# Outpatient Medication Use and Health Outcomes in Post–Acute Coronary Syndrome Patients

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**Objective:** To investigate the pattern of postdischarge evidence-based outpatient medication use and its impact on subsequent hospital readmissions in post–acute coronary syndrome (ACS) patients.

**Study Design:** Prospective observational study.

**Methods:** A telephone survey was conducted to collect information from discharge to 8 months after discharge for 433 patients hospitalized with a primary diagnosis of ACS in 5 mid-Michigan hospitals. The survey data were then merged with chart review data from the initial hospitalization. We first conducted a longitudinal descriptive analysis of the utilization patterns of patient self-reported medication use from discharge to the 8-month survey. Then, multivariable logit analysis was used to estimate the effect of post-ACS medication use on self-reported hospital readmission at 3 months and 8 months after discharge. Propensity score matching was used to counter the possible bias induced by self-selection of outpatient medication use.

**Results:** The pattern of outpatient medication use was dynamic. Most changes to medication regimens occurred within 3 months after discharge, with fewer changes in the subsequent 5 months. Taking a β-blocker, angiotensin-converting enzyme inhibitor, or angiotension receptor blocker significantly reduced the probability of hospital readmission 3 months after discharge. Propensity score matching produced similar statistically significant results. Rehospitalization within 3 months after discharge was a strong predictor of later hospital readmission up to 8 months.

**Conclusion:** Timely and appropriate medication adjustment in outpatient settings appears to be critically important to reduce hospital readmission among ACS patients.

***(Am J Manag Care. 2006;12:581-587)***

Cardiovascular disease is one of the major threats to people's health in the United States. Each year, acute coronary syndrome (ACS) episodes result in more than 1.4 million hospital admissions and 20% of deaths from all causes.[1] Randomized clinical trials have established a set of medications widely recognized to improve survival and quality of life of ACS patients. The national practice guidelines from the American College of Cardiology (ACC) and American Heart Association (AHA) promote continuous use of these evidence-based medications after ACS to prevent death and secondary complications.[2] These medications include angiotensin-converting enzyme inhibitors (ACEIs) (or angiotension receptor blockers [ARBs] as appropriate), β-blockers, lipid-lowering medications, and aspirin. Despite the general consensus regarding their clinical efficacy, previous research has consistently shown underprescription and inadequate utilization of these medications in outpatient clinical settings.[3-8] These problems have been attributed to inconsistent acceptance of practice guidelines as well as problems with coordination among inpatient physicians, outpatient physicians, pharmacists, patients themselves, and insurance companies.

Hospital discharge offers a major opportunity for quality improvement intervention, because it is the linkage point between inpatient care and outpatient care. ACC and AHA have particularly targeted discharge for application of practice guidelines to prescribe evidence-based medicines. Existing research is encouraging, suggesting that both filling prescriptions and adherence to cardiac medications are improved by complete hospital discharge recommendations.[3,9,10] However, outpatient care for ACS patients is more complicated than adherence versus nonadherence to discharge medications because of the complex healthcare environment and long-term course of follow-up. Patients may add, switch, or drop their discharge medications due to transfer of care to another physician, change in health condition, medication side effects, or changes in insurance coverage. Compared with the body of existing research that focuses on effectiveness of quality improvement interventions in hospitals,[3,11,12] little health services research has focused on outpatient care after an acute episode of cardiovascular disease to investigate patterns of long-term medication use and its impact on health outcomes in patients with ACS or acute myocardial infarction (AMI).



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This project was funded in part by the Agency for Healthcare Research & Quality grants R01 HS10531 and R01 HS09514-S1.

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The purposes of this investigation were to (1) analyze patterns of medication use from discharge to 8 months in patients with an initial ACS diagnosis in any of the 5 mid-Michigan hospitals participating in this study and (2) use multivariable regression analysis to investigate how the use of these medications affected subsequent rates of hospital readmission.

## METHODS

### Data

We evaluated postdischarge cardiovascular health behaviors and medication use in patients hospitalized for ACS in 5 mid-Michigan hospitals from 2002 to 2003. Inclusion criteria were aged 21 years or older, a working diagnosis of ACS or AMI in the medical record, and a documented serum troponin I level equal to or greater than the upper limits of normal for that hospital during hospitalization. Exclusion criteria included inability to speak English or complete study interviews or discharge to a nonhome setting.

The study data came from 2 sources: medical record review and postdischarge patient telephone survey. Demographic features, clinical examination results, in-hospital procedure, and most importantly, discharge medication data were collected from review of hospital medical records. All medical record data including medication use were collected by trained nurse chart abstractors supervised by the study community project manager. Each chart abstractor used a standard data collection sheet and made periodic reference to a chart abstraction manual concerning specific data fields and parameters. Ongoing chart abstractor team meetings were conducted to review and refine chart audit processes, and maintain reliability of data entry.

Posthospital telephone surveys lasting approximately 30 to 40 minutes were conducted by trained survey researchers from the Institute for Public Policy and Social Research of Michigan State University at 3 time points: after discharge from the index hospital (mean of 14.1 days after discharge [SD = 9.6 days]), 3 months after discharge, and 8 months after discharge. In the telephone interview, patients were asked by interviewers to collect the bottles of each of their currently used prescription medications and read off the names as well as the dosage of the medications. Interviewers also asked about changes in medication use, including adding, dropping, or switching medications since the prior interview. The hospital readmission also was reported, but differentiated from emergency department visits in the survey. Patients were specifically asked to tell interviewers whether they had ever visited a hospital emergency department and/or been admitted to a hospital for at least 1 night at 3 months and 8 months after their initial hospital discharge. However, the survey did not determine whether an emergency department visit led to a hospital readmission, or the specific reason for hospital readmission. Reasons for readmission, therefore, include cardiac and noncardiac diseases. Participation in any hospital- or home-based cardiac rehabilitation program was also assessed during the telephone survey, and patients were systematically asked about rehabilitation participation since the prior interview. Information related to health behaviors (eg, smoking, drinking) was also collected.

### Sample

A total of 719 patients were enrolled in the initial study, of whom 527 (73%) completed a postdischarge baseline interview. Among those who completed a baseline interview, 433 (82%) completed a 3-month interview, and 381 (88%) of these patients also completed an 8-month interview. Based on the Michigan vital statistics record, the mortality rate was very low (n = 10). No demographic features or hospital care variables differed between the survivors who dropped out of the survey and those who remained in the study. However, smoking, depression, and having better functional status were predictive of attrition, after adjusting for mortality. Because the focus of this study was the impact of evidence-based medication use on health outcomes for *post-ACS* patients, we included only the 433 patients who completed at least both a baseline interview and a 3-month follow-up interview.

### Measurements

Study measures came from the chart abstract and phone survey. Patients' demographic characteristics and clinical information, including diagnoses, comorbidities, clinical examination results, and discharge medication, were obtained from chart review. Although the baseline survey collected information about medication use shortly after discharge, we used medication prescribed at discharge as the more reliable measurement of medication availability. Outpatient medication use at 3 months or 8 months, hospital readmission, enrollment in rehabilitation services, and health-related behaviors came from the baseline, 3-month, and 8-month surveys.

We categorized the medications into 2 groups for this analysis: (1) *cardiac medications*, which are the drugs recommended by ACC and AHA to treat cardiovascular disease and its related symptoms, including ACEIs, ARBs, β-blockers, lipid-lowering medications (almost entirely comprised of statin medications), and aspirin and (2) all *other medications* prescribed for noncardiac-related clinical conditions.

Severity of ACS and general health status measures include ejection fraction, Duke Activity Status Index (DASI), and Charlson Comorbidity Index (CCI).[13] As an overall measure of cardiac functioning, ejection fraction was measured during the initial hospitalization, and hence was obtained from the chart review for the entire study sample and dichotomized at an ejection fraction less than or equal to 35%.[14,15] The DASI was used to measure patients' functional status. It is a weighted composite score computed from answers to questions about 12 activities of daily living of progressive intensity. DASI scores have been shown to be highly correlated with oxygen uptake on treadmill exercise,[16] and has adequate sensitivity to show clinical changes in physical function for both surgical cardiac patients[17,18] and nonsurgical cardiac patients.[19,20] In addition, this tool has been demonstrated to be significantly correlated with other measures of cardiovascular fitness.[21] Scale scores for the DASI range from 0 to 58.2 points, with a higher composite score indicating greater functional capacity. In our study, the 12 DASI daily activities were evaluated at baseline survey for each subject. We then calculated the DASI score based on the survey data.

CCI was used as the measurement of comorbidity.[13] Patients' composite CCI score was the weighted sum of the presence of 19 medical conditions documented in their medical record including diabetes, myocardial infarction, peripheral vascular disease, and so forth. The CCI score in this study was calculated by the comorbidities reported in the chart review.

**Descriptive Analyses**

We first performed a descriptive analysis of patterns of cardiac medication use and instances of postdischarge hospital readmission. The purpose of the descriptive analysis was to examine the dynamic features of postacute care for ACS, particularly changing patterns of outpatient prescription medication use.

**Multivariable Regression Analyses**

After the descriptive analysis, we performed multivariable logit regression modeling using Stata software (StataCorp, College Station, Tex) to estimate the association between cardiac medication use and hospital readmission at 3 months or 8 months after initial hospitalization for ACS patients. The dependent variables in the model were hospital readmission at 3 months or 8 months after discharge. The major independent variables included whether the patient reported using 1 or more selected cardiac medications—including ACEIs/ARBs, β-blockers, or both; lipid-lowering medications; or aspirin—by the time of the 3-month or 8-month surveys. Other independent variables included patient demographics (age, sex, race, marital status, years of education), socioeconomic status (whether a patient's household income was below the national poverty level), clinical and health status variables (ejection fraction, DASI, CCI), health-related behaviors (smoking, drinking), and participation in either formal or informal cardiac rehabilitation. We set the threshold of significance at $P = .1$ for the statistical analysis.

**Propensity Score Matching**

Our study is a prospective observational study, with surveys at 3 months and 8 months that captured information about the period preceding the interview. Without experimental assignment of medications to respondents, the use of postdischarge cardiac medications may correlate with health outcomes. For example, healthier patients or patients with more sufficient discharge medication are more likely to tolerate ACEIs and β-blockers, and they are also the ones who will have better outcomes, regardless of their medication use.[22-24] Therefore, we used the propensity score matching method to first predict the propensity to use ACEIs/ARBs or β-blockers at 3 months or 8 months conditional on patients' demographic features, health status (ejection fraction, DASI, CCI), and discharge medication. Then we compared the outcomes among patients who had the same propensity to receive postdischarge cardiac medications conditional on whether they *actually* used them or not using Epanechnikov kernel–based matching with the default bandwidth at 0.06 in Stata to calculate the average treatment effect of postdischarge medication use on hospital readmission. We also bootstrapped the standard errors of the average treatment effect with 1000 repetitions to test the significance of the average treatment effect.

## RESULTS

**Patients' Characteristics**

**Table 1** summarizes characteristics of the 433 patients who participated in both the discharge survey and the 3-month survey. The study sample included older adults with a mean age of more than 60 years (SD = 11.51 years); the majority (64%) were male. Approximately 15% of the sample had poor heart function, with ejection fractions less than or equal to 35%. The average DASI score at discharge was 32.48, which represented higher functional status than that found in the Bypass Angioplasty Revascularization Investigation study (mean DASI = 21).[25] The study sample showed a moderate average level of comorbidity, with an average CCI score of 1.65 and standard deviation of 1.31.

**Table 1.** Patients' Demographics and Health Status at Discharge (N = 433)

| Characteristic | Mean (SD) |
|---|---|
| Age, y | 60.13 (11.51) |
| Male | 64% |
| Race | |
| White | 78% |
| Black | 10% |
| Hispanic and other nonwhite | 12% |
| Marital status | |
| Married | 70% |
| Single | 3% |
| Divorced or separated | 15% |
| Widowed | 12% |
| Years of education | 12.65 (2.21) |
| Household income (in thousands of dollars) | 39.41 (3.55) |
| Clinical and general health status | |
| Ejection fraction ≤ 35% | 15% |
| DASI score | 32.48 (17.21) |
| CCI | 1.65 (1.31) |
| Cardiac health–related behavior | |
| Currently smoking | 10% |
| Former smoker | 55% |
| Currently drinking alcohol moderately | 73% |
| Currently drinking alcohol heavily | 6% |

DASI indicates Duke Activity Status Index; CCI, Charlson Comorbidity Index.

**Postdischarge Healthcare Utilization**

**Table 2** depicts the dynamic nature of the postdischarge healthcare, including cardiac medications, in greater detail. At discharge, 273 patients, approximately 65% of the sample, were on a β-blocker, and 230 were on an ACEI/ARB. At 3 months after discharge, these numbers increased, with 323 on a β-blocker and 268 on an ACEI/ARB. The number of people on a lipid lowering-medication increased from 283 at discharge to 310 at the 3-month interview. There was a minor increase in the number of patients on aspirin from 351 at discharge to 374 at 3 months.

For the 381 patients who completed the 8-month survey, we found the number of people on prescribed cardiac medications did not change appreciably from 3 months to 8 months, with 257 patients on a β-blocker at 3 months and 279 at 8 months. Similarly, the number of patients on an ACEI increased unsubstantially from 200 to 228. There were also minor changes in number of people on aspirin from the 3-month to the 8-month survey.

Most of the changes in medication use occurred between the index hospital discharge and the 3-month survey. For example, among the 323 patients who were on a β-blocker at 3 months after discharge, 65% of them had been discharged with a β-blocker, and 35% had added a β-blocker during this time interval. Among the 268 patients who were on an ACEI/ARB at the 3-month survey, 60% were discharged with an ACEI/ARB prescription, and 40% added this medication after discharge. Similarly, among the 208 people who were taking a lipid-lowering medication at the 3-month survey, 57% were discharged with a prescription, and 43% added it. The only type of medication with consistently high use was aspirin. For those who were on aspirin at 3 months, 94% were discharged with an aspirin recommendation.

A high percentage of patients reported taking cardiac medications at both the 3-month to the 8-month surveys. For example, 92% of the patients on a β-blocker at 8 months also reporting used it at the 3-month survey, and 83% of those on an ACEI/ARB used it at the time of the 3-month survey. Concerning inpatient care, 124 patients were readmitted to a hospital between discharge and 3 months, and 76 patients were readmitted between 3 months and 8 months. It is interesting to note that among the 76 patients who were hospitalized between 3 months and 8 months, 30 (40%) of these patients had been previously readmitted between discharge and the 3-month survey.

**Effect of Medication Use on Hospital Readmission**

The results of multivariable logit regression of outpatient prescription drug use on hospital readmission are shown in **Table 3**, demonstrating that patients who were taking a β-blocker or an ACEI/ARB at 3 months were significantly *less* likely to be readmitted to a hospital. Taking a β-blocker only (coefficient = 0.68, $P < .05$), an ACEI/ARB only (coefficient = 1.09, $P < .05$), or both (coefficient = −0.69, $P < .1$) all were associated with a lower probability of hospital readmission by 3 months after discharge. Use of β-blockers, ACEIs/ARBs, lipid-lowering medications, or aspirin did *not* have a significant effect on readmission rates between 3 months and 8 months. However, readmission to the hospital between discharge and 3 months did significantly predict hospitalization again at a later time (coefficient = 0.94, $P < .05$). As expected, health status/severity of illness was important. People with a lower ejection fraction (ejection fraction ≤35%, coefficient = 0.68, $P < .1$) or

**Table 2.** Dynamics of Postdischarge Healthcare for Patients With Acute Coronary Syndrome

| | From Discharge to 3-Month Survey | | From 3-Month to 8-Month Survey | |
|---|---|---|---|---|
| **Postdischarge Healthcare** | **Discharge (N = 433)** | **3 Months (N = 433)** | **3 Months (N = 381)** | **8 Months (N = 381)** |
| Report taking a β-blocker | 273 | 323 | 257 | 279 |
| Used to take a β-blocker and still taking it | | 65% of 323 | | 92% of 279 |
| Added a β-blocker | | 35% of 323 | | 8% of 279 |
| Report taking an ACEI or ARB | 230 | 268 | 200 | 228 |
| Used to take an ACEI/ARB and still taking it | | 60% of 268 | | 88% of 228 |
| Added an ACEI/ARB | | 40% of 268 | | 12% of 228 |
| Report taking a lipid-lowering medication | 256 | 208 | 168 | 195 |
| Used to take a lipid-lowering medication and still taking it | | 57% of 208 | | 86% of 195 |
| Added lipid-lowering medication | | 43% of 208 | | 14% of 195 |
| Report taking aspirin | 351 | 374 | 280 | 330 |
| Used to take aspirin and still taking it | | 94% of 374 | | 85% of 330 |
| Added aspirin | | 6% of 374 | | 15% of 330 |
| Readmitted to hospital | | 124 | | 76 |
| Readmitted to hospital in both time periods | | | | 30 |

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

higher DASI score (coefficient = –0.02, $P < .05$) were more likely to have had a hospital readmission by the time of the 8-month survey.

### Propensity Score Matching Results

The propensity score matching results are depicted in **Table 4**, together with the calculated analytical treatment effect from the logit regression. The average treatment effect of taking ACEIs/ARBs or β-blockers from propensity score matching is –0.158, with the bootstrapped standard error at 0.083 ($P < .1$). This means that, on average, the predicted probability of hospital readmission for those who take ACEIs/ARBs or β-blockers is 0.158 lower than the probability for those who don't take these medications. This result is very similar to the calculated average effect of taking β-blockers or ACEIs/ARBs on hospital readmission at 3 months obtained from the logit regression at –0.154, with an analytical standard error of 0.03 ($P < .05$). Therefore, the propensity score matching confirmed that after controlling for possible selection bias in postdischarge medication use due to either better health conditions or more sufficient discharge prescriptions, the use of ACEIs/ARBs or β-blockers at 3 months after discharge was still demonstrated to significantly reduce the probability of hospital readmission.

## DISCUSSION

From these results, we suggest that in addition to hospital discharge, the period within 3 months after discharge appears to be critical for initiating and/or adjusting medication therapy for ACS patients. Based on this study, most of the postdischarge adjustments in medications occurred during this time interval. Taking at least 1 type of β-blocker or ACEI/ARB within this period helped reduce significantly the probability of hospital readmission for ACS patients. Once patients were readmitted during this critical period, they were more likely to be admitted to the hospital a second time or more. Although we did not assess the relationship between mortality and outpatient medication use in this study, Mukherjee et al[26] found that the use of combination evidence-based medical therapies was independently and strongly associated with lower 6-month mortality in patients with ACS. Although we are not sure as to the exact mechanism, this study suggests that patients in this study were more likely to use their cardiac medica-

**Table 3.** Multivariate Logit Regression Results of Outpatient Medication Use on Hospital Readmission

| Postdischarge Healthcare | Coefficient (SE) Readmission at 3 Months (N = 433) | Readmission at 8 Months (N = 381) |
|---|---|---|
| Types of outpatient cardiac medication | | |
| β-Blocker only | −0.68* (0.38) | −0.14 (0.72) |
| ACEI/ARB only | −1.09† (0.46) | −0.56 (0.49) |
| Both ACEI/ARB and β-blocker | −0.69† (0.35) | 0.07 (0.29) |
| Lipid-lowering medication | −0.05 (0.20) | −0.12 (0.42) |
| Daily aspirin | −0.38 (0.34) | −0.15 (0.31) |
| Readmitted to hospital between discharge and 3-month survey | | 0.94* (0.31) |
| Health condition | | |
| Ejection fraction ≤35% | 0.28 (0.34) | 0.68 (0.38) |
| DASI score | −0.02* (0.01) | −0.02* (0.01) |
| CCI | −0.11 (1.08) | 0.13 (0.11) |
| Cardiac rehabilitation | | |
| Complete formal rehabilitation | −1.00* (0.47) | −1.25 (0.82) |
| Currently attending formal rehabilitation | 0.12 (0.32) | 0.32 (0.72) |
| Complete informal rehabilitation | −0.02 (0.87) | −0.52 (1.18) |
| Currently attending informal rehabilitation | −0.47† (0.23) | 0.31 (0.33) |
| Health behavior | | |
| Currently smoking | −0.14 (0.43) | 0.18 (0.51) |
| Former smoker | −0.14 (0.24) | −0.14 (0.34) |
| Drinking alcohol | −0.26 (0.24) | 0.27 (0.29) |
| Demographics | | |
| Age | −0.01 (0.01) | −0.01 (0.01) |
| Female | −0.04 (0.25) | −0.14 (0.32) |
| Black | −1.13† (0.64) | −0.22 (0.84) |
| Other nonwhite | 1.16* (0.54) | 0.27 (0.71) |
| Single, divorced, or separated | −0.49 (0.70) | −0.37 (0.94) |
| Widowed | 0.47 (0.70) | 1.19 (0.85) |
| Years of education | 0.01 (0.05) | 0.05 (0.07) |
| Income below poverty level | 0.07 (0.36) | −0.37 (0.47) |

*Statistically significant at the 95% confidence interval.
†Statistically significant at the 90% confidence interval.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DASI, Duke Activity Status Index; CCI, Charlson Comorbidity Index.

tions up to 8 months after hospital discharge and maintain better health conditions if they used them up to 3 months after discharge.

Such results also suggest that outpatient physicians could be as important for ACS patients as the inpatient physicians who write the discharge prescriptions. The outpatient physicians are responsible for the continuous care of ACS patients after their discharge from the hospital. Reviewing patients' health status, setting up reasonable recovery goals, and motivating patients to adhere to their discharge prescription or adjust their prescriptions to fit their health needs are critical tasks of outpatient physicians. Although other studies have shown the importance of hospital discharge medications, our results demonstrate that a focus on the months shortly after discharge may be equally important for attention to medication therapy.

We did not find that taking lipid-lowering medications had a significant effect on hospital readmission rates for up to 8 months after discharge. This may be because lipid-lowering medications need a longer time frame to show benefit. In general, hospital readmissions within several months after ACS are due to congestive heart failure, for which ACEIs/ARBs and β-blockers have more benefit. We did find that aspirin is efficacious in preventing hospital readmission with negative point estimates, but the results were not statistically significant. We suspect this is due to ceiling effects, as more than 80% of the patients were on aspirin constantly in this study.

This study does have some limitations. First, we experienced expected attrition in a sample of patients hospitalized for ACS (27% from baseline to the 8-month survey). During the follow-up period, better functional status but the presence of more depression and smoking were significant predictors of attrition. It is not possible to know whether our results held true for those who dropped out. Second, we did not know the reasons for rehospitalization from the self-report data. However, based on the statistically significant relationship between cardiac medication use, heart function measurement (ejection fraction, DASI), and the probability of hospital readmission, but the nonstatistically significant relationship between comorbidity measurement (CCI) and hospital readmission, it is possible that the majority of the hospital readmission in this study were due to cardiac-related conditions. Third, the propensity score matching confirmed the consistency of our estimation of the efficacy of cardiac medication use after discharge. However, we cannot determine the reason for the adjustment of prescription medication therapy between discharge and 3 months. Possible reasons include seeing a specialist versus an internist, the quality of care delivered by outpatient physicians, or the presence or absence of contraindications to any of the medications. Future research to specifically address these issues may provide further insight.

**Table 4.** Propensity Score Matching of the Effects of Cardiac Medication Use on Hospital Readmission at 3 Months After Discharge

| | Net Effects of ACEI/ARB or β-Blocker Use on Probability of Hospital Readmission |
|---|---|
| Propensity score matching (bootstrapped SE) | –0.158* (0.083) |
| Estimated average treatment effect (analytical SE) | –0.154† (0.03) |

*Statistically significant at the 90% confidence interval.
†Statistically significant at the 95% confidence interval.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

***Acknowledgment***

The authors wish to thank Manfred Strommel, PhD, for his contribution to the manuscript. We are also grateful to the 2 anonymous reviewers for their comments to improve this article. The authors take responsibility for any errors occurring in the manuscript.

## CONCLUSION

Our study sheds light on the association between medication use and health outcomes among ACS patients, showing the combined effect of discharge prescriptions and subsequent use of medications in outpatient clinical settings. The effort made by the outpatient physicians could be as important as that of the inpatient care physicians who write discharge prescriptions in promoting the use of outpatient medications shown previously to be effective for ACS patients. Further research on quality improvement interventions for chronically ill patients should focus on the outpatient care provided after acute inpatient events.

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