

# Did HEDIS Get it Right? Evaluating the Quality of a Quality Measure

## Adherence to $\beta$ -Blockers and Cardiovascular Outcomes After Myocardial Infarction

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**Background:** As an example of the process that could be used to evaluate and optimize the performance of quality measures in routine practice, we evaluated whether the Healthcare Effectiveness Data and Information Set (HEDIS) measure assessing the “persistence of  $\beta$ -blocker treatment after a heart attack” correlates with post-myocardial infarction (MI) outcomes and whether or not there are alternative specifications of this construct which are better predictors and/or may be more easily applied.

**Research Design:** The study included a retrospective cohort of 8672 post-MI patients 18 years old and above. We assessed the strength of the association between the different adherence measures and the composite clinical outcome using multivariable Cox models. We compared the predictive capacity of each adherence definition model to one that did not contain adherence by computing the change in C-statistics and the continuous net reclassification improvement indices (NRIs).

**Results:** Adherence was associated with clinical outcome reductions, with hazard ratios ranging from 0.48 (95% CI, 0.27–0.85) to 0.81 (95% CI, 0.67–0.99). None of the adherence measures, including the HEDIS definition, significantly changed the C-statistic relative to a model that did not include adherence. However, the short-term adherence measure (having 72 d covered during the first

90 d postdischarge) showed a large change in NRI (correctly reclassifying 12% of cases and 16% of noncases; NRI: 28%; 95% CI, 22%–38%), although did not significantly differ from the change in NRI with the HEDIS measure.

**Conclusions:** We identified an adherence measure that showed a predictive ability as good as that of the HEDIS definition to measure  $\beta$ -blocker use after MI, halving the time of assessment required, and thus, allowing for the implementation of quality improvement interventions in a more timely manner.

**Key Words:** quality measures, quality assessment, medication adherence, secondary prevention, myocardial infarction, risk prediction

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Performance measures are frequently used to monitor health care delivery, target quality improvement interventions, and structure reimbursement contracts.<sup>1–3</sup> Although these metrics are intended to be evidence based and generally measure processes of care and surrogate markers that are strongly associated with morbidity and mortality,<sup>4</sup> good performance on quality measures does not always translate into better patient outcomes.<sup>5–10</sup> For example, only 25% of the Center for Medicare and Medicaid Services inpatient performance measures for heart failure were associated with lower rates of postdischarge mortality or rehospitalization.<sup>5,6</sup>

There are several potential explanations for the lack of association between some quality measures and better outcomes. The evidence supporting quality measures generally originates from randomized clinical trial data where targeted patients are recruited and care is closely observed, while the measures themselves are applied in routine practice where patients may have multiple comorbidities and where monitoring and treatment adherence are comparatively low.<sup>11</sup> In addition, the emergence of newer evidence may make some measures inaccurate.<sup>12,13</sup> There are also many different ways in which quality measures can be defined (eg, good glycemic control may be defined based on a range of hemoglobin A1c values),<sup>14,15</sup> with cut-points being chosen somewhat

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arbitrarily; in these cases misspecification can diminish the association with the outcomes of interest.<sup>16</sup>

Accordingly, establishing whether quality measures optimally reflect the clinical outcomes they seek to maximize is of substantial clinical and policy importance. Further, the choice of analytic methods for conducting their assessment needs to be clarified. Complementary to typical approaches, which rely on associations with the outcomes of interest, the use of classic prediction metrics, such as *C*-statistic, or recently developed metrics such as the continuous net reclassification index (NRI), could be a useful approach to more accurately select and evaluate quality measures.

In 2006, the NCQA introduced a new Healthcare Effectiveness Data and Information Set (HEDIS) measure assessing the “persistence of  $\beta$ -blocker treatment after a heart attack.” This metric, the first one in HEDIS related to long-term medication adherence, may have been specified in many alternative ways. Given the increasing attention being paid to medication adherence as a strategy for improving health quality while reducing spending,<sup>17–19</sup> an empiric determination of how to optimally define this measure is desirable. Further, the process of evaluating this metric could easily be used to evaluate and optimize the performance of quality measures in routine practice.

Accordingly, we evaluated whether this HEDIS measure correlates with post-myocardial infarction (MI) outcomes and whether or not there are alternative specifications of this construct which are better predictors and/or may be more easily applied.

## METHODS

### Study Design and Population

We assembled a retrospective cohort of adult patients 65 years of age or younger who received health care and pharmacy benefits through Aetna, a large commercial insurer in the United States, and were discharged alive after hospitalization for MI between January 2007 and October 2009. We designed our study to mirror the way in which HEDIS evaluates post-MI  $\beta$ -blocker adherence. In specific, subjects were identified based upon discharge diagnoses codes of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) 410.x1 (in the primary or secondary position) or DRG 121, 122, 516, 526. The discharge date was considered the index date for our analyses and we included only those patients who were continuously insured for at least 365 days before and, based upon the HEDIS criteria, for at least 135 days of the 180 days after their index date.

On the basis of the criteria applied by HEDIS, we excluded patients discharged directly to a nonacute facility such as a nursing home or rehabilitation facility and those identified as having a potential contraindication to  $\beta$ -blocker therapy. Contraindications were defined as having any inpatient or outpatient records in the preceding 12 months up until 180 days after the index date of primary or secondary diagnosis of asthma (ICD-9 code 493), hypotension (ICD-9 code 458), heart block greater than first degree (ICD-9 codes 426.0, 426.12, 426.13, 426.2–426.4, 426.51–426.54, and 426.7), sinus bradycardia (ICD-9 code 427.81), or chronic

obstructive pulmonary disease (COPD) (ICD-9 codes 491.2, 496, and 506.4). Patients prescribed inhaled corticosteroids were also excluded.

If a patient had >1 eligible admission, only the first one was evaluated. Patients discharged from one hospital and admitted to another within 1 day were considered as transfers between acute care facilities and were treated as single contiguous admissions. The institutional review board of Brigham and Women’s Hospital approved this study.

### Adherence Measures

We assessed  $\beta$ -blocker adherence during the 6 months after hospital discharge using different adherence measures and we classified patients as being adherent or not (ie, a binary measure) based on each of these definitions (Table 1). The measures either evaluated medication availability or persistence. The availability measures assessed the proportion of days that patients had medication available to them over the 180-day period after hospital discharge. For example, the HEDIS measure defined patients as being adherent if they had  $\beta$ -blocker available to them for  $\geq 135$  of the 180 days after hospital discharge. The persistence measures assessed continuous exposure to medication starting with the initial prescription and allowing for certain predetermined gaps between successive prescription refills until patients were assumed to have discontinued their medication. For example, the 15-day gap measure defined patients as being adherent if they did not have gaps  $\geq 15$  days without medication available after the initial prescription and until 180 days after hospital discharge. We also assessed adherence during a shorter timeframe (3 mo) based on having  $\geq 72$  days ( $\geq 80\%$ ) of medications available and having a gap of  $\leq 15$  days, although for these measures we still evaluated outcomes beginning 181 days after discharge as described below. Short timeframe adherence was defined as 3

**TABLE 1.** Measures of Adherence Evaluated After Hospital Discharge

Types of Measures	Definitions of Adherence
Availability measures	
Based on the number of prescriptions filled during the 180 d after discharge	$\geq 3$ prescriptions $\geq 6$ prescriptions
Based on days’ supply during the 180 d after hospital discharge	$\geq 135$ d ( $\geq 75\%$ ) with $\beta$ -blocker available* $\geq 144$ d ( $\geq 80\%$ ) with $\beta$ -blocker available $\geq 180$ d ( $\geq 100\%$ ) with $\beta$ -blocker available
Based on days’ supply during the 90 d after hospital discharge <sup>†</sup>	$\geq 72$ d ( $\geq 80\%$ ) with $\beta$ -blocker available
Persistence measures	
Based on the total days without medication available during the 180 d after hospital discharge	Maximum gap of 0 d Maximum gap of 15 d Maximum gap of 30 d
Based on the total days without medication available during the 90 d after hospital discharge <sup>†</sup>	Maximum gap of 15 d

\*The HEDIS measure.

<sup>†</sup>Outcomes were assessed beginning 181 days after hospital discharge (see the text for details).

months, as this was the minimum amount of follow-up time to accommodate patients who filled 90-day prescriptions.

## Outcome

We sought to validate the adherence definitions by evaluating their ability to accurately predict a composite outcome of acute MI, unstable angina, congestive heart failure, or death within the 181–365 days after the discharge date. These outcomes were assessed using validated claims algorithms.<sup>20</sup>

## Covariates

We used recorded diagnoses in inpatient and outpatient claims to assess the presence of comorbid conditions during the 12-month period before the discharge date that may confound the relationship between adherence and the occurrence of our composite cardiovascular outcome. The following variables were included: age at index date, sex, hypertension, diabetes, lipid disorder, congestive heart failure, COPD or asthma, cerebrovascular disease, peripheral vascular disease, chronic kidney disease, malignancy, arthritis, and dementia. The use of the following medications in the year prior the index hospitalization was also assessed: antiplatelets (clopidogrel, prasugrel, and ticlopidine), statins, ACEI/ARBs,  $\beta$ -blockers, calcium channel blockers, diuretics, nitrates, digoxin, and warfarin. In addition, we also defined the characteristics of the index MI including year of hospitalization, length of stay for the index admission, angiography, revascularization interventions such as percutaneous coronary intervention, stent, coronary-artery bypass grafting, and, systemic thrombolysis and intracoronary thrombolysis. Furthermore, we assessed the concomitant use of other post-MI medications, defined as having at least 1 filled prescription for any statin, ACEI/ARB, or antiplatelets (clopidogrel, prasugrel, and ticlopidine) within 180 days after discharge from the index MI hospitalization.

## Statistical Analysis

We used descriptive statistics to summarize the characteristics of post-MI cohort. We also described patient characteristics stratifying by whether or not they were adherent to their prescribed  $\beta$ -blocker using the reference (HEDIS) definition (having at least 135 d covered). To test differences, we used one-way analysis of variance for continuous variables and the  $\chi^2$  tests for dichotomous ones.

We fit a Cox model to predict the composite cardiovascular outcome with only clinical and demographic covariates and then added to this model a covariate that defined patients as being adherent or not based upon each adherence definition shown in Table 1 (ie, 1 at a time). On the basis of these models, we first evaluated the strength of the association between each adherence measure and the clinical composite outcome, by estimating the corresponding hazard ratios and their 95% confidence intervals (CIs). Then, we assessed the discriminative ability of each definition by comparing the change in *C*-statistic and continuous NRIs and their 95% CIs.

The *C*-statistic indicates the discriminative ability of a prediction model and can be interpreted as the probability

that the model assigns a higher predicted risk to a case as compared with a noncase.<sup>21</sup> Useless predictions such as a coin flip result in a *C*-statistic of 0.5 (no discrimination), whereas a perfect prediction model has a *C*-statistic of 1, and is achieved if the predicted risks for all the cases are higher than those for all noncases, with no overlap. We assessed the difference in *C*-statistic for survival<sup>22,23</sup> between models with and without each adherence measure using bootstrapping. To overcome limitations of *C*-statistic, which is insensitive to further improvements in prediction once a good prediction model has been built, complementarily, we used the continuous NRI to quantify the overall improvement in reclassification. Moreover, the examination of the event and nonevent reclassification components of the NRI (indicating the amount of correct reclassification among individuals who do and do not have experience of the outcome of interest) offers additional insight by helping to explain how the different measures work and thus facilitating their interpretation. This metric does not require the specification of categories of risk and relies on the proportions of cases correctly assigned a higher model probability after adding the adherence measure to the model and noncases correctly assigned a lower model probability after adding the adherence measure.<sup>24</sup> CIs were estimated using bootstrapping. *C*-statistics and NRI were calculated at 1 year of follow-up. In a supplemental analysis, we evaluated whether the best performing measure differed from the HEDIS definition by estimating the 95% bootstrap CI for the difference in the estimates of the NRI based on 1000 replications.

All statistical analyses were performed using the SAS version 9.2 (SAS Institute Inc., Cary, NC).

## Sensitivity Analysis

To further assess the robustness of our findings, we performed additional analyses. First, we repeated our analysis after excluding days patients spent in the hospital from the denominators of the adherence measures. Second, to confirm the consistency of the results in a wider population that could also benefit from  $\beta$ -blocker therapy, we also evaluated the predictive ability of each adherence measure using the same approach described above but also including those with potential contraindications to  $\beta$ -blockers.

## RESULTS

The study cohort included 8672 post-MI patients without contraindications to receive  $\beta$ -blockers. The mean (SD) age of the patients was 59.7 (12.5) years and 28.5% of the cohort were female. Sixty-nine percent of patients had newly initiated a  $\beta$ -blocker after their MI (Table 2). On the basis of the HEDIS definition, adherent patients were more likely than nonadherent to have undergone revascularization procedures during the index hospitalization, and to concomitantly use statins, ACEI/ARBs, and antiplatelet therapy with their prescribed  $\beta$ -blocker.

## Adherence Rates by Definition and Associations With Clinical Outcomes

Rates of full adherence ranged from 7% to 73% depending on the definition applied (Fig. 1), with the most

**TABLE 2.** Patient Characteristics

	All (N = 8672)	Adherent* (N = 5165)	Non Adherent* (N = 3507)	P <sup>†</sup>
Age [mean (SD)]	59.7 (12.5)	59.7 (12.2)	59.7 (13.1)	0.913
Female	2468 (28.5)	1359 (26.3)	1109 (31.6)	<0.001
Medication use before hospitalization <sup>‡</sup>				
β-blocker	2726 (31.4)	1510 (29.2)	1216 (34.7)	<0.001
Statin	3466 (40.0)	1994 (38.6)	1472 (42.0)	0.002
ACEI or ARB	3507 (40.4)	2054 (39.8)	1453 (41.4)	0.121
Calcium channel blockers	1612 (18.6)	915 (17.7)	697 (19.9)	0.011
Diuretic	1928 (22.2)	1179 (22.8)	749 (21.4)	0.106
Nitrates	911 (10.5)	452 (8.8)	459 (13.1)	<0.001
Digoxin	174 (2.0)	86 (1.7)	88 (2.5)	0.006
Warfarin	47 (0.5)	19 (0.4)	28 (0.8)	0.007
Antiplatelet	869 (10.0)	401 (7.8)	468 (13.3)	<0.001
Concomitant medication use <sup>§</sup>				
Statin	7442 (85.8)	4709 (91.2)	2733 (77.9)	<0.001
ACEI or ARB	6179 (71.3)	3968 (76.8)	2211 (63.0)	<0.001
Antiplatelet	6465 (74.6)	4151 (80.4)	2314 (66.0)	<0.001
Coexisting illness <sup>‡</sup>				
Hypertension	5169 (59.6)	3071 (59.5)	2098 (59.8)	0.734
Diabetes	2402 (27.7)	1321 (25.6)	1081 (30.8)	<0.001
Lipid disorder	4179 (48.2)	2607 (50.5)	1572 (44.8)	<0.001
Congestive heart failure	1408 (16.2)	808 (15.6)	600 (17.1)	0.069
Cardiovascular disease	1115 (12.9)	587 (11.4)	528 (15.1)	<0.001
Peripheral vascular disease	138 (1.6)	73 (1.4)	65 (1.9)	0.108
COPD or asthma	156 (1.8)	80 (1.5)	76 (2.2)	0.034
Chronic renal disease	976 (11.3)	496 (9.6)	480 (13.7)	<0.001
Malignancy	1108 (12.8)	657 (12.7)	451 (12.9)	0.848
Arthritis	1127 (13.0)	635 (12.3)	492 (14.0)	0.018
Dementia	229 (2.6)	96 (1.9)	133 (3.8)	<0.001
Procedure on index hospitalization				
Angiography	7369 (85.0)	4547 (88.0)	2822 (80.5)	<0.001
Percutaneous coronary intervention	829 (9.6)	537 (10.4)	292 (8.3)	0.001
Stent	4849 (55.9)	3181 (61.6)	1668 (47.6)	<0.001
Coronary-artery bypass grafting	682 (7.9)	410 (7.9)	272 (7.8)	0.757
Systemic thrombolysis	69 (0.8)	43 (0.8)	26 (0.7)	0.639
Intracoronary thrombolysis	46 (0.5)	24 (0.5)	22 (0.6)	0.306
Length hospitalization [mean (SD)]	4.8 (3.6)	4.7 (3.6)	4.8 (3.7)	0.228

All values correspond to n (%), unless otherwise stated.

\*Adherent is defined based on the HEDIS adherence measure (having at least 135 d covered).

<sup>†</sup>Using analysis of variance for continuous variables and the  $\chi^2$  for dichotomous variables.

<sup>‡</sup>Medication use before hospitalization and coexisting illnesses were assessed on the basis of all filled prescriptions and available diagnoses during the 12-month period preceding the index hospitalization. Medication use was defined as the filling of at least 1 prescription during this period.

<sup>§</sup>Concomitant use of other post-MI medications, defined as having at least 1 filled prescription within 180 days after discharge from the index MI hospitalization.

ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers; COPD, chronic obstructive pulmonary disease.

restrictive definitions (having  $\geq 180$  d covered, having  $\geq 6$  prescriptions, or having no allowable gap without days supply) yielding the lowest adherence rates.

All of the adherence measures except 2 (filling at least 3 or 6 prescriptions) were associated with reductions in hospitalization for major vascular events and mortality (Table 3), with hazard ratios ranging from 0.48 (95% CI, 0.27–0.85) to 0.81 (95% CI, 0.67–0.99).

### Predictive Capacity of the Adherence Measures

None of the adherence measures examined, including the HEDIS definition, significantly improved the C-statistic relative to a model that did not include a covariate for β-blocker adherence (Table 3). However, several of the adherence measures significantly improved the correct reclassification of cases and noncases (Table 3). Of these, the greatest improvement in reclassification was observed with the short-term availability measure (having 72 d covered during the first 90 d postdischarge), which correctly

reclassified 12% of cases and 16% of noncases (continuous NRI: 28%; 95% CI, 22%–38%), whereas the HEDIS measures reclassified correctly 2% of cases and 20% of noncases (continuous NRI: 22%; 95% CI, 14%–32%). The differences between the NRI values for these 2 adherence measures did not reach statistical significance (6%; 95% CI, –2%–14%).

### Sensitivity Analysis

Our findings remained unchanged in secondary analyses after excluding days patients spent in the hospital from the denominators of the adherence measures. Our results were also very similar when we repeated our analysis among all patients discharged from hospital for MI (n = 15,552) and not only those without potential contraindications to β-blocker treatment (Table 4), although in this cohort, the short-term availability measure (having 72 d covered during the first 90 d postdischarge), apart from showing the greatest improvement in reclassification (continuous NRI: 32%; 95% CI, 26%–36%), was also the only measure to improve the

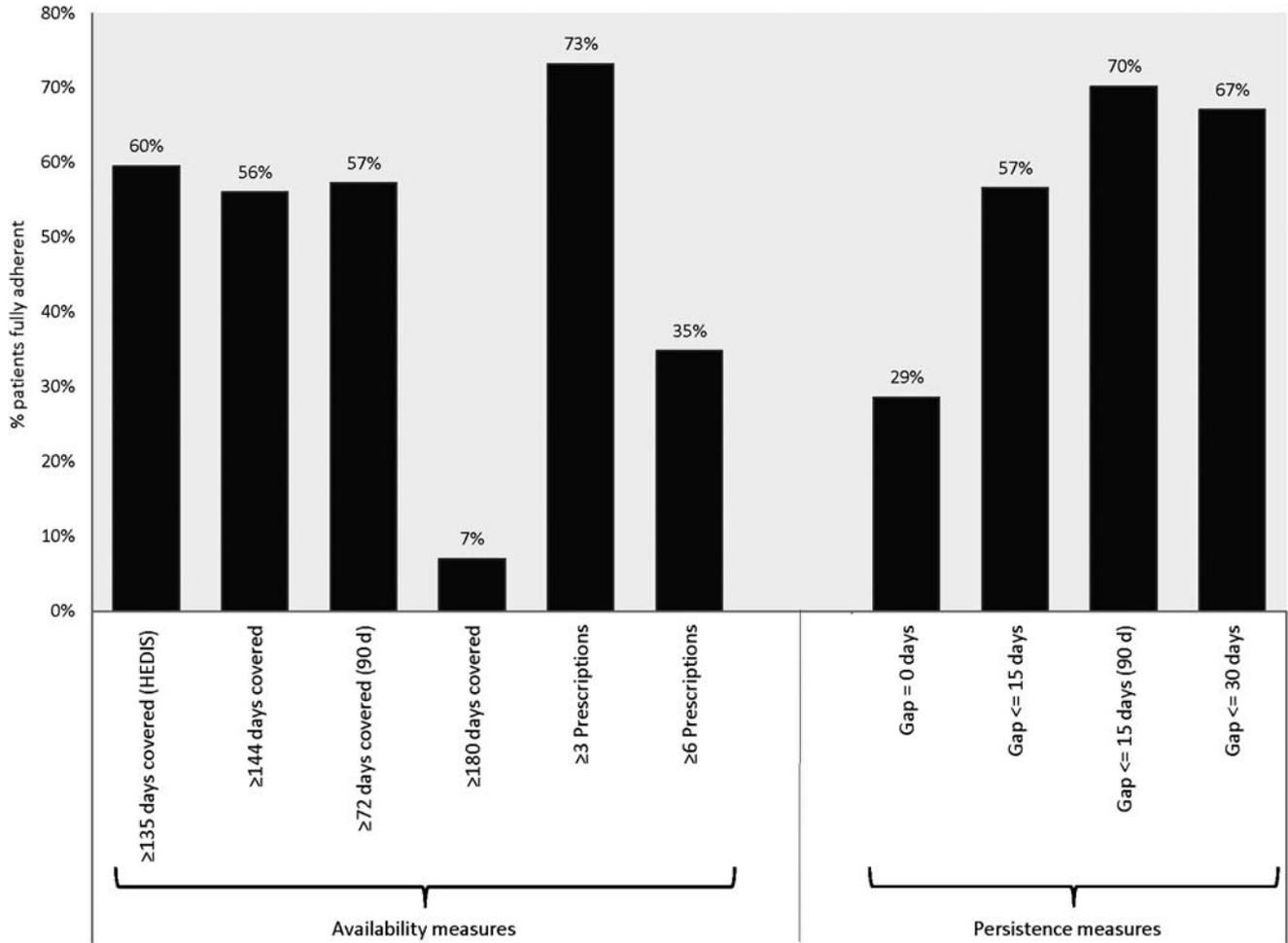


FIGURE 1. Adherence rates to beta-blockers by definition.

discrimination ability when added to the full model that did not include adherence (C-statistic: 0.769 with vs. 0.766 without the adherence measure;  $P=0.0232$ ).

### DISCUSSION

Performance measures are created and used with the goal of improving health care quality, and therefore it is

TABLE 3. Predictive Ability of Different Definitions of Post-MI beta-Blocker Adherence (N=8672)

Adherence Criteria	HR (95% CI)	C-Statistic	P*	Continuous NRI (95% CI)	RI Cases	RI Controls
Long-term (180 d) measures						
Availability measures						
> 135 d covered	0.77 (0.64–0.94)	0.754	0.2210	0.22 (0.14–0.32)	0.02	0.20
> 144 d covered	0.77 (0.64–0.94)	0.754	0.2577	0.24 (0.16–0.35)	0.10	0.13
> 180 d covered	0.48 (0.27–0.85)	0.755	0.1025	–0.00 (–0.06–0.06)	0.79	–0.79
≥ 3 prescriptions	0.90 (0.73–1.10)	0.751	0.8596	0.15 (0.05–0.25)	–0.32	0.47
≥ 6 prescriptions	0.83 (0.67–1.02)	0.751	0.9402	0.07 (0.09–0.25)	0.47	–0.29
Persistence measures						
Maximum gap 0 d	0.73 (0.58–0.91)	0.753	0.2748	0.12 (0.05–0.18)	0.52	–0.41
Maximum gap 15 d	0.76 (0.63–0.91)	0.755	0.1137	0.16 (0.07–0.27)	0.01	0.14
Maximum gap 30 d	0.81 (0.67–0.99)	0.752	0.7524	0.09 (–0.00–0.20)	–0.25	0.35
Short-term (90 d) measures						
> 72 d covered	0.79 (0.65–0.96)	0.754	0.1637	0.28 (0.22–0.38)	0.12	0.16
Maximum gap 15 d	0.79 (0.65–0.97)	0.753	0.4511	0.12 (0.04–0.21)	–0.29	0.41

\*Correspond to the difference between the C-statistic of full-adjusted model (all variables included in Table 2) without adherence measure (C-statistic: 0.751) and the C-statistic of adjusted model adding each adherence measure.  
 CI indicates confidence interval; HR, hazard ratio; NRI, net reclassification index; RI, reclassification index.

**TABLE 4.** Predictive Ability of Different Definitions of Post-MI  $\beta$ -Blocker Adherence (N = 15,552)

Adherence Criteria	HR (95% CI)	C-Statistic	P*	NRI (> 0)	RI Cases	RI Controls
Long-term (180 d) measures						
Availability measures						
> 135 d covered	0.78 (0.70–0.88)	0.768	0.1258	0.23 (0.17–0.29)	0.08	0.14
> 144 d covered	0.77 (0.68–0.86)	0.768	0.0791	0.25 (0.19–0.30)	0.17	0.08
> 180 d covered	0.72 (0.53–0.98)	0.767	0.2304	–0.01 (0.05–0.02)	0.81	–0.82
≥ 3 prescriptions	0.98 (0.87–1.11)	0.766	0.6449	0.12 (0.07–0.18)	–0.29	0.41
≥ 6 prescriptions	0.82 (0.72–0.94)	0.767	0.1707	0.18 (0.12–0.21)	0.51	–0.33
Persistence measures						
Maximum gap 0 d	0.76 (0.67–0.87)	0.768	0.3280	0.12 (0.06–0.17)	0.55	–0.44
Maximum gap 15 d	0.79 (0.70–0.88)	0.768	0.1983	0.15 (0.09–0.20)	0.05	0.10
Maximum gap 30 d	0.86 (0.76–0.96)	0.767	0.5748	0.09 (0.02–0.14)	–0.21	0.30
Short-term (90 d) measures						
> 72 d covered	0.74 (0.66–0.84)	0.769	0.0232	0.32 (0.26–0.36)	0.22	0.09
Maximum gap 15 d	0.84 (0.74–0.94)	0.767	0.2993	0.12 (0.06–0.18)	–0.24	0.35

\*Correspond to the difference between the C-statistic of full-adjusted model (all variables included in Table 2) without adherence measure (C-statistic: 0.766) and the C-statistic of adjusted model adding each adherence measure.

CI indicates confidence interval; HR, hazard ratio; NRI, net reclassification index; RI, reclassification index.

imperative to understand whether they efficiently and accurately predict the outcomes they seek to promote. This is particularly true as the evidence supporting many measures comes from clinical trials, rather than real-world settings, because measures do not always reflect current evidence and because the precise criteria used to define a measure are often somewhat arbitrarily chosen. In fact, the limited literature that has evaluated the relationship between quality measures has in many cases failed to show a positive relationship.<sup>5–10</sup>

We evaluated the predictive capacity of a relatively new HEDIS measure and compared its predictive ability with that of alternative metrics that could have been chosen to assess the same construct. We found that although the specific way in which HEDIS defined this measure, having a  $\beta$ -blocker available for at least 135 of the 180 days after MI, does predict adverse cardiovascular outcomes, other measures that seem to do so with at least the same accuracy, offer potential advantages with regard to how quickly they can be assessed. In specific, the greatest improvement in reclassification—although not statistically different from the HEDIS measure—was observed with the short-term availability measure (80% of days covered during the first 90 d postdischarge). Further, when all patients discharged from hospital for MI were included in the analysis, and not only patients without potential contraindications to  $\beta$ -blockers, the short-term availability measure showed also a significant improvement in discrimination based upon a change in C-statistic.

To the best of our knowledge, this is the first time the performance of alternative ways of defining a single quality measure have been compared and we believe that our approach could be more generally useful for optimizing the performance of other similar metrics. In our analysis we used 2 statistics that are frequently used to evaluate prediction rules: the C-statistic and the continuous NRI, both derived from multivariable Cox proportional hazards models.<sup>25</sup> Although the C-statistic has been the standard measure for assessing performance of predictive models and produces results that are easily interpretable, it is very difficult to

demonstrate incremental improvement in this measure after a relatively good prediction model has been built. For example, several traditional Framingham risk factors, such as LDL cholesterol, would have not been included in this well-known risk score as its inclusion in the model fails to improve C-statistic relative to a model without it.<sup>26,27</sup> To overcome C-statistic limitations,<sup>27</sup> other metrics such as the continuous NRI have been proposed. The latter measure has the advantage of being a much more sensitive measure of discrimination than the C-statistic, but overall, both metrics do not rely on risk categories nor on the incidence rates of the disease and thus can be compared among different populations supporting the reliability of these metrics across different settings.<sup>24</sup> For this reason, complementary to assessment of associations, exploring the C-statistic and recently developed metrics such as the continuous NRI could be a useful approach to more accurately select optimal quality measures and evaluate their validity.

Our results also have specific relevance for the care of post-MI patients. Coronary heart disease remains the leading cause of death in the United States and other developed countries<sup>28,29</sup> and adherence to evidence-based post-MI medications, including  $\beta$ -blockers, remains extremely poor.<sup>30–38</sup> Thus, measures such as post-MI  $\beta$ -blocker adherence remain very reasonable targets for quality improvement activities.<sup>30–34</sup> That said, the precise way in which this quality measure should be defined has thus far been unclear. Our results suggest that measures based upon prescription filling during the first 3 months after discharge, rather than 6 months as in the current HEDIS measure, could predict adverse cardiovascular outcomes with at least the same accuracy. Further, this measure could be implemented more quickly and would thus allow for the identification of those patients who could most benefit from quality improvement interventions during the highly vulnerable early post-MI time period.

The prescription rates observed for antiplatelet and ACEI/ARB after MI were lower than expected but consistent with previously published data from the same insurer,<sup>17</sup> and with

rates reported among Medicare beneficiaries.<sup>39</sup> In the case of antiplatelet agents, it is important to note that we only evaluated agents requiring a prescription—clopidogrel, prasugrel, and ticlopidine. As the patient cohort consisted of patients with acute MI but not necessarily ST-segment elevation (STEMI), some unstable angina/non-STEMI patients would appropriately not have received clopidogrel after their event. Further, the use of ACEI/ARBs is a grade 1A recommendation only for STEMI patients with left ventricular dysfunction (and a 2A recommendation for others). As such, lack of prescribing these agents for all patients may not be entirely surprising.

There are several limitations to this study. First, due to its observational nature, our study may be affected by unmeasured confounding. In the multivariate analyses, we adjusted for a wide range of expected confounders and although some residual confounding may still be present, the association between  $\beta$ -blocker adherence and clinical outcomes is not expected to be entirely explained by confounding by the healthy adherer effect.<sup>40</sup> Further, we sought primarily to compare measures, rather than to estimate the impact of adherence on outcomes, and thus any bias should apply relatively equally to the measures we assessed. Second, our analysis relied on pharmacy claims, but patients may not consume all of their filled medications. Validation studies show a very high concordance between claims-based measures and pill counts in cardiovascular disease.<sup>41</sup> In the US context this is perhaps not surprising as virtually all patients must pay some amount out-of-pocket for their prescriptions and are unlikely to purchase medications when they have supplies in their possession. Thus, we would anticipate a high degree of consistency between refill claims and actual medication consumption. Although some degree of overestimation of adherence is possible, we do not expect this to have affected our measures differentially as all were based upon administrative claims. Further, for all of the measures we evaluated, patients defined as being adherent based upon claims did indeed have lower rates of cardiovascular outcomes. Third, for our primary analysis we tried to reproduce as closely as possible the population assessed by the HEDIS measure. However, it could be argued that patients with relative contraindications to  $\beta$ -blocker therapy, such as COPD, heart failure, etc., may also benefit from therapy.<sup>42,43</sup> In any case, as shown in the sensitivity analysis, results were consistent when using the whole post-MI cohort. Finally, we evaluated relatively young patients who had been discharged from the hospital after MI and who were covered by a large national insurer, and our results may not be generalizable to patients with other conditions, older populations, or to those who receive health benefits through other means.

In conclusion, although explicit criteria exist for the development of performance measures so that they can accurately reflect health care quality,<sup>4</sup> our results suggest that further efforts are needed to prospectively validate and test measures. Although the current definition of the HEDIS measure for post-MI  $\beta$ -blocker adherence does seem to predict clinical outcomes, we identified other definitions that did so with at least the same accuracy. These optimal quality measures showed advantages of relevance for post-MI pa-

tient care, having a shorter time of assessment and therefore allowing for the implementation of quality improvement interventions in a more timely manner.

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