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ORIGINAL RESEARCH

An Electronic Order Set for Acute Myocardial Infarction Is Associated With Improved Patient Outcomes Through Better Adherence to Clinical Practice Guidelines

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BACKGROUND: Adherence to evidence-based recommendations for acute myocardial infarction (AMI) remains unsatisfactory.

OBJECTIVE: Quantifying association between using an electronic AMI order set (AMI-OS) and hospital processes and outcomes.

DESIGN: Retrospective cohort study.

SETTING: Twenty-one community hospitals.

PATIENTS: A total of 5879 AMI patients were hospitalized between September 28, 2008 and December 31, 2010.

MEASUREMENTS: We ascertained whether patients were treated using the AMI-OS or individual orders (a la carte). Dependent process variables were use of evidence-based care; outcome variables were mortality and rehospitalization.

RESULTS: Use of individual and combined therapies improved outcomes (eg, 50% lower odds of 30-day mortality for patients with ≥3 therapies). The 3531 patients treated using the AMI-OS were more likely to receive evidence-based therapies (eg, 50% received 5 different therapies vs 36% a la carte). These patients had lower 30-day mortality (5.7% vs 8.5%) than the 2348 treated using a la carte orders. Although AMI-OS patients' predicted mortality risk was lower (3.2%) than that of a la carte patients (4.8%), the association of improved processes and outcomes with the use of the AMI-OS persisted after risk adjustment. For example, after inverse probability weighting, the relative risk for inpatient mortality in the AMI-OS group was 0.67 (95% confidence interval: 0.52-0.86). Inclusion of use of recommended therapies in risk adjustment eliminated the benefit of the AMI-OS, highlighting its mediating effect on adherence to evidence-based treatment.

CONCLUSIONS: Use of an electronic order set is associated with increased adherence to evidence-based care and better AMI outcomes. *Journal of Hospital Medicine* 2014;9:155–161. © 2014 Society of Hospital Medicine

Although the prevalence of coronary heart disease and death from acute myocardial infarction (AMI) have declined steadily, about 935,000 heart attacks still occur annually in the United States, with approximately one-third of these being fatal.[1–3] Studies have demonstrated decreased 30-day and longer-term mortality in AMI patients who receive evidence-based treatment, including aspirin, β-blockers, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), anticoagulation therapy, and statins.[4–7] Despite clinical practice guidelines (CPGs) outlining evidence-based care and considerable efforts to implement processes that improve patient outcomes, delivery of effective therapy remains suboptimal.[8] For example, the Hospital Quality Alliance Program[9] found that in AMI patients, use of aspirin on admission was only 81% to 92%, β-blocker on admission 75% to 85%, and ACE inhibitors for left ventricular dysfunction 71% to 74%.

Efforts to increase adherence to CPGs and improve patient outcomes in AMI have resulted in variable degrees of success. They include promotion of CPGs,[4–7] physician education with feedback, report cards, care paths, registries,[10] Joint Commission standardized measures,[11] and paper checklists or order sets (OS).[12,13]

In this report, we describe the association between use of an evidence-based, electronic OS for AMI (AMI-OS) and better adherence to CPGs. This AMI-OS was implemented in the inpatient electronic medical records (EMRs) of a large integrated healthcare delivery system, Kaiser Permanente Northern California (KPNC). The purpose of our investigation was to determine (1) whether use of the AMI-OS was associated with improved AMI processes and patient outcomes, and (2) whether these associations persisted after risk adjustment using a comprehensive severity of illness scoring system.

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MATERIALS AND METHODS

This project was approved by the KPNC institutional review board.

Under a mutual exclusivity arrangement, salaried physicians of The Permanente Medical Group, Inc., care for 3.4 million Kaiser Foundation Health Plan, Inc. members at facilities owned by Kaiser Foundation Hospitals, Inc. All KPNC facilities employ the same information systems with a common medical record number and can track care covered by the plan but delivered elsewhere.[14] Our setting consisted of 21 KPNC hospitals described in previous reports,[15–18] using the same commercially available EMR system that includes computerized physician order entry (CPOE). Deployment of the customized inpatient Epic EMR (www.epicsystems.com), known internally as KP HealthConnect (KPHC), began in 2006 and was completed in 2010.

In this EMR's CPOE, physicians have options to select individual orders (a la carte) or they can utilize an OS, which is a collection of the most appropriate orders associated with specific diagnoses, procedures, or treatments. The evidence-based AMI-OS studied in this project was developed by a multidisciplinary team (for detailed components see Supporting Appendix 1–Appendix 5 in the online version of this article).

Our study focused on the first set of hospital admission orders for patients with AMI. The study sample consisted of patients meeting these criteria: (1) age $\geq$18 years at admission; (2) admitted to a KPNC hospital for an overnight stay between September 28, 2008 and December 31, 2010; (3) principal diagnosis was AMI (International Classification of Diseases, 9th Revision [ICD-9][19] codes 410.00, 01, 10, 11, 20, 21, 30, 31, 40, 41, 50, 51, 60, 61, 70, 71, 80, 90, and 91); and (4) KPHC had been operational at the hospital for at least 3 months to be included (for assembly descriptions see Supporting Appendices 1–5 in the online version of this article). At the study hospitals, troponin I was measured using the Beckman Access AccuTnI assay (Beckman Coulter, Inc., Brea, CA), whose upper reference limit (99th percentile) is 0.04 ng/mL. We excluded patients initially hospitalized for AMI at a non-KPNC site and transferred into a study hospital.

The data processing methods we employed have been detailed elsewhere.[14,15,17,20–22] The dependent outcome variables were total hospital length of stay, inpatient mortality, 30-day mortality, and all-cause rehospitalization within 30 days of discharge. Linked state mortality data were unavailable for the entire study period, so we ascertained 30-day mortality based on the combination of KPNC patient demographic data and publicly available Social Security Administration decedent files. We ascertained rehospitalization by scanning KPNC hospitalization databases, which also track out-of-plan use.

The dependent process variables were use of aspirin within 24 hours of admission, β-blockers, anticoagulation, ACE inhibitors or ARBs, and statins. The primary independent variable of interest was whether or not the admitting physician employed the AMI-OS when admission orders were entered. Consequently, this variable is dichotomous (AMI-OS vs a la carte).

We controlled for acute illness severity and chronic illness burden using a recent modification[22] of an externally validated risk-adjustment system applicable to all hospitalized patients.[15,16,23–25] Our methodology included vital signs, neurological status checks, and laboratory test results obtained in the 72 hours preceding hospital admission; comorbidities were captured longitudinally using data from the year preceding hospitalization (for comparison purposes, we also assigned a Charlson Comorbidity Index score[26]).

End-of-life care directives are mandatory on admission at KPNC hospitals. Physicians have 4 options: full code, partial code, do not resuscitate, and comfort care only. Because of small numbers in some categories, we collapsed these 4 categories into "full code" and "not full code." Because patients' care directives may change, we elected to capture the care directive in effect when a patient first entered a hospital unit other than the emergency department (ED).

Two authors (M.B., P.C.L.), one of whom is a board-certified cardiologist, reviewed all admission electrocardiograms and made a consensus determination as to whether or not criteria for ST-segment elevation myocardial infarction (STEMI) were present (ie, new ST-segment elevation or left bundle branch block); we also reviewed the records of all patients with missing troponin I data to confirm the AMI diagnosis.

Statistical Methods

We performed unadjusted comparisons between AMI-OS and non–AMI-OS patients using the *t* test or the χ^2 test, as appropriate.

We hypothesized that the AMI-OS plays a mediating role on patient outcomes through its effect on adherence to recommended treatment. We evaluated this hypothesis for inpatient mortality by first fitting a multivariable logistic regression model for inpatient mortality as the outcome and either the 5 evidence-based therapies or the total number of evidence-based therapies used (ranging from 0–2, 3, 4, or 5) as the dependent variable controlling for age, gender, presence of STEMI, troponin I, comorbidities, illness severity, ED length of stay (LOS), care directive status, and timing of cardiac catheterization referral as covariates to confirm the protective effect of these therapies on mortality. We then used the same model to estimate the effect of AMI-OS on inpatient mortality, substituting the therapies with AMI-OS as the dependent variable and using the same covariates. Last, we included both the therapies and the AMI-OS in the model to evaluate their combined effects.[27]

We used 2 different methods to estimate the effects of AMI-OS and number of therapies provided on the

outcomes while adjusting for observed baseline differences between the 2 groups of patients: propensity risk score matching, which estimates the average treatment effect for the treated,[28,29] and inverse probability of treatment weighting, which is used to estimate the average treatment effect.[30–32] The propensity score was defined as the probability of receiving the intervention for a patient with specific predictive factors.[33,34] We computed a propensity score for each patient by using logistic regression, with the dependent variable being receipt of AMI-OS and the independent variables being the covariates used for the multivariate logistic regression as well as ICD-9 code for final diagnosis. We calculated the Mahalanobis distance between patients who received AMI-OS (cases) and patients who did not received AMI-OS (controls) using the same set of covariates. We matched each case to a single control within the same facility based on the nearest available Mahalanobis metric matching within calipers defied as the maximum width of 0.2 standard deviations of the logit of the estimated propensity score.[29,35] We estimated the odds ratios for the binary dependent variables based on a conditional logistic regression model to account for the matched pairs design.[28] We used a generalized linear model with the log-transformed LOS as the outcome to estimate the ratio of the LOS geometric mean of the cases to the controls. We calculated the relative risk for patients receiving AMI-OS via the inverse probability weighting method by first defining a weight for each patient. [We assigned a weight of $1/ps_i$ to patients who received the AMI-OS and a weight of $1/(1-ps_i)$ to patients who did not receive the AMI-OS, where ps_i denotes the propensity score for patient i]. We used a logistic regression model for the binary dependent variables with the same set of covariates described above to estimate the adjusted odds ratios while weighting each observation by its corresponding weight. Last, we used a weighted generalized linear model to estimate the AMI-OS effect on the log-transformed LOS.

RESULTS

Table 1 summarizes the characteristics of the 5879 patients. It shows that AMI-OS patients were more likely to receive evidence-based therapies for AMI (aspirin, β-blockers, ACE inhibitors or ARBs, anticoagulation, and statins) and had a 46% lower mortality rate in hospital (3.51 % vs 6.52%) and 33% lower rate at 30 days (5.66% vs 8.48%). AMI-OS patients were also found to be at lower risk for an adverse outcome than non–AMI-OS patients. The AMI-OS patients had lower peak troponin I values, severity of illness (lower Laboratory-Based Acute Physiology Score, version 2 [LAPS2] scores), comorbidity burdens (lower Comorbidity Point Score, version 2 [COPS2] and Charlson scores), and global predicted mortality risk. AMI-OS patients were also less likely to have required intensive care. AMI-OS patients were at higher risk of death than non–AMI-OS patients with respect to only 1 variable (being full code at the time of admission), but although this difference was statistically significant, it was of minor clinical impact (86% vs 88%).

Table 2 shows the result of a logistic regression model in which the dependent variable was inpatient mortality and either the 5 evidence-based therapies or the total number of evidence-based therapies are the dependent variables. β-blocker, statin, and ACE inhibitor or ARB therapies all had a protective effect on mortality, with odds ratios ranging from 0.48 (95% confidence interval [CI]: 0.36-0.64), 0.63 (95% CI: 0.45-0.89), and 0.40 (95% CI: 0.30-0.53), respectively. An increased number of therapies also had a beneficial effect on inpatient mortality, with patients having 3 or more of the evidence-based therapies showing an adjusted odds ratio (AOR) of 0.49 (95% CI: 0.33-0.73), 4 or more therapies an AOR of 0.29 (95% CI: 0.20-0.42), and 0.17 (95% CI: 0.11-0.25) for 5 or more therapies.

Table 3 shows that the use of the AMI-OS is protective, with an AOR of 0.59 and a 95% CI of 0.45-0.76. Table 3 also shows that the most potent predictors were comorbidity burden (AOR: 1.07, 95% CI: 1.03-1.10 per 10 COPS2 points), severity of illness (AOR: 1.09, 95% CI: 1.07-1.12 per 10 LAPS2 points), STEMI (AOR: 3.86, 95% CI: 2.68-5.58), and timing of cardiac catheterization referral occurring immediately prior to or during the admission (AOR: 0.37, 95% CI: 0.27-0.51). The statistical significance of the AMI-OS effect disappears when both AMI-OS and the individual therapies are included in the same model (see Supporting Information, Appendices 1–5, in the online version of this article).

Table 4 shows separately the average treatment effect (ATE) and average treatment effect for the treated (ATT) of AMI-OS and of increasing number of therapies on other outcomes (30-day mortality, LOS, and readmission). Both the ATE and ATT show that the use of the AMI-OS was significantly protective with respect to mortality and total hospital LOS but not significant with respect to readmission. The effect of the number of therapies on mortality is significantly higher with increasing number of therapies. For example, patients who received 5 therapies had an average treatment effect on 30-day inpatient mortality of 0.23 (95% CI: 0.15-0.35) compared to 0.64 (95% CI: 0.43-0.96) for 3 therapies, almost a 3-fold difference. The effects of increasing number of therapies were not significant for LOS or readmission. A sensitivity analysis in which the 535 STEMI patients were removed showed essentially the same results, so it is not reported here.

To further elucidate possible reasons why physicians did not use the AMI-OS, the lead author reviewed 105 randomly selected records where the

TABLE 1. Description of Study Cohort

	Patients Initially Managed Using		
	AMI Order Set, N = 3,531[†]	A La Carte Orders, N = 2,348[†]	P Value*
Age, y, median (mean ±SD)	70 (69.4 ±13.8)	70 (69.2 ±13.8)	0.5603
Age (% >65 years)	2,134 (60.4%)	1,415 (60.3%)	0.8949
Sex (% male)	2,202 (62.4%)	1,451 (61.8%)	0.6620
STEMI (% with)[‡]	166 (4.7%)	369 (15.7%)	<0.0001
Troponin I (% missing)	111 (3.1%)	151 (6.4%)	<0.0001
Troponin I median (mean ±SD)	0.57 (3.0 ±8.2)	0.27 (2.5 ±8.9)	0.0651
Charlson score median (mean ±SD)[§]	2.0 (2.5 ±1.5)	2.0 (2.7 ±1.6)	<0.0001
COPS2, median (mean ±SD)[¶]	14.0 (29.8 ±31.7)	17.0 (34.3 ±34.4)	<0.0001
LAPS2, median (mean ±SD)[¶]	0.0 (35.6 ±43.5)	27.0 (40.9 ±48.1)	<0.0001
Length of stay in ED, h, median (mean ±SD)	5.7 (5.9 ±3.0)	5.7 (5.4 ±3.1)	<0.0001
Patients receiving aspirin within 24 hours[#]	3,470 (98.3%)	2,202 (93.8%)	<0.0001
Patients receiving anticoagulation therapy[#]	2,886 (81.7%)	1,846 (78.6%)	0.0032
Patients receiving β-blockers[#]	3,196 (90.5%)	1,926 (82.0%)	<0.0001
Patients receiving ACE inhibitors or ARBs[#]	2,395 (67.8%)	1,244 (53.0%)	<0.0001
Patients receiving statins[#]	3,337 (94.5%)	1,975 (84.1%)	<0.0001
Patient received 1 or more therapies	3,531 (100.0%)	2,330 (99.2%)	<0.0001
Patient received 2 or more therapies	3,521 (99.7%)	2,266 (96.5%)	<0.0001
Patient received 3 or more therapies	3,440 (97.4%)	2,085 (88.8%)	<0.0001
Patient received 4 or more therapies	3,015 (85.4%)	1,646 (70.1%)	<0.0001
Patient received all 5 therapies	1,777 (50.3%)	866 (35.9%)	<0.0001
Predicted mortality risk, %, median, (mean ±SD)**	0.86 (3.2 ±7.4)	1.19 (4.8 ±10.8)	<0.0001
Full code at time of hospital entry (%)[††]	3,041 (86.1%)	2,066 (88.0%)	0.0379
Admitted to ICU (%)[‡‡]			
Direct admit	826 (23.4%)	567 (24.2%)	0.5047
Unplanned transfer	222 (6.3%)	133 (5.7%)	0.3262
Ever	1,283 (36.3%)	1,169 (49.8%)	<0.0001
Length of stay, h, median (mean ±SD)	68.3 (109.4 ±140.9)	68.9 (113.8 ±154.3)	0.2615
Inpatient mortality (%)	124 (3.5%)	153 (6.5%)	<0.0001
30-day mortality (%)	200 (5.7%)	199 (8.5%)	<0.0001
All-cause rehospitalization within 30 days (%)	576 (16.3%)	401 (17.1%)	0.4398
Cardiac catheterization procedure referral timing			
1 day preadmission to discharge	2,018 (57.2%)	1,348 (57.4%)	0.1638
2 days preadmission or earlier	97 (2.8%)	87 (3.7%)	
After discharge	149 (4.2%)	104 (4.4%)	
No referral	1,267 (35.9%)	809 (34.5%)	

NOTE: **Abbreviations:** ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; AMI-OS, acute myocardial infarction order set; ARBs, angiotensin receptor blockers; COPS2, Comorbidity Point Score, version 2; CPOE, computerized physician order entry; ED, emergency department; ICU, intensive care unit; LAPS2, Laboratory-based Acute Physiology Score, version 2; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.

*χ^2 or *t* test, as appropriate. See text for further methodological details.

[†]AMI-OS is an evidence-based electronic checklist that guides physicians to order the most effective therapy by CPOE during the hospital admission process. In contrast, a la carte means that the clinician did not use the AMI-OS, but rather entered individual orders via CPOE. See text for further details.

[‡]STEMI as evident by electrocardiogram. See text for details on ascertainment.

[§]See text and reference 31 for details on how this score was assigned.

[¶]The COPS2 is a longitudinal, diagnosis-based score assigned monthly that integrates all diagnoses incurred by a patient in the preceding 12 months. It is a continuous variable that can range between a minimum of zero and a theoretical maximum of 1,014, although <0.05% of Kaiser Permanente hospitalized patients have a COPS2 exceeding 241, and none have had a COPS2 >306. Increasing values of the COPS2 are associated with increasing mortality. See text and references 20 and 27 for additional details on the COPS2.

[¶]The LAPS2 integrates results from vital signs, neurological status checks, and 15 laboratory tests in the 72 hours preceding hospitalization into a single continuous variable. Increasing degrees of physiologic derangement are reflected in a higher LAPS2, which can range between a minimum of zero and a theoretical maximum of 414, although <0.05% of Kaiser Permanente hospitalized patients have a LAPS2 exceeding 227, and none have had a LAPS2 >282. Increasing values of LAPS2 are associated with increasing mortality. See text and references 20 and 27 for additional details on the LAPS2.

[#]See text for details of specific therapies and how they were ascertained using the electronic medical record.

**Percent mortality risk based on age, sex, diagnosis, COPS2, LAPS2, and care directive using a predictive model described in text and in reference 22.

[††]See text for description of how end-of-life care directives are captured in the electronic medical record.

[‡‡]Direct admit means that the first hospital unit in which a patient stayed was the ICU; transfer refers to those patients transferred to the ICU from another unit in the hospital.

AMI-OS was not used, 5 records from each of the 21 study hospitals. This review found that in 36% of patients, the AMI-OS was not used because emergent catheterization or transfer to a facility with percutaneous coronary intervention capability occurred. Presence of other significant medical conditions, including critical illness, was the reason in 17% of these cases, patient or family refusal of treatments in 8%, issues around end-of-life care in 3%, and specific medical contraindications in 1%. In the remaining 34%, no reason for not using the AMI-OS could be identified.

TABLE 2. Logistic Regression Model for Inpatient Mortality to Estimate the Effect of Evidence-Based Therapies

	Multiple Therapies Effect		Individual Therapies Effect	
Outcome Number of outcomes	Death 277		Death 277	
	AOR*	95% CI†	AOR*	95% CI†
Age in years				
18–39	Ref		Ref	
40–64	1.02	(0.14–7.73)	1.01	(0.13–7.66)
65–84	4.05	(0.55–29.72)	3.89	(0.53–28.66)
85+	4.99	(0.67–37.13)	4.80	(0.64–35.84)
Sex				
Female	Ref			
Male	1.05	(0.81–1.37)	1.07	(0.82–1.39)
STEMI‡				
Absent	Ref		Ref	
Present	4.00	(2.75–5.81)	3.86	(2.64–5.63)
Troponin I				
≤0.1 ng/ml	Ref		Ref	
>0.1 ng/ml	1.01	(0.72–1.42)	1.02	(0.73–1.43)
COPS2§ (AOR per 10 points)	1.05	(1.01–1.08)	1.04	(1.01–1.08)
LAPS2§ (AOR per 10 points)	1.09	(1.06–1.11)	1.09	(1.06–1.11)
ED LOS¶ (hours)				
<6	Ref		Ref	
6–7	0.74	(0.53–1.03)	0.76	(0.54–1.06)
>=12	0.82	(0.39–1.74)	0.83	(0.39–1.78)
Code Status#				
Full Code	Ref			
Not Full Code	1.08	(0.78–1.49)	1.09	(0.79–1.51)
Cardiac procedure referral				
None during stay	Ref			
1 day pre adm until discharge	0.40	(0.29–0.54)	0.39	(0.28–0.53)
Number of therapies received				
2 or less	Ref			
3	0.49	(0.33–0.73)		
4	0.29	(0.20–0.42)		
5	0.17	(0.11–0.25)		
Aspirin therapy			0.80	(0.49–1.32)
Anticoagulation therapy			0.86	(0.64–1.16)
Beta Blocker therapy			0.48	(0.36–0.64)
Statin therapy			0.63	(0.45–0.89)
ACE inhibitors or ARBs			0.40	(0.30–0.53)
C Statistic	0.814		0.822	
Hosmer-Lemeshow *p* value	0.509		0.934	

NOTE: Abbreviations: ACE = angiotensin converting enzyme; ARB = angiotensin receptor blockers.

*Adjusted odds ratio.

†95% confidence interval.

‡ST-segment elevation myocardial infarction present.

§See text and preceding table for details on COmorbidity Point Score, version 2 and Laboratory Acute Physiology Score, version 2.

¶Emergency department length of stay.

#See text for details on how care directives were categorized.

TABLE 3. Logistic Regression Model for Inpatient Mortality to Estimate the Effect of Acute Myocardial Infarction Order Set

Outcome Number of outcomes	Death 277	
	AOR*	95% CI†
Age in years		
18–39	Ref	
40–64	1.16	(0.15–8.78)
65–84	4.67	(0.63–34.46)
85+	5.45	(0.73–40.86)
Sex		
Female	Ref	
Male	1.05	(0.81–1.36)
STEMI‡		
Absent	Ref	
Present	3.86	(2.68–5.58)
Troponin I		
≤0.1 ng/ml	Ref	
>0.1 ng/ml	1.16	(0.83–1.62)
COPS2§ (AOR per 10 points)	1.07	(1.03–1.10)
LAPS2§ (AOR per 10 points)	1.09	(1.07–1.12)
ED LOS¶ (hours)		
<6	Ref	
6–7	0.72	(0.52–1.00)
>=12	0.70	(0.33–1.48)
Code status#		
Full code	Ref	
Not full code	1.22	(0.89–1.68)
Cardiac procedure referral		
None during stay	Ref	
1 day pre adm until discharge	0.37	(0.27–0.51)
Order set employed**		
No	Ref	
Yes	0.59	(0.45–0.76)
C Statistic	0.792	
Hosmer-Lemeshow *p* value	0.273	

*Adjusted odds ratio.

†95% confidence interval.

‡ST-segment elevation myocardial infarction present.

§See text and preceding table for details on COmorbidity Point Score, version 2 and Laboratory Acute Physiology Score, version 2.

¶Emergency department length of stay.

#See text for details on how care directives were categorized.

**See text for details on the order set.

DISCUSSION

We evaluated the use of an evidence-based electronic AMI-OS embedded in a comprehensive EMR and found that it was beneficial. Its use was associated with increased adherence to evidence-based therapies, which in turn were associated with improved outcomes. Using data from a large cohort of hospitalized AMI patients in 21 community hospitals, we were able to use risk adjustment that included physiologic illness severity to adjust for baseline mortality risk. Patients in whom the AMI-OS was employed tended to be at lower risk; nonetheless, after controlling for confounding variables and adjusting for bias using propensity scores, the AMI-OS was associated with increased use of evidence-based therapies and decreased mortality. Most importantly, it appears that the benefits of the OS were not just due to increased receipt of individual recommended therapies, but to increased concurrent receipt of multiple recommended therapies.

TABLE 4. Adjusted Odds Ratio (95% CI) or Mean Length-of-Stay Ratio (95% CI) in Study Patients

Outcome	Order Set*	3 Therapies†	4 Therapies†	5 Therapies†
Average treatment effect‡				
Inpatient mortality	0.67 (0.52–0.86)	0.64 (0.43–0.96)	0.37 (0.25–0.54)	0.23 (0.15–0.35)
30-day mortality	0.77 (0.62–0.96)	0.68 (0.48–0.98)	0.34 (0.24–0.48)	0.26 (0.18–0.37)
Readmission	1.03 (0.90–1.19)	1.20 (0.87–1.66)	1.19 (0.88–1.60)	1.30 (0.96–1.76)
LOS, ratio of the geometric means	0.91 (0.87–0.95)	1.16 (1.03–1.30)	1.17 (1.05–1.30)	1.12 (1.00–1.24)
Average treatment effect on the treated§				
Inpatient mortality	0.69 (0.52–0.92)	0.35 (0.13–0.93)	0.17 (0.07–0.43)	0.08 (0.03–0.20)
30-day mortality	0.84 (0.66–1.06)	0.35 (0.15–0.79)	0.17 (0.07–0.37)	0.09 (0.04–0.20)
Readmission	1.02 (0.87–1.20)	1.39 (0.85–2.26)	1.36 (0.88–2.12)	1.23 (0.80–1.89)
LOS, ratio of the geometric means¶	0.92 (0.87–0.97)	1.18 (1.02–1.37)	1.16 (1.01–1.33)	1.04 (0.91–1.19)

NOTE: **Abbreviations:** CI, confidence interval; LOS, length of stay.

*Refers to comparison in which the reference group consists of patients who were not treated using the acute myocardial infarction order set.

†Refers to comparison in which the reference group consists of patients who received 2 or less of the 5 recommended therapies.

‡See text for description of average treatment effect methodology.

§See text for description of average treatment effect on the treated and matched pair adjustment methodology.

¶See text for details on how we modeled LOS.

Modern EMRs have great potential for significant improvements in the quality, efficiency, and safety of care provided,[36] and our study highlights this potential. However, a number of important limitations to our study must be considered. Although we had access to a very rich dataset, we could not control for all possible confounders, and our risk adjustment cannot match the level of information available to clinicians. In particular, the measurements available to us with respect to cardiac risk are limited. Thus, we have to recognize that the strength of our findings does not approximate that of a randomized trial, and one would expect that the magnitude of the beneficial association would fall under more controlled conditions. Resource limitations also did not permit us to gather more time course data (eg, sequential measurements of patient instability, cardiac damage, or use of recommended therapies), which could provide a better delineation of differences in both processes and outcomes.

Limitations also exist to the generalizability of the use of order sets in other settings that go beyond the availability of a comprehensive EMR. Our study population was cared for in a setting with an unusually high level of integration.[1] For example, KPNC has an elaborate administrative infrastructure for training in the use of the EMR as well as ensuring that order sets are not just evidence-based, but that they are perceived by clinicians to be of significant value. This infrastructure, established to ensure physician buy-in, may not be easy to replicate in smaller or less-integrated settings. Thus, it is conceivable that factors other than the degree of support during the EMR deployments can affect rates of order set use.

Although our use of counterfactual methods included illness severity (LAPS2) and longitudinal comorbidity burden (COPS2), which are not yet available outside highly integrated delivery services employing comprehensive EMRs, it is possible they are insufficient. We cannot exclude the possibility that other biases or patient characteristics were present that led clinicians to preferentially employ the electronic order set in some patients but not in others. One could also argue that future studies should consider using overall adherence to recommended AMI treatment guidelines as a risk adjustment tool that would permit one to analyze what other factors may be playing a role in residual differences in patient outcomes. Last, one could object to our inclusion of STEMI patients; however, this was not a study on optimum treatment strategies for STEMI patients. Rather, it was a study on the impact on AMI outcomes of a specific component of computerized order entry outside the research setting.

Despite these limitations, we believe that our findings provide strong support for the continued use of electronic evidence-based order sets in the inpatient medical setting. Once the initial implementation of a comprehensive EMR has occurred, deployment of these electronic order sets is a relatively inexpensive but effective method to foster compliance with evidence-based care.

Future research in healthcare information technology can take a number of directions. One important area, of course, revolves around ways to promote enhanced physician adoption of EMRs. Our audit of records where the AMI-OS was not used found that specific reasons for not using the order set (eg, treatment refusals, emergent intervention) were present in two-thirds of the cases. This suggests that future analyses of adherence involving EMRs and CPOE implementation should take a more nuanced look at how order entry is actually enabled. It may be that understanding how order sets affect care enhances clinician

acceptance and thus could serve as an incentive to EMR adoption. However, once an EMR is adopted, a need exists to continue evaluations such as this because, ultimately, the gold standard should be improved patient care processes and better outcomes for patients.

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References

1. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med*. 2010;362(23):2155–2165.
2. Rosamond WD, Chambless LE, Heiss G, et al. Twenty-two-year trends in incidence of myocardial infarction, coronary heart disease mortality, and case fatality in 4 US communities, 1987–2008. *Circulation*. 2012;125(15):1848–1857.
3. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125(1):e2–e220.
4. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *J Am Coll Cardiol*. 2007;50(7):e1–e157.
5. Antman EM, Hand M, Armstrong PW, et al. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2008;51(2):210–247.
6. Jernberg T, Johanson P, Held C, Svennblad B, Lindback J, Wallentin L. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. *JAMA*. 2011;305(16):1677–1684.
7. Puymirat E, Simon T, Steg PG, et al. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *JAMA*. 2012; 308(10):998–1006.
8. Motivala AA, Cannon CP, Srinivas VS, et al. Changes in myocardial infarction guideline adherence as a function of patient risk: an end to paradoxical care? *J Am Coll Cardiol*. 2011;58(17):1760–1765.
9. Jha AK, Li Z, Orav EJ, Epstein AM. Care in U.S. hospitals—the Hospital Quality Alliance program. *N Engl J Med*. 2005;353(3):265–274.
10. Desai N, Chen AN, et al. Challenges in the treatment of NSTEMI patients at high risk for both ischemic and bleeding events: insights from the ACTION Registry-GWTG. *J Am Coll Cardiol*. 2011;57:E913–E913.
11. Williams SC, Schmaltz SP, Morton DJ, Koss RG, Loeb JM. Quality of care in U.S. hospitals as reflected by standardized measures, 2002–2004. *N Engl J Med*. 2005;353(3):255–264.
12. Eagle KA, Montoye K, Riba AL. Guideline-based standardized care is associated with substantially lower mortality in medicare patients with acute myocardial infarction. *J Am Coll Cardiol*. 2005;46(7): 1242–1248.
13. Ballard DJ, Ogola G, Fleming NS, et al. Impact of a standardized heart failure order set on mortality, readmission, and quality and costs of care. *Int J Qual Health Care*. 2010;22(6):437–444.
14. Selby JV. Linking automated databases for research in managed care settings. *Ann Intern Med*. 1997;127(8 pt 2):719–724.
15. Escobar G, Greene J, Scheirer P, Gardner M, Draper D, Kipnis P. Risk adjusting hospital inpatient mortality using automated inpatient, outpatient, and laboratory databases. *Med Care*. 2008;46(3):232–239.
16. Liu V, Kipnis P, Gould MK, Escobar GJ. Length of stay predictions: improvements through the use of automated laboratory and comorbidity variables. *Med Care*. 2010;48(8):739–744.
17. Escobar GJ, Greene JD, Gardner MN, Marelich GP, Quick B, Kipnis P. Intra-hospital transfers to a higher level of care: contribution to total hospital and intensive care unit (ICU) mortality and length of stay (LOS). *J Hosp Med*. 2011;6(2):74–80.
18. Liu V, Kipnis P, Rizk NW, Escobar GJ. Adverse outcomes associated with delayed intensive care unit transfers in an integrated healthcare system. *J Hosp Med*. 2012;7(3):224–230.
19. International Classification of Diseases, 9th Revision-Clinical Modification. 4th ed. 3 Vols. Los Angeles, CA: Practice Management Information Corporation; 2006.
20. Go AS, Hylek EM, Chang Y, et al. Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *JAMA*. 2003;290(20):2685–2692.
21. Escobar GJ, LaGuardia J, Turk BJ, Ragins A, Kipnis P, Draper D. Early detection of impending physiologic deterioration among patients who are not in intensive care: development of predictive models using data from an automated electronic medical record. *J Hosp Med*. 2012;7(5):388–395.
22. Escobar GJ, Gardner M, Greene JG, David D, Kipnis P. Risk-adjusting hospital mortality using a comprehensive electronic record in an integrated healthcare delivery system. *Med Care*. 2013;51(5):446–453.
23. Kipnis P, Escobar GJ, Draper D. Effect of choice of estimation method on inter-hospital mortality rate comparisons. *Med Care*. 2010;48(5): 456–485.
24. van Walraven C, Escobar GJ, Greene JD, Forster AJ. The Kaiser Permanente inpatient risk adjustment methodology was valid in an external patient population. *J Clin Epidemiol*. 2010;63(7):798–803.
25. Wong J, Taljaard M, Forster AJ, Escobar GJ, van Walraven C. Derivation and validation of a model to predict daily risk of death in hospital. *Med Care*. 2011;49(8):734–743.
26. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613–619.
27. MacKinnon DP. Introduction to Statistical Mediation Analysis. New York, NY: Lawrence Erlbaum Associates; 2008.
28. Imbens GW. Nonparametric estimation of average treatment effects under exogenity: a review. *Rev Econ Stat*. 2004;86:25.
29. Rosenbaum PR. Design of Observational Studies. New York, NY: Springer Science+Business Media; 2010.
30. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28:24.
31. Robins JM, Rotnitzky A, Zhao LP. Estimation of regression coefficients when some regressors are not always observed. *J Am Stat Assoc*. 1994(89):846–866.
32. Lunceford JK, Davidian M. Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study. *Stat Med*. 2004;23(19):2937–2960.
33. Rosenbaum PR. Discussing hidden bias in observational studies. *Ann Intern Med*. 1991;115(11):901–905.
34. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998;17(19):2265–2281.
35. Feng WW, Jun Y, Xu R. A method/macro based on propensity score and Mahalanobis distance to reduce bias in treatment comparison in observational study, 2005. www.lexjansen.com/pharmasug/2006/publichealthresearch/pr05.pdf. Accessed on September 14, 2013.
36. Ettinger WH. Using health information technology to improve health care. *Arch Intern Med*. 2012;172(22):1728–1730.