

# Are Co-Morbidities Associated with Guideline Adherence? The MI-Plus Study of Medicare Patients

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**BACKGROUND/OBJECTIVES:** The impact of co-morbid illnesses on adherence to guideline recommendations in chronic illness is of growing concern. We tested a framework [Piette and Kerr, *Diabetes Care*. 29(3):725–31, 2006] of provider adherence to guidelines in the presence of co-morbid conditions, which suggests that the effect of co-morbid conditions depends on treatment recommendations for the co-morbid conditions and how symptomatic they are.

**METHODS:** We conducted an exploratory analysis to assess the framework using chart audit data for 1,240 post-acute myocardial infarction (AMI) Medicare beneficiaries in Alabama. We assessed level of guideline-adherent post-AMI care from chart-based quality indicators and constructed scores reflecting how much care for the co-morbid condition was similar to post-AMI care (concordance) and how symptomatic the co-morbid condition is, based on expert opinion.

**RESULTS:** Patients had a mean age of 74 years, mean co-morbidities of 2, and 61% were white. Both concordance and symptomatic scores were positively associated with guideline compliance, with correlations of 0.32 and 0.14, respectively ( $p < 0.001$  for each). We found positive correlations between highly concordant co-morbid conditions and post-AMI quality scores and negative correlations between highly symptomatic conditions and post-AMI quality scores; both findings support the framework. However, the framework performed less well for conditions that were not highly concordant or highly symptomatic, and the magnitudes of the associations were not large.

**CONCLUSIONS:** The framework was related to the association of co-morbid conditions with adherence by providers to guideline-recommended treatment for post-AMI patients. The framework holds promise for evaluating and possibly predicting guideline adherence.

**KEY WORDS:** acute myocardial infarction; guideline adherence; co-morbid disease; multi-morbidity; older patients; theory testing.

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## BACKGROUND

In a recent conference report, Werner and colleagues<sup>1</sup> describe proceedings of a Society of General Internal Medicine conference focusing on methods of measuring quality of care for patients with multiple clinical conditions. Issues of multiple co-morbidities, particularly among elderly patients<sup>2–8</sup>, are beginning to receive attention, especially in diseases like diabetes, where the burden and mortality risk from co-morbidities may outweigh risks from the disease itself<sup>9–15</sup>. Despite disease burden due to other major diseases, including coronary artery disease<sup>16</sup>, there has been less examination of guideline-concordance behavior patterns for diseases other than diabetes.

Medicare patients who have suffered an acute myocardial infarction (AMI) often present to primary care physicians with multiple co-morbidities. Boyd estimates that 50% of all Medicare beneficiaries have at least two chronic diseases<sup>17</sup>, and within the PROSPER study population (elderly with established vascular disease), 61% had hypertension, 11% diabetes, and 28% smoked<sup>7</sup>. Optimal evidence-based care of such patients often involves the application of multiple guidelines, which adds complexity to the task of the primary care physician. At the same time, the concurrence of co-morbidities may increase patients' risk of subsequent AMI and death. Thus, patients with the most to gain from guideline-adherent care present the most challenge to the busy practitioner<sup>18,19</sup>. In addition, Boyd suggests that applying multiple guidelines to older patients may not be in the patient's best interest because of risks of polypharmacy and concomitant side effects<sup>20</sup>.

In a recent paper focused on diabetes, Piette and Kerr<sup>10</sup> describe a framework for conceptualizing how co-morbidities of different types might affect adherence both with guideline-recommended therapies and with patient self-care recommendations. They suggest that when treatment recommendations for health problems co-morbid with diabetes are on the same treatment pathway—when they are either very consistent with or at least pose no serious treatment conflict with guideline-recommended treatment for diabetes—patients are more likely

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to receive guideline-recommended treatment for diabetes. They also suggest that when co-morbid conditions have a greater symptom burden than diabetes, the co-morbid condition can dominate and have a negative impact on adherence to guideline-recommended care in diabetes.

Applying this framework to ambulatory post-AMI patients, the subject of our analysis, specific co-morbidities may have a differential impact on guideline adherence in ambulatory AMI patients. In particular, co-morbid diseases in which the drug treatment is not in conflict with the recommended drug treatment for post-AMI care (or, using the term from the Piette and Kerr paper, treatment for the co-morbid condition is *concordant* with post-AMI care), and where the diseases often co-occur, are likely to increase the chances of receiving appropriate treatment.

In this paper, we present data from a study focused on ambulatory patients with a history of AMI and their receipt of guideline-recommended therapies. We evaluate the framework in the context of AMI.

## CONCEPTUAL FRAMEWORK

Following Piette and Kerr, we conceptualized a co-morbid condition as “concordant” if it represented part of the same overall pathophysiologic risk profile and was likely to be part of the treatment and self-management plan for AMI. A condition was labeled “not concordant” if it did not directly represent part of the same overall pathophysiology and was not likely to be part of the direct treatment and self-management plan for AMI. We labeled a condition “symptomatic” if it commonly manifests symptoms, and “asymptomatic” if not. Table 1 shows our predictions regarding the association of these scores with post-AMI guideline-recommended treatment adherence.

## METHODS

The overall study was designed as a group-randomized controlled trial to test the effect of Internet-delivered physician education on physicians’ adherence to post-AMI guideline-recommended treatments. In this sub-analysis, we assessed effects of patient co-morbidities on receipt of these guideline-recommended treatments at baseline (before randomization and intervention).

### Sample

MI-Plus recruitment was targeted to community-based primary care physicians in Alabama caring for eight or more post-AMI patients. These physicians were identified by linking a database purchased from a commercial vendor (SK&A Information Services) by the Division of Continuing Medical Edu-

cation, University of Alabama School of Medicine, to Medicare claims data. The Quality Improvement Organization (QIO) for Alabama matched AMI cases to physicians by linking inpatient and outpatient claims files (1999–2004). AMI cases were identified using ICD-9 codes 410.xx (acute AMI) and 412.xx (old AMI). Most cases were identified using 410.xx, and all patients had had a hospital admission for an AMI within the 12 months prior to chart abstraction. We received only aggregated information with no patient identifiers. To be eligible for randomization, all physicians had to confirm at enrollment that they cared for Medicare post-AMI patients. Institutional Review Board approval for the study was granted from the University of Alabama at Birmingham.

A total of 1,240 patient charts from 139 physician offices were abstracted for the baseline measurement of performance of physicians in the MI-Plus study. Up to ten patient charts were abstracted for each physician by trained nurse abstractors, who collected demographic and clinical data using a computerized abstraction template. For quality assurance purposes, five percent of the charts were reabstracted for each treatment group with an overall inter-rater reliability rate of 91.3%.

### Variables Included in the Analysis

Relevant co-morbid conditions for each patient were collected using the chart problem list or the physician’s visit diagnosis in the office visit narrative. Co-morbid conditions of interest included those affecting cardiovascular risk and that have specific treatment guidelines, or whose presence may complicate treatment due to potentially conflicting drug regimens, or real or perceived contraindications to drug therapy indicated for post-AMI care. These include hypertension, hyperlipidemia, diabetes mellitus, current smoking, emphysema or asthma, depression, obesity, chronic kidney disease, and chronic heart failure. We defined obesity using height and weight data (body mass index  $\geq 30$  kg/m<sup>2</sup>), as well as using the ICD-9 diagnosis code for obesity. We accepted either.

We used indicators of adherence to guideline-recommended therapy that conform to widely used standards<sup>21,22</sup>, many of which have been shown to be associated with risk of mortality after AMI<sup>23</sup>. Broadly applicable indicators allow comparison of the same indicators of physician guideline adherence in patients with multiple co-morbidities and patients with no co-morbidities. MI-Plus indicators that meet this requirement include (1) aspirin use, (2) beta blocker use, (3) treatment for elevated low density lipoprotein cholesterol (LDL-c) using appropriate lipid lowering agents, and (4) use of angiotensin-converting enzyme inhibitors (ACE-I) for patients with diabetes and hypertension, or (5) use of ACE-I for patients with documented left ventricular dysfunction or chronic heart failure.

We constructed a composite quality score, which summarizes the individual indicators. For each patient, the score took a value of 1 for each indicator if one of these conditions was met: (1) there was information in the patient chart that the patient received the guideline-indicated therapy and they met the criteria for the indicator; (2) the patient was not eligible for the therapy either because of contraindication or because s/he did not meet the criteria for the indicator. Otherwise, the score took a value of 0. We summed scores for all five indicators, creating an ordinal variable valued between 0 and 5, where 0

**Table 1. Expected Relationships Among Two Key Dimensions of Piette and Kerr’s Framework**

	Concordant	Not concordant
Symptomatic	Very likely	?
Asymptomatic	?	Very unlikely

indicated that none of the indicators were met for that patient, even though some were indicated, and 5 meant that all indicated indicators were satisfied. If an indicator was not relevant to a particular patient, then their score would still be 5.

Finally, we considered the effect of combined co-morbid conditions on the quality score indicating the degree to which the patient received post-AMI guideline-recommended therapies. We created two separate counts of co-morbid conditions as follows: in the first, which we called the concordant score, we assigned weights to the nine co-morbid conditions. The weights varied from 1 to 3, where 1 implies low concordance and 3 implies high concordance. We created the weights by having six board-certified internal medicine clinicians rank the nine co-morbidities by degree of concordance, based on their clinical judgment as to the degree to which the treatment recommendations for each health problem were aligned with the treatment recommendations for post-AMI care or potentially discrepant, then split the rankings into three groups, assigning the three weights. In using this order to construct the score, we were attempting to build on the nature of comorbidity concordance with ischemic heart disease. Final scores were: 1 for chronic obstructive pulmonary disease/asthma and depression; 2 for smoking, obesity, depression, and chronic kidney disease; and 3 for hypertension, hyperlipidemia, diabetes, and chronic heart failure. In the second score, which we called symptomatic, we used a similar process to determine weights based on degree of expected symptoms, past or present, for each co-morbid condition. Final scores were: 1 for hypertension and hyperlipidemia; 2 for smoking, obesity, depression, and chronic kidney disease; and 3 for diabetes, chronic obstructive pulmonary disease/asthma, and chronic heart failure.

## Data Analysis

We analyzed data at the patient level. We assessed patient characteristics, grouping patients by the nine co-morbidities. We assessed associations between (1) concordant scores and quality scores, and (2) symptomatic scores and quality scores, respectively, using generalized linear models (GLM). We assessed bivariate relationships between each co-morbidity and each of the five quality indicators separately, using t-tests, comparing mean composite scores for patients without and with each of the conditions. Finally, we conducted multivariable regression analysis to examine quality scores, controlling for confounding by the following factors: sex, race (white/non-white), age (65–74, over 75 years old), and insurance status. We estimated three models: the concordance and symptomatic scores each separately, and both together.

We used generalized estimating equations (GEE) to correct for autocorrelation and adjusted all bivariate inferences for multiple comparisons using the Bonferroni correction. We also used Pearson's correlations to assess bivariate correlations.

## RESULTS

Mean age among all patients was 74 years; 40% were women, and 61% were white (Table 2). On average, patients had two co-morbid diseases. The most common co-morbidity was hypertension, followed by hyperlipidemia, diabetes, chronic heart

**Table 2. Characteristics of 1,240 Ambulatory Post-MI Patients and Their Scores for Guideline Adherence, Comorbidity Concordance, and Symptomatic Comorbidity: The MI-Plus Study**

Patient characteristics	
Mean age (SD)	74.2 (SD 9.9)
% Female	40%
% White	61%
Presence of comorbid diseases	
% with hypertension	73%
% with hyperlipidemia	61%
% with diabetes	37%
% current smoking	11%
% with emphysema/asthma	24%
% with depression	13%
% obese	23%
% with chronic kidney disease	11%
% with chronic heart failure	29%
Score values	
Mean quality score (SD) <sup>a</sup>	2.22 (1.21)
Mean concordance score (SD) <sup>b</sup>	7.10 (3.72)
Mean symptomatic score (SD) <sup>c</sup>	5.25 (3.37)

<sup>a</sup>Range 0–5; reflects adherence to five guideline-based indicators, with higher score signifying higher adherence

<sup>b</sup>Range 0–20; reflects concordance of patient's co-morbidities with post-AMI status (shared pathophysiology and management) with higher score signifying higher concordance; concordance weight for each comorbidity in Table 2

<sup>c</sup>Range 0–20; reflects extent to which co-morbidities are symptomatic, with higher score signifying higher concordance; concordance weight for each comorbidity in Table 2

failure, chronic obstructive pulmonary disease/asthma, obesity, depression, smoking, and chronic kidney disease.

We found that both the concordance and symptomatic scores are positively correlated with the composite quality score ( $p < 0.001$ ): as the concordance and symptomatic scores increase, so does the quality score. The correlation between the quality and concordance scores was 0.32 ( $p < 0.001$ ), and the correlation between the quality and symptomatic score was 0.14 ( $p < 0.001$ ).

Viewing each condition individually, performance on all post-AMI guideline-recommended indicators was fairly high, ranging from a low of 52% for beta-blocker treatment of patients with chronic obstructive pulmonary disease/asthma to a high of 88% for lipid-lowering treatment among patients with hyperlipidemia as a co-morbidity (Table 3). Using the quality score (0 to 5) to assess concordance with recommendations across all indicators simultaneously (Table 4), the mean score overall was 2.21 for the whole sample, and varied from 1.99 for patients with chronic obstructive pulmonary disease/asthma to 2.68 for patients with diabetes.

In multivariable analysis (Table 5), we found that each of the two scores was significantly and positively related to the quality score even after controlling for possible confounding variables. However, when we entered both together into the equation, the concordance score remains positively associated with the quality score, while the symptomatic score becomes negatively associated; both are still significant. In a fourth model, where we entered both concordance and symptomatic scores and their interaction, we found that both were significant, the symptomatic score remains negative, and the interaction term is negative and significant, but small in size (results not shown). We also determined that the change in sign was not due to multi-collinearity between concordance and symptomatic scores.

**Table 3. Adherence with Five Quality Indicators Used in the Composite Quality Score of Guideline Adherence by Co-Morbid Condition for 1,240 Ambulatory Post-AMI Patients in the MI-Plus Study**

	Condition (total N=1,240)								
	Hypertension	Hyperlipidemia	Diabetes	Current smoker	Chronic obstructive pulmonary disease	Depression	Obesity	Chronic kidney disease	Chronic heart failure
	n=879	n=730	n=445	n=128	n=289	n=158	n=273	n=134	n=345
Guideline concordance indicator									
Aspirin prescribed at discharge	76%	83%	75%	74%	73%	71%	72%	71%	74%
Beta blockers prescribed at discharge	63%	65%	65%	56%	52%	54%	58%	68%	68%
Lipid-lowering agent prescribed at discharge	75%	88%	80%	66%	63%	73%	78%	74%	69%
ACE inhibitors prescribed at discharge among diabetic patients	74%	76%	74%	73%	71%	62%	77%	67%	78%
ACE inhibitors prescribed at discharge among patients with chronic heart failure	75%	72%	67%	86%	71%	69%	80%	61%	72%

## DISCUSSION

The original framework proposed by Piette and Kerr<sup>10</sup> centered on diabetes as the chronic condition of interest. In our study, we centered on heart disease, and more specifically, on ambulatory treatment following an acute myocardial infarction. In our analysis, focused on care for patients who have recently had an AMI, we found that more concordant conditions, i.e., those with more pathophysiologic and management overlap with the post-AMI condition of interest in this analysis, increased the likelihood that patients received treatments recommended by guidelines for patients with ischemic heart disease; conversely, when co-morbid conditions were not concordant, guideline-recommended AMI treatments were less likely received. However, the expected associations between a condition being symptomatic and guideline adherence being higher were less consistent, and the magnitude of the associations was not large.

We find the Piette and Kerr framework useful for two reasons: first, it could help order co-morbid conditions and force more thoughtfulness about how patients with multiple chronic conditions could be treated. Second, by offering

testable propositions, if the framework has empirical foundation and if a direct link to improved outcomes is found, it could be used in the future to target patient groups or providers for education and knowledge translation activities to promote improved adherence to guideline recommendations. It can also provide a framework to improve the degree to which the guidelines take into account co-morbid conditions that are not concordant with post-AMI treatment guidelines, or attempt to improve recognition of asymptomatic conditions. For both these reasons, we believe that further investigation similar to ours, but focusing on different “centering” chronic conditions is essential. In addition, longitudinal studies in which temporal sequencing can be measured definitively are also important for establishing causality.

Issues of concordance depend heavily on which disease or health problem is the center of the investigation. To a patient who is classified “with diabetes” primarily, heart disease is a co-morbid condition. Conversely, to a post-AMI patient, diabetes is co-morbid. While the question of which disease is used to center the observations is important for assessing concordance of co-morbid conditions, it should not affect symptomatology of co-morbid conditions that are

**Table 4. Quality Scores and Their Difference for Patients With and Without Specific Co-Morbidities, Unadjusted Means**

Condition	Mean quality score for patients with condition	Mean quality score for patients without the condition	Difference	P value
Hypertension	2.37	1.91	0.45	<0.0001
Hyperlipidemia	2.56	1.75	0.81	<0.0001
Diabetes	2.68	1.99	0.69	<0.0001
Current smoker	2.07	2.26	-0.19	0.05
Chronic obstructive pulmonary disorder/asthma	1.99	2.33	-0.34	<0.0001
Depression	2.08	2.27	-0.19	0.04
Obesity	2.40	2.24	0.16	0.03
Chronic kidney disease	2.32	2.23	0.09	0.38
Chronic heart failure	2.31	2.22	0.10	0.16



Table 5. Adjusted Association Between Composite Quality Score and the Concordance/Symptomatic Scores

Variable	Model 1		Model 2		Model 3	
	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value
Female	-0.04	0.50	-0.05	0.45	-0.07	0.25
White	-0.10	0.38	-0.14	0.23	-0.07	0.48
Age 65–74	0.25	0.02	0.24	0.03	0.21	0.04
Age 75+	0.14	0.16	0.10	0.36	0.10	0.30
Have Medicare + Medicaid	-0.23	0.01	-0.26	0.01	-0.17	0.06
Have Medicare + other insurance	0.12	0.17	0.14	0.15	0.10	0.26
Concordance score	0.14	<0.0001	–	–	0.26	<0.0001
Symptomatic score	–	–	0.09	<0.0001	-0.15	<0.0001

**Notes:**

Model 1 includes the concordance score alone

Model 2 includes the symptomatic score alone

Model 3 includes both scores

characteristics of the co-morbid condition, not of the condition of focus. This observation may explain the unexpected findings in terms of symptomatology, in that the indicators on which the quality score for guideline adherence are based are focused on the post-AMI condition, not the co-morbidity. Because the post-AMI condition is, by definition, symptomatic in this group (even though in general, ischemic heart disease is often asymptomatic, these patients were recently diagnosed with AMI), one might not expect asymptomaticity of the co-morbid condition to diminish adherence to indicators for the post-AMI condition, as long as the co-morbidities are concordant. This is, indeed, what we observed with hypertension and hyperlipidemia.

Our finding that the sign on the symptomatic score changed direction when we included both concordance and symptomatic scores in the model suggests that there is a complex relationship between the two scores. The fact that neither interaction nor multi-collinearity explains this result leads us to conclude that including one score without the other in a model is likely to lead to omitted variable bias, or confounding. We do not have a clear explanation for this relationship, and we believe that this finding should be tested by others using more robust methods for obtaining the scores, as we note in our Limitations section. This relationship may be specific to post-AMI care and the set of co-morbid conditions that may affect guideline-recommended care specific to this health problem.

Despite the utility this framework might have for clinical practice in the future, we should perhaps also be seeking to develop a different kind of framework. The health-care community is beginning to acknowledge that the presence of multiple chronic conditions in an individual patient may alter the optimal approach to each of these conditions for that individual. A framework that would aid in prioritizing treatments *without* being centered on a single condition might be very useful clinically. While our symptomatic score is independent of the “centering” condition in a framework à la Piette and Kerr, our concordant score is clearly dependent on the centering condition. In parallel with efforts to refine the current model, we should also perhaps think about “meta-guidelines” that are not based on a single condition or diagnosis or on the simple juxtaposition of condition-specific guidelines.

## Limitations

There are limits on the generalizability of our findings. Our data come from one state and from patients whose physicians participated in the longitudinal study of an educational intervention to improve post-AMI care. Although this is a limitation, in the context of an exploratory study to assess the application of a new theoretical framework to understand characteristics of co-morbid conditions and adherence to guideline-recommended treatments, it is reasonable to begin with low generalizability. A more serious limitation is that we used a limited sample of clinicians to rate the co-morbid conditions to derive the weights used to score concordance and symptomatology. While this is a serious limitation, and a more robust exploration of the phenomenon we are investigating will require a more robust approach to assessing weights, we believe that our panel of clinicians was expert and that it is likely that replication will confirm most of the weights we used. There are also some issues related to contraindications for some post-AMI guideline recommendations, such as the possibility that clinicians may consider ACE inhibitors contraindicated in patients with chronic kidney disease. We believe that it is very important for further research to be conducted to assess the relationships we report in different post-AMI samples as well as in other chronic conditions. Finally, our analysis extends only to whether or not a guideline-recommended medication was prescribed, not whether or not it was taken by the patient. Full compliance with guideline-recommended therapies requires both provider and patient action. In this study, we could only assess provider action.

## Summary

A consensus is emerging that guidelines and evidence on which to base treatment decisions need to take into account the realities of highly co-morbid, complex patients being cared for by providers in our health-care systems. There are competing hypotheses that may explain some of these findings, and we believe that further investigation along these lines will yield promising new insights and approaches. Possible approaches may include the ability to target patient groups for more specific interventions to improve adherence to guideline-recommended care or the development of new guidelines that are not single condition-specific and may aid in prioritizing evidence-based treatment.

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