respect to the presence or absence of the four denominator inclusion criteria, Heart Failure, the use of Beta Blockers, the presence of LVSD and use of ACE or ARBs. We would note that ejection fraction (EF) values from all three datasets were difficult to obtain given the ongoing challenges with collecting this data in discrete fields in EHRs. Because of this limited data, the testing provided in this document represents patients who are self-identified African American or black with a diagnosis of heart failure who were currently receiving ACE or ARB and beta-blocker therapy. Because a diagnosis of left ventricular systolic dysfunction (LVSD) or an EF <40% is a requirement for prescribing those two medications, if the EF or LVSD value was missing, we assumed that it was present if all of the other inclusion factors were met.

The files were also coded for the use of the fixed-dose combination therapy, diagnoses of lupus erythematosus, hypotension, peripheral neuropathy and the use of PDE5 medications. The data also included patient demographics (age and gender).

The following table shows the distribution, by age and gender, for each of the datasets.

Gender	Age	Dataset 1*		Dataset 2		Dataset 3	
		Number	Percent	Number	Percent	Number	Percent
Female	18-45	312	8.5%	16	26.2%	94	6.2%
	45-65	1,456	39.7%	28	45.9%	697	45.8%
	65+	1,902	51.8%	17	27.9%	730	48.0%
Subtotal		**3,670**		**61**		**1,521**	
Male							
	18-45	315	11.7%	14	16.7%	142	9.5%
	45-65	1,295	48.2%	49	58.3%	852	56.9%
	65+	1,079	40.1%	21	25.0%	503	33.6%
Subtotal		**2,689**		**84**		**1,497**	
TOTAL		**6,359**		**145**		**3,018**	

*Dataset 1 did not provide gender for 25 of the 6,384 patients.

1.7. If there are differences in the data or sample used for different aspects of testing (e.g., reliability, validity, exclusions, risk adjustment), identify how the data or sample are different for each aspect of testing reported below.

Dataset 1: Used for measure score reliability testing (signal-to-noise ratio), exclusions, and performance scores

Datasets 2 and 3: Used for data element reliability testing (inter-rater reliability), data element validity testing (comparison

of the electronic report to the patient record), and exclusions

1.8 What were the patient-level sociodemographic (SDS) variables that were available and analyzed in the data or sample used? For example, patient-reported data (e.g., income, education, language), proxy variables when SDS data are not collected from each patient (e.g. census tract), or patient community characteristics (e.g. percent vacant housing, crime rate).

Not applicable

2a2. RELIABILITY TESTING

***Note**: If accuracy/correctness (validity) of data elements was empirically tested, separate reliability testing of data elements is not required – in 2a2.1 check critical data elements; in 2a2.2 enter "see section 2b2 for validity testing of data elements"; and skip 2a2.3 and 2a2.4.*

2a2.1. What level of reliability testing was conducted? (*may be one or both levels*)

☒ **Critical data elements used in the measure** (*e.g., inter-abstractor reliability; data element reliability must address ALL critical data elements*)

☒ **Performance measure score** (e.g., *signal-to-noise analysis*)

2a2.2. For each level checked above, describe the method of reliability testing and what it tests (*describe the steps—do not just name a method; what type of error does it test; what statistical analysis was used*)

Dataset 1:

We calculated the signal-to-noise ratio to determine the reliability of the fixed dose therapy using the EHR data. Signal-to-noise is calculated as the ratio of variance between sites to the within variance of the site. We use the following guideline for describing reliability (Fleiss, 2003):

Excellent	0.76 – 1.00
Good	0.61 – 0.75
Fair	0.41 – 0.60
Poor	0.00 – 0.40

Reference: Fleiss, J. L., Levin, B. and Paik, M. C. (2003). *Statistical Methods for Rates and Proportions*, Third Edition, John Wiley & Sons, New York.

Datasets 2 and 3:

We calculated inter-rater reliability on a subset of manually abstracted charts during the validity testing (comparison of the electronic report to the gold standard – patient record). For each set of manually abstracted charts, 30 of these charts were re-abstracted by a second nurse reviewer and we calculated the κ statistic of each of the elements where there was less than 100% agreement between the two raters.

2a2.3. For each level of testing checked above, what were the statistical results from reliability testing? (e.*g., percent agreement and kappa for the critical data elements; distribution of reliability statistics from a signal-to-noise analysis*)

Dataset 1:

In this sample, there were 4,692 eligible patients in 303 sites with 73 patients on the fixed-dose combination therapy. The number of patients for which the therapy was appropriate (eligible denominator) varied from 4 or fewer patients for approximately half of the sites. Thirty-three (33) sites had 20 or more patients eligible for the denominator.

To estimate reliability, a "unit" of observation was defined as a site. Sites with more patients provide more "information" about the signal. All sites were used to calculate the "signal", and noise was calculated from all sites, as well as only those sites with 20 or more patients.

The estimate and 95% credible interval for overall reliability is 0.702 (0.184, 0.964) for all sites, regardless of the number of patients.

When only the subset of sites with 20 or more patients was used in the calculation of noise, the estimate is 0.858 (0.433, 0.990).

Datasets 2 and 3:
We calculated inter-rater reliability for 30 patients for each dataset. Below are the κ statistics and confidence intervals for each of the data elements:

	Inpatient encounter	**Heart Failure Diagnosis**	**Fixed-dose therapy in the outpatient setting**	**Fixed-dose therapy in the inpatient setting**
Dataset 2	0.867 (0.69, 1.00)	0.87 (0.62, 1.00)	100% Agreement	0.875 (0.708, 1.00)
Dataset 3	0.933 (0.803, 1.00)	100% Agreement	0.783 (0.374, 1.00)	0.866 (0.687, 1.00)

The remaining elements, for which there was 100% agreement, are:

- Outpatient encounter
- Sex
- Race
- Age
- Ejection Fraction
- ACE/ARB
- Beta-Blocker
- Severe or Symptomatic Hypotension
- Severe Lupus Erythematosus
- Unstable Angina
- Peripheral Neuritis
- PDE5

2a2.4 What is your interpretation of the results in terms of demonstrating reliability? (i.*e., what do the results mean and what are the norms for the test conducted?*)

Dataset 1:

The measure score demonstrated good agreement regardless of sample size and excellent agreement if limited to sites with 20 or more patients. We anticipate that these agreement rates will further improve as additional sites are added and performance scores improve.

Dataset 2:

When adjusting for agreement by chance, the κ statistics show excellent agreement between the two abstractors. The estimates for inpatient encounter, heart failure diagnosis, and fixed-dose therapy in the inpatient setting are somewhat uncertain, but this is likely due to the small number of patients for whom inter-rater reliability rates were calculated. Even with these small numbers, there is good agreement between the two abstractors.

Dataset 3:

Most elements also have 100% (excellent) agreement between the abstractors in this dataset. Inpatient encounter, fixed-dose therapy in the inpatient and outpatient settings have κ statistics, which show
good to excellent agreement. Similar to the findings in Dataset 2, it is likely that this is due to the small number of patient charts abstracted.

2b2. VALIDITY TESTING

2b2.1. What level of validity testing was conducted? (*may be one or both levels*)

☒ **Critical data elements** (*data element validity must address ALL critical data elements*)

☐ **Performance measure score**

☐ **Empirical validity testing**

☐ **Systematic assessment of face validity of performance measure score as an indicator** of quality or resource use (*i.e., is an accurate reflection of performance on quality or resource use and can distinguish good from poor performance*)

2b2.2. For each level of testing checked above, describe the method of validity testing and what it tests (*describe the steps—do not just name a method; what was tested, e.g., accuracy of data elements compared to authoritative source, relationship to another measure as expected; what statistical analysis was used)*

Datasets 2 and 3:

Each testing partner was asked to produce an automated report of patient-level data using the eMeasure specifications (HQMF). We selected a random sample of patients for comparison of the electronically produced data to the gold standard (visual inspection of the medical record). We estimated data element validity by comparing each element in the patient record to the EHR electronic report. We used percent agreement to understand the extent of validity found. We did not provide a κ statistic given the smaller number of charts abstracted. A very small amount of variation between the EHR and the manual abstraction can lead to a κ statistic that is not very useful and provides limited value to understanding the accuracy of the electronically-produced data.

2b2.3. What were the statistical results from validity testing? (*e.g., correlation; t-test*) **Dataset 2:**

For the 98 patients included in the random sample, we calculated the percent agreement comparing each element in the electronic report from the EHR to the manually-abstracted patient charts. For all elements, we included all data in the calculation, regardless of denominator inclusion and exclusion.

	% Agreement
Heart Failure	79
LVSD	63
ACE/ARB	100
Beta Blocker	99
Hypotension	100
Lupus Erythmatosus	100
Unstable Angina	100
Peripheral Neuritis	100
PDE5	100
Fixed Dose	99

Dataset 3:

The same comparison and calculations were completed to compare the EHR and the manual abstracts of patients in the 100 patient random sample.

	% Agreement
Heart Failure	78
LVSD	59
ACE/ARB	89
Beta Blocker	78
Hypotension	99
Lupus Erythmatosus	100
Unstable Angina	99
Peripheral Neuritis	100
PDE5	98
Fixed Dose	100

2b2.4. What is your interpretation of the results in terms of demonstrating validity? (i*.e., what do the results mean and what are the norms for the test conducted?*)

Dataset 2:

The data show good agreement between the EHR and manually abstracted (gold standard) data, indicating high validity for all but two of the elements in the EHR data. LVSD and heart failure show moderate validity in EHR data according to the percent agreement. The disagreements for the heart failure element were typically due to variance in documentation within the medical record (narrative text vs. discrete field). LVSD has historically been a challenge since capture of this element in all electronic measures requires an ejection fraction (EF) value. Few EHR vendors have incorporated EF as a discrete field. Fewer yet are using standard coding. Physician practices and hospitals must identify workflow solutions to ensure that the data are included in a discrete field. The frequency with which the EF value is documented in discrete fields will increase as EHR vendors and providers work together to address the ongoing challenges in collecting this critical data element.

Dataset 3:
Results similar to those of Dataset 2 are seen here with most of the data elements demonstrating high validity. In addition to heart failure and LVSD, abstractors identified some challenges in the documentation of ACE/ARB and beta blocker where medication lists found in hospital discharge instructions were not reconciled in the outpatient record. These findings demonstrate the importance of providers implementing workflows and improving data exchange to ensure that information that is critical for patient care is captured in the patient record.

2b3. EXCLUSIONS ANALYSIS

NA ☐ no exclusions — *skip to section 2b4*

2b3.1. Describe the method of testing exclusions and what it tests (*describe the steps—do not just name a method; what was tested, e.g., whether exclusions affect overall performance scores; what statistical analysis was used*)

The measure is calculated by identifying all patients in the denominator who meet the numerator. For those patients who did not receive the fixed-dose, we then looked to see if there was an appropriate exclusion. If an exclusion is identified, then the patient is removed from the denominator. Using all three datasets, we looked at the denominator exclusion rates to determine frequency and variability across providers. We were unable to complete statistical testing given the generally low exclusion rates.

2b3.2. What were the statistical results from testing exclusions? (*include overall number and percentage of individuals excluded, frequency distribution of exclusions across measured entities, and impact on performance measure scores*)

We summarized the denominator exclusions across all three datasets. Note that Dataset 1 was unable to provide information on the severity of hypotension and lupus diagnoses. As a result, we anticipate that the exclusion rates are overestimated in this dataset.

	Denominator Before Exclusions	Total Number of Exclusions	Exclusion Rate
Dataset 1	6,384	1,675	26.2%
Dataset 2	145	0	0%
Dataset 3	1,547*	0	0%

*Number of patients in Dataset 3 that met all denominator inclusion criteria.

Next, we summarized the exclusion rates in Dataset 1 across the 303 sites. Datasets 2 and 3 did not have exclusions, so additional information cannot be provided.

	Denominator Before Exclusions	Number of Exclusions	Exclusion Rate
Sum	6,384	1,675	26.2%
Min	1	0	0%
Average	19.83	5.2	21.8%
Max	6	6	100%

Here we show the frequency of exclusions in Dataset 1. Note that the exclusions are not mutually exclusive, so the number of exclusions in this table sums to more than 1,675.

Hypotension	PDE5	Lupus Erythematosus	Unstable Angina	Peripheral Neuritis
1,035	608	126	61	4

2b3.3. What is your interpretation of the results in terms of demonstrating that exclusions are needed to prevent unfair distortion of performance results? (*i.e., the value outweighs the burden of increased data collection and analysis. Note: **If patient preference is an exclusion**, the measure must be specified so that the effect on the performance score is transparent, e.g., scores with and without exclusion*)

We were unable to complete statistical testing on the exclusions given the generally low rates. As noted above, we believe that the total number of exclusions provided in Dataset 1 are overestimated given the lack of specificity on the severity of two of the exclusions (hypotension and lupus erythematosus). As the ability to capture the severity of diagnoses improves through implementation of this measure and as performance on the measure increases, we anticipate that the exclusion rates will decrease to better reflect the patient populations for whom prescription of this drug is appropriate.

Even with this data collection limitation, we continue to include these two exclusions to align with the FDA prescribing guidance and support clinician discretion on whether prescribing the medication is appropriate for each individual patient since the calculation first looks to determine if the fixed dose is prescribed and then determines if an exclusion is documented. In addition, the validity testing discussed in section 2b2 demonstrates that there is 100% agreement between the EHR data and the manual abstraction of the patient record for these exclusions. This agreement indicates that the measure can identify those patients for whom fixed dose combination therapy is appropriate or not. Any potential challenges in collecting these data elements, particularly those that require information on the severity of the condition, will be monitored as the measure is implemented.

2b4. RISK ADJUSTMENT/STRATIFICATION FOR OUTCOME OR RESOURCE USE MEASURES

If not an intermediate or health outcome, or PRO-PM, or resource use measure, skip to section 2b5.

2b4.1. What method of controlling for differences in case mix is used?

☒ **No risk adjustment or stratification**

☐ **Statistical risk model with** Click here to enter number of factors **risk factors**
☐ **Stratification by** Click here to enter number of categories **risk categories**
☐ **Other,** Click here to enter description

2b4.2. If an outcome or resource use measure is not risk adjusted or stratified, provide rationale and analyses to demonstrate that controlling for differences in patient characteristics (case mix) is not needed to achieve fair comparisons across measured entities.

Not applicable

2b4.3. Describe the conceptual/clinical and statistical methods and criteria used to select patient factors (clinical factors or sociodemographic factors) used in the statistical risk model or for stratification by risk (*e.g., potential*

factors identified in the literature and/or expert panel; regression analysis; statistical significance of p<0.10; correlation of x or higher; patient factors should be present at the start of care)

Not applicable

2b4.4a. What were the statistical results of the analyses used to select risk factors?

Not applicable

2b4.4b. Describe the analyses and interpretation resulting in the decision to select SDS factors (e.g. prevalence of the factor across measured entities, empirical association with the outcome, contribution of unique variation in the outcome, assessment of between-unit effects and within-unit effects)

Not applicable

2b4.5. Describe the method of testing/analysis used to develop and validate the adequacy of the statistical model or stratification approach (*describe the steps—do not just name a method; what statistical analysis was used*)

Provide the statistical results from testing the approach to controlling for differences in patient characteristics (case mix) below.

If stratified, skip to 2b4.9

Not applicable

2b4.6. Statistical Risk Model Discrimination Statistics (*e.g., c-statistic, R-squared*)**:**

Not applicable

2b4.7. Statistical Risk Model Calibration Statistics (*e.g., Hosmer-Lemeshow statistic*): Not applicable

2b4.8. Statistical Risk Model Calibration – Risk decile plots or calibration curves: Not applicable

2b4.9. Results of Risk Stratification Analysis: Not applicable

2b4.10. What is your interpretation of the results in terms of demonstrating adequacy of controlling

for differences in patient characteristics (case mix)? (i.*e., what do the results mean and what are the norms for the test conducted*)

Not applicable

2b4.11. Optional Additional Testing for Risk Adjustment (*not required, but would provide additional support of adequacy of risk model, e.g., testing of risk model in another data set; sensitivity analysis for missing data; other methods that were assessed*)

Not applicable

2b5. IDENTIFICATION OF STATISTICALLY SIGNIFICANT & MEANINGFUL DIFFERENCES IN PERFORMANCE

2b5.1. Describe the method for determining if statistically significant and clinically/practically meaningful differences in performance measure scores among the measured entities can be identified (*describe the steps—do not just name a method; what statistical analysis was used? Do not just repeat the information provided related to performance gap in 1b)*

We are unable to perform statistical testing of differences due to small sample sizes. We provided the descriptive statistics below, which demonstrate that generally performance is poor across the three datasets and there is significant room for improvement. As this measure is implemented and performance improves, we will conduct further analyses to identify meaningful differences in performance across clinicians and practices.

2b5.2. What were the statistical results from testing the ability to identify statistically significant and/or clinically/practically meaningful differences in performance measure scores across measured entities? (e.g., *number and percentage of entities with scores that were statistically significantly different from mean or some benchmark, different from expected; how was meaningful difference defined*)

Overall performance in each dataset was:

	Fixed Dose Prescribed	Total Patients	Performance Score
Dataset 1:			
Sum	73	4692	1.6%
Min	0	437	0.0%
Avg	0.2	15.7	1.1%
Max	1	3	33.3%
Dataset 2:			
Sum	1	145	0.7%
Min	0	2	0.0%
Avg	0.1	10.4	0.4%

Max	1	20	5.0%
Dataset 3:			
Sum	0.0	1547	0.0%
Min	0.0	2	0.0%
Avg	0.0	171.9	0.0%
Max	0.0	1392	0.0%

We further analyzed performance by age and gender.

Dataset 1:

Gender	Age		Fixed Dose Prescribed	Total Patients	Performance Score
Female	18-45				
		Sum	7	237	3.0%
		Min	0	15	0.0%
		Avg	0.1	2.8	1.0%
		Max	1	2	50.0%
Female	45-65				
		Sum	21	1162	1.8%
		Min	0.0	103.0	0.0%
		Avg	0.1	6.2	2.6%
		Max	1.0	1.0	100.0%
Female	65+				
		Sum	20	1542	1.3%
		Min	0	140	0.0%
		Avg	0.1	7.6	0.3%
		Max	1	3	33.3%
Male	18-45				
		Sum	3	234	1.3%
		Min	0	25	0.0%
		Avg	0.0	3.2	1.7%
		Max	1	1	100.0%
Male	45-65				
		Sum	12	829	1.4%
		Min	0	81	0.0%
		Avg	0.1	5.4	1.4%
		Max	1	2	50.0%
Male	65+				
		Sum	10	688	1.5%
		Min	0	73	0.0%
		Avg	0.1	4.7	1.3%
		Max	1	1	100.0%

Dataset 2:

Gender	Age		Fixed Dose Prescribed	Total Patients	Performance Score
Female	18-45				
		Sum	0	16	0.0%
		Min	0	1	0.0%
		Avg	0	2.7	0.0%
		Max	0	1	0.0%
Female	45-65				
		Sum	0	28	0.0%
		Min	0	5	0.0%
		Avg	0	2.5	0.0%
		Max	0	5	0.0%
Female	65+				
		Sum	0	17	0.0%
		Min	0	2	0.0%
		Avg	0	5.7	0.0%
		Max	0	2	0.0%
Male	18-45				
		Sum	0	14	0.0%
		Min	0	1	0.0%
		Avg	0	2.3	0.0%
		Max	0	1	0.0%
Male	45-65				
		Sum	1	49	2.0%
		Min	0	1	0.0%
		Avg	0.1	4.9	1.1%
		Max	1	9	11.1%
Male	65+				
		Sum	0	21	0.0%
		Min	0	2	0.0%
		Avg	0	3	0.0%
		Max	0	2	0.0%

Dataset 3:

Gender	Age		Fixed Dose Prescribed	Total Patients	Performance Score
Female	18-45				
		Sum	0	36	0.0%
		Min	0	1	0.0%
		Avg	0	7.2	0.0%
		Max	0	30	0.0%
Female	45-65				
		Sum	0	359	0.0%
		Min	0	1	0.0%

	Avg	0	39.9	0.0%
	Max	0	313	0.0%
Female 65+				
	Sum	0	345	0.0%
	Min	0	1	0.0%
	Avg	0	49.3	0.0%
	Max	0	309	0.0%
Male 18-45				
	Sum	0	76	0.0%
	Min	0	1	0.0%
	Avg	0	19	0.0%
	Max	0	71	0.0%
Male 45-65				
	Sum	0	473	0.0%
	Min	0	1	0.0%
	Avg	0	52.6	0.0%
	Max	0	434	0.0%
Male 65+				
	Sum	0	258	0.0%
	Min	0	1	0.0%
	Avg	0	32.3	0.0%
	Max	0	235	0.0%

2b5.3. What is your interpretation of the results in terms of demonstrating the ability to identify statistically significant and/or clinically/practically meaningful differences in performance across measured entities? (i.*e., what do the results mean in terms of statistical and meaningful differences?*)

Overall rates ranged from 0.0% to 33.3% with an average performance rate of no more than 1.1%, which demonstrates that generally performance on this measure is poor across the three datasets and there is
significant room for improvement. As implementation of this measure increases and performance improves, we will conduct further analyses to identify meaningful differences in performance across clinicians and practices.

2b6. COMPARABILITY OF PERFORMANCE SCORES WHEN MORE THAN ONE SET OF SPECIFICATIONS

If only one set of specifications, this section can be skipped.

Note: *This criterion is directed to measures with more than one set of specifications/instructions (e.g., one set of specifications for how to identify and compute the measure from medical record abstraction and a different set of specifications for claims or eMeasures). It does not apply to measures that use more than one source of data in one set of specifications/instructions (e.g., claims data to identify the denominator and medical record abstraction for the numerator).* ***If comparability is not demonstrated, the different specifications should be submitted as separate measures.***

2b6.1. Describe the method of testing conducted to demonstrate comparability of performance scores for the same entities across the different data sources/specifications (*describe the steps—do not just name a method; what statistical analysis was used*)

Not applicable

2b6.2. What were the statistical results from testing comparability of performance scores for the same entities when using different data sources/specifications? (*e.g., correlation, rank order*)

Not applicable

2b6.3. What is your interpretation of the results in terms of demonstrating comparability of performance measure scores for the same entities across the different data sources/specifications? (i.*e., what do the results mean and what are the norms for the test conducted*)

Not applicable

2b7. MISSING DATA ANALYSIS AND MINIMIZING BIAS

2b7.1. Describe the method of testing conducted to identify the extent and distribution of missing data (or nonresponse) and demonstrate that performance results are not biased due to systematic missing data (or differences between responders and nonresponders) and how the specified handling of missing data minimizes bias (*describe the steps—do not just name a method; what statistical analysis was used*)

As described in 2b2 above, data element validity testing enabled us to identify the extent and distribution of missing data between the report produced from the EHR and a manual abstraction of the patient record. These agreement rates provide useful information on the degree to which missing data from the electronically-produced measure may misrepresent clinician and practice performance.
Sensitivity analyses could not be completed due to small sample sizes.

2b7.2. What is the overall frequency of missing data, the distribution of missing data across providers, and the results from testing related to missing data? (*e.g., results of sensitivity analysis of the effect of various rules for missing data/nonresponse; if no empirical sensitivity analysis, identify the approaches for handling missing data that were considered and pros and cons of each*)

Most of the data elements required to compute this measure demonstrated 100% agreement between the electronic report and visual inspect of the patient chart. For those data elements where 100% agreement was not achieved such as LVSD, moderate validity was demonstrated.

2b7.3. What is your interpretation of the results in terms of demonstrating that performance results are not biased due to systematic missing data (or differences between responders and nonresponders) and how the specified handling of missing data minimizes bias**?** (i.*e., what do the results mean in terms of supporting the selected approach*

for missing data and what are the norms for the test conducted; if no empirical analysis, provide rationale for the selected approach for missing data)

LVSD has historically been a challenge since capture of this element in all electronic measures requires an ejection fraction (EF) value. Few EHR vendors have incorporated EF as a discrete field, fewer yet are using standard coding and practices and hospitals must identify workflow solutions to ensure that the data is included in a discrete field. The frequency with which the EF value is documented in discrete fields can increase as EHR vendors and providers work together to address the ongoing challenges in collecting this critical data element. Even with the challenges in collecting this data element, all of the data elements required to compute this measure had moderate to high agreement rates between the electronic report and the visual inspection of the patient record, which demonstrates that the measure can be collected via EHRs and used to represent performance.

3. Feasibility

Extent to which the specifications including measure logic, require data that are readily available or could be captured without undue burden and can be implemented for performance measurement.

3a. Byproduct of Care Processes

For clinical measures, the required data elements are routinely generated and used during care delivery (e.g., blood pressure, lab test, diagnosis, medication order).

3a.1. **Data Elements Generated as Byproduct of Care Processes.**

Generated or collected by and used by healthcare personnel during the provision of care (e.g., blood pressure, lab value, diagnosis, depression score)

If other:

3b. Electronic Sources

The required data elements are available in electronic health records or other electronic sources. If the required data are not in electronic health records or existing electronic sources, a credible, near-term path to electronic collection is specified.

3b.1. **To what extent are the specified data elements available electronically in defined fields?** *(i.e., data elements that are needed to compute the performance measure score are in defined, computer-readable fields)*

ALL data elements are in defined fields in electronic health records (EHRs)

3b.2. **If ALL the data elements needed to compute the performance measure score are not from electronic sources, specify a credible, near-term path to electronic capture, OR provide a rationale for using other than electronic sources.**

3b.3. **If this is an eMeasure, provide a summary of the feasibility assessment in an attached file or make available at a measure-specific URL.**

Attachment **Attachment:**

National_Minority_Quality_Forum_Feasibility_Assessment_of_Fixed_Dose_Therapy_Measure_090216.pdf

3c. Data Collection Strategy

Demonstration that the data collection strategy (e.g., source, timing, frequency, sampling, patient confidentiality, costs associated with fees/licensing of proprietary measures) can be implemented (e.g., already in operational use, or testing demonstrates that it is ready to put into operational use). For eMeasures, a feasibility assessment addresses the data elements and measure logic and demonstrates the eMeasure can be implemented or feasibility concerns can be adequately addressed.

3c.1. **Describe what you have learned/modified as a result of testing and/or operational use of the measure regarding data collection, availability of data, missing data, timing and frequency of data collection, sampling, patient confidentiality, time and cost of data collection, other feasibility/implementation issues.**
IF a PRO-PM, consider implications for both individuals providing PROM data (patients, service recipients, respondents) and those whose performance is being measured.
The feasibility assessment of the eMeasure showed that the data elements are currently coded in EHRs in a manner that enables data capture in a standardized format and within current clinical workflows. Challenges remain with the collection of ejection fraction values to determine left ventricular systolic dysfunction, which is no different than other measures that require this data element.

These results along with the findings from the reliability and validity testing demonstrate that the measure as specified will produce results that are feasible, reliable and valid and no indications of unintended consequences have been identified that would warrant modifications to the measure. In addition, the overall poor performance rates further emphasize the significant gap in care that this measure addresses.

3c.2. **Describe any fees, licensing, or other requirements to use any aspect of the measure as specified** *(e.g., value/code set, risk model, programming code, algorithm)*.
Not applicable

4. Usability and Use

Extent to which potential audiences (e.g., consumers, purchasers, providers, policy makers) are using or could use performance results for both accountability and performance improvement to achieve the goal of high-quality, efficient healthcare for individuals or populations.

4a. Accountability and Transparency

Performance results are used in at least one accountability application within three years after initial endorsement and are publicly reported within six years after initial endorsement (or the data on performance results are available). If not in use at the time of initial endorsement, then a credible plan for implementation within the specified timeframes is provided.

4.1. **Current and Planned Use**
NQF-endorsed measures are expected to be used in at least one accountability application within 3 years and publicly reported within 6 years of initial endorsement in addition to performance improvement.

Planned	Current Use (for current use provide URL)
Payment Program	Quality Improvement (external benchmarking to organizations) http://www.heart.org/HEARTORG/HealthcareResearch/GetWithTheGuidelines/GetWithTheGuidelines-HF/Get-With-The-Guidelines-Heart-Failure_UCM_306087_SubHomePage.jsp Get with the Guideline-Heart Failure Registry

4a.1. **For each CURRENT use, checked above, provide:**

- Name of program and sponsor
- Purpose
- Geographic area and number and percentage of accountable entities and patients included

A similar measure focused on hospital performance is currently used for quality improvement and benchmarking purposes in the American Heart Association´s Get with the Guidelines-Heart Failure registry. Information on the geographic area, number and percentage of hospitals, providers and patients is not available on the registry web site.

4a.2. **If not currently publicly reported OR used in at least one other accountability application (e.g., payment program, certification, licensing) what are the reasons?** (*e.g., Do policies or actions of the developer/steward or accountable entities restrict access to performance results or impede implementation?*)

This is a newly developed and tested measure intended to be used and reported at the clinician level. Information on additional uses including accountability applications will be provided at the time of maintenance. NMQF is dedicated to ensuring that this measure is implemented widely and submitted the measure for consideration by the Centers for Medicare & Medicaid Services (CMS) for consideration in the Merit-based Incentive Payment System (MIPS). This measure was included on the Measures Under Consideration (MUC) list released by CMS in November 2016. It was proposed for the MIPS program and will be considered by the Measures Application Partnership in the 2016 review cycle.

4a.3. **If not currently publicly reported OR used in at least one other accountability application, provide a credible plan for implementation within the expected timeframes -- any accountability application within 3 years and publicly reported within 6 years of initial endorsement.** (*Credible plan includes the specific program, purpose, intended audience, and timeline for implementing the measure within the specified timeframes. A plan for accountability applications addresses mechanisms for data aggregation and reporting.*)

This is a newly developed and tested measure intended to be used and reported at the clinician level. Information on additional uses including accountability applications will be provided at the time of maintenance. NMQF is dedicated to ensuring that this measure is implemented widely and submitted the measure for consideration by the Centers for Medicare & Medicaid Services (CMS) for consideration in the Merit-based Incentive Payment System (MIPS). This measure was included on the Measures Under Consideration (MUC) list released by CMS in November 2016. It was proposed for the MIPS program and will be considered by the Measures Application Partnership in the 2016 review cycle.

4b. Improvement

Progress toward achieving the goal of high-quality, efficient healthcare for individuals or populations is demonstrated. If not in use for performance improvement at the time of initial endorsement, then a credible rationale describes how the performance results could be used to further the goal of high-quality, efficient healthcare for individuals or populations.

4b.1. **Progress on Improvement. (Not required for initial endorsement unless available.)**

Performance results on this measure (current and over time) should be provided in 1b.2 and 1b.4. Discuss:

- **Progress (trends in performance results, number and percentage of people receiving high-quality healthcare)**
- **Geographic area and number and percentage of accountable entities and patients included**

NMQF partnered with three organizations to test this measure as outlined in 1b.2 and 1b.4.

Final results show that there is overall poor performance on the measure. Specifically, the clinical registry demonstrated that only 1.1% of all eligible patients are currently receiving the FDA-approved fixed dose combination therapy across 303 practices in the Southeast, less than 1% of all patients were prescribed the medication in the federally qualified and community health center sample, and 0% in the integrated delivery system in the South.

Specific performance results from each dataset are included below.

Dataset 1:

A clinical registry that contains data from approximately 30 different electronic health records systems (EHRs), covering over 500 sites or practices throughout the southeast, and representing in excess of 3 million patients. We received an extract of their EHR that includes all patients meeting the denominator criteria for the measure. We used calendar year 2014 for this dataset. The dataset included 6,384 patients with 1,415 clinicians across 321 sites.

Dataset 2:

A network of federally-qualified and community health centers in the Midwest. We received an extract of their EHR (GE Centricity) that included all patients meeting the denominator criteria for the measure. In addition, we manually reviewed 98 randomly selected charts for patients in this EHR subset of patients. We used calendar year 2015 for this dataset. The dataset included 145 patients across 14 sites.

Dataset 3:

An integrated inpatient and outpatient delivery system in the South. We received an extract from their EHR (Epic) of all patients meeting the denominator criteria for the measure. In addition, we used a simple random sample of 100 patients identified in the EHR for a manual abstraction of the patient chart data for the elements required for the measure. We used calendar year 2015 for this dataset. The dataset included 3,018 patients with 825 clinicians across 10 sites.

Dataset 1:

Sum 1.6%

Min 0.0%

Avg 1.1%
Max 33.3%

Dataset 2:
Sum 0.7%
Min 0.0%
Avg 0.4%
Max 5.0%

Dataset 3:
Sum 0.0%
Min 0.0%
Avg 0.0%
Max 0.0%

4b.2. **If no improvement was demonstrated, what are the reasons? If not in use for performance improvement at the time of initial endorsement, provide a credible rationale that describes how the performance results could be used to further the goal of high-quality, efficient healthcare for individuals or populations.**
Testing of the measure demonstrated that there is overall poor performance on the measure. Specifically, the clinical registry demonstrated that only 1.1% of all eligible patients are currently receiving the FDA-approved fixed dose combination therapy across 303 practices in the Southeast, less than 1% of all patients were prescribed the medication in the federally qualified and community health center sample, and 0% in the integrated delivery system in the South. These overall poor performance rates further emphasize the significant gap in care that this measure addresses.

4c. Unintended Consequences

The benefits of the performance measure in facilitating progress toward achieving high-quality, efficient healthcare for individuals or populations outweigh evidence of unintended negative consequences to individuals or populations (if such evidence exists).

4c.1. **Were any unintended negative consequences to individuals or populations identified during testing; OR has evidence of unintended negative consequences to individuals or populations been reported since implementation? If so, identify the negative unintended consequences and describe how benefits outweigh them or actions taken to mitigate them.**
Testing of the measure demonstrated that the measure as specified will produce results that are reliable and valid and the data is feasible to collect. No indications of unintended consequences have been identified that would warrant modifications to the measure at this time. In addition, the overall poor performance rates further emphasize the significant gap in care that this measure addresses.

5. Comparison to Related or Competing Measures

If a measure meets the above criteria and there are endorsed or new related measures (either the same measure focus or the same target population) or competing measures (both the same measure focus and the same target population), the measures are compared to address harmonization and/or selection of the best measure.

5. Relation to Other NQF-endorsed Measures
Are there related measures (conceptually, either same measure focus or target population) or competing measures (conceptually both the same measure focus and same target population)? If yes, list the NQF # and title of all related and/or competing measures.
Yes

5.1a. **List of related or competing measures (selected from NQF-endorsed 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)

5.1b. **If related or competing measures are not NQF endorsed please indicate measure title and steward.**

Previously endorsed measure:

0162: ACEI or ARB for left ventricular systolic dysfunction - Heart Failure (HF) Patients (CMS)
0610: Heart Failure - Use of ACE Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB) Therapy (ActiveHealth Management)
0615: Heart Failure - Use of Beta Blocker Therapy (ActiveHealth Management)

5a. Harmonization

The measure specifications are harmonized with related measures;
OR
The differences in specifications are justified

5a.1. **If this measure conceptually addresses EITHER the same measure focus OR the same target population as NQF-endorsed measure(s):**
Are the measure specifications completely harmonized?
Yes

5a.2. **If the measure specifications are not completely harmonized, identify the differences, rationale, and impact on interpretability and data collection burden.**
Measure specifications for the target population and medication therapies for ACEI, ARB, and beta-blocker are completely harmonized with 0081 and 0083.

5b. Competing Measures

The measure is superior to competing measures (e.g., is a more valid or efficient way to measure);
OR
Multiple measures are justified.

5b.1. **If this measure conceptually addresses both the same measure focus and the same target population as NQF-endorsed measure(s):**
Describe why this measure is superior to competing measures (e.g., a more valid or efficient way to measure quality); OR provide a rationale for the additive value of endorsing an additional measure. (Provide analyses when possible.)
Not applicable

Appendix

A.1 Supplemental materials may be provided in an appendix. All supplemental materials (such as data collection instrument or methodology reports) should be organized in one file with a table of contents or bookmarks. If material pertains to a specific submission form number, that should be indicated. Requested information should be provided in the submission form and required attachments. There is no guarantee that supplemental materials will be reviewed.

No appendix **Attachment:**

Contact Information

Co.1 **Measure Steward (Intellectual Property Owner):** National Minority Quality Forum
Co.2 **Point of Contact:** Gretchen, Wartman, gwartman@nmqf.org, 202-223-7560-
Co.3 **Measure Developer if different from Measure Steward:** National Minority Quality Forum
Co.4 **Point of Contact:** Gretchen, Wartman, gwartman@nmqf.org, 202-223-7560-

Additional Information

Ad.1 **Workgroup/Expert Panel involved in measure development**
Provide a list of sponsoring organizations and workgroup/panel members' names and organizations. Describe the members' role in measure development.
Writing Committee members:

Ola Akinboboye, MD, MPH, MBA, FACC, FACP

Associate Professor of Clinical Medicine, Weill Medical College of Cornell University
Medical Director, Queens Heart Institute
Rosedale, NY

Bryan Curry, MD, FACC
Department of Cardiology
Howard University Hospital
Washington, DC

Anekwe E. Onwuanyi, MD, FACC
Professor of Medicine and Chief of Cardiology, Morehouse School of Medicine
Medical Director, Heart Failure Program, Grady Health System
Atlanta, GA

David N. Smith, MD, FACP, FACC
Assistant Clinical Professor of Medicine
Yale School of Medicine
New Haven, CT

Modele O. Ogunniyi, MD, MPH, FACC, FACP, FAHA
Assistant Professor of Medicine
Division of Cardiology, Department of Medicine
Emory University School of Medicine
Assistant Medical Director, Grady Heart Failure Program
Atlanta, GA

Elizabeth Ofili, MD, MPH, FACC
Professor of Medicine
Director and Senior Associate Dean
Clinical Research Center & Clinical and Translational Research
Morehouse School of Medicine
Atlanta, GA

This committee advised on the underlying evidence, measure statements construction, and detailed specifications during the development of the Fixed-dose combination therapy measure. They will continue to provide input and clinical expertise as the measure is tested and finalized and during every measure update.

Measure Developer/Steward Updates and Ongoing Maintenance
Ad.2 **Year the measure was first released:** 2015
Ad.3 **Month and Year of most recent revision:** 06, 2015
Ad.4 **What is your frequency for review/update of this measure?** Specifications are updated annually; supporting guidelines reviewed 3 years or as evidence changes
Ad.5 **When is the next scheduled review/update for this measure?** 12, 2016

linking permissions, please visit NMQF's Terms of Use page (http://heartfailurequalityimprovementinitiative.com/terms-of-use/). Neither the NMQF, nor its members shall be responsible for any use of the Measures.

Ad.7 **Disclaimers:** These Measures are intended to assist physicians in enhancing quality of care. Measures are designed for use by any physician who manages the care of a patient for a specific condition, or for prevention. These performance Measures are not clinical guidelines and do not establish a standard of medical care, and have not been tested for all potential applications. NMQF encourages the testing and evaluation of its Measures.

THE MEASURES AND SPECIFICATIONS ARE PROVIDED "AS IS" WITHOUT WARRANTY OF ANY KIND.

Ad.8 **Additional Information/Comments:** Not applicable