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Medication Adherence and Readmission In Medicare Myocardial Infarction

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Abstract

Objectives—To examine the relationship between 6-month medication adherence and 1-year down-stream heart-disease related readmission among patients who survived a myocardial infarction (MI).

Study Design—Retrospective, nested case-control analysis of Medicare fee-for-service beneficiaries who were discharged alive post-MI in 2008 (n = 168,882).

Methods—Patients in the case group had their first heart-disease related readmission post-MI discharge during 6-9 months and/or 9-12 months. We then used propensity score matching mechanism to identify patients in the control group who had similar characteristics, but did not have a readmission in the same time window. Adherence was defined as the average 6-month medication possession ratio (MPR) prior to the first date of the time-window of defining readmission.

Results—After controlling for demographic, insurance coverage and clinical characteristics, patients who had a heart-disease related readmission had worse adherence, with MPR of 0.70 and 0.74 in the case and control groups. Odds ratio of MPR 0.75 was 0.79 (95% CI 0.75-0.83) among those with a readmission relative to those without.

Conclusion—Our study shows that better 6-month medication adherence may reduce heartdisease related readmissions within a year after an MI.

According to the American Heart Association, 7.9 million Americans have a history of myocardial infarction (MI) and 450,000 deaths occur each year in the US because of new and recurrent MI.¹ Readmissions after MI are common and costly; for example, 30-day all-cause readmission after MI in 2006-2008 Medicare was 22.5%, 24.8%, and 23.0% among elderly White, Black, and Hispanic patients, respectively.^{2,3} Previous research on readmissions has focused primarily on 30-day all-cause readmission and has examined the association between readmissions and hospital-level factors. The focus on 30-day

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readmissions was stimulated in part because under the Affordable Care Act (ACA), Congress directed the Centers for Medicare & Medicaid Services (CMS) to reduce payments to hospitals with higher-than-expected 30-day readmission rates. However, as a recent article notes,⁴ the policymakers' emphasis on 30-day readmission may be misguided, because the majority of readmissions take place outside the 30-day window; and patientlevel factors outside the hospital's control may drive a considerable part of hospital readmission rates, especially for longer term readmission.

One key patient-level factor affecting readmission rates is believed to be patients' compliance to essential medications, including β -blockers, lipid-lowering agents, aspirins, and either an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker (ARB). Because these drugs have been shown very effective by clinical trials, they have become important components of lifelong medical therapy for these patients.⁵ Clinical guidelines now recommend that all patients with an acute MI receive these medications.⁶

Previous studies have shown that better medication adherence could reduce medical spending, ⁷⁻¹¹ partially due to reduced hospitalization and emergency department use. However, previous researchers measured adherence and expenditures concurrently. Adherence has to be measured during a specific time period, while as readmissions can occur at any time during that period. We expect that readmissions are more likely to be influenced by drug adherence a short time before the reference period. In other words, both adherence and the likelihood of readmission are time-dependent variables. To solve the problem of time dependent variables, we use a retrospective nested case-control study design to examine the relationship between adherence and readmission 1-year post MI. This method is commonly used in medicine and health service research, but it has not been used to study adherence and readmission. We hypothesize that patients with better 6-month adherence to essential medications used to treat MI are less likely to have down-stream readmissions related to heart diseases.

METHODS

Study design

The key challenge to studying the effect of adherence on readmission is that both adherence and the likelihood of readmission are time dependent variables and have to be measured during a specific period of time. For example, if we study the effect of 6-month adherence on the rates of readmission within 1-year post discharge, we cannot simply compare the 1year readmission rates among individuals with good or bad 6-month adherence. We need to ensure the time period used to measure adherence occurred within a reasonably short period before period in which we measure readmission, so we are more confident to infer the adherence affects readmission. We attempt to address time dependency using a nested casecontrol design because it allowed us to measure adherence before a readmission may have occurred. Specifically, we identified the case group as beneficiaries who had their first heartdisease related readmission post-MI discharge during two *pre-specified small time windows* within a year post MI: 6-9 months and 9-12 months post-MI. We chose a minimum of 6month follow-up period for two reasons: first, short-term readmissions (e.g., 30-day readmission) are more likely due to hospital factors than patient medication adherence;

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We then used propensity score matching mechanism to identify the control group as beneficiaries who had similar characteristics, measured by the observed covariates as in the case group, but did not have a readmission in the same time window. For both the case and control groups, the main exposure variable, adherence, was defined as the average 6-month medication possession ratio (MPR) prior to the first date of the time-window of defining readmission. The first heart-disease related readmission day for each beneficiary in the case group was used as the index date for two purposes: the start date from which we traced it back for 6-month to define adherence; the anchor date for the matched individuals in the control group to define adherence.

Data source and case/control groups

We used 2008 and 2009 pharmacy and medical claims data for all fee-for-service Medicare beneficiaries with Parts A, B, and D coverage who had an MI in 2008. MI was defined as having at least 1 inpatient claim with a primary or secondary diagnosis code as ICD9 410.X1 by the Centers for Medicare & Medicaid Services' chronic condition warehouse.

We first identified beneficiaries who (1) were discharged alive and on studied medications after an MI in 2008, (2) had a heart-disease related readmission (primary and secondary ICD9 diagnosis codes 390 - 459), and (3) were enrolled in a stand-alone Part D plan continuously for 6 months after the discharge index date (first discharge date for MI in 2008). We excluded those patient who were readmitted within the first 6 months after discharge or who died.

Propensity score matching

Adjustment variables—To ensure that the case and control groups are comparable, we used propensity score matching method. In calculating propensity scores, we first conducted a logistic model with the response variable as having a heart-disease related readmission between 6 to 9 months post discharge index date (i.e., an indicator for case/control groups). In the model, we accounted for individual-level characteristics for demographic, insurance coverage, and health status. The demographic variables included gender, age group (from 34 years of age, 35 to 50, 51 to 64, 65 to 74, 75 to 84, and 85), and race or ethnic group (non-Hispanic White, non-Hispanic Black, Hispanic, Asian, and others/unknown, all relative to White). Part D data have an enhanced Research Triangle Institute Race Code verified by first and last name algorithms which is much more accurate than the usual race variable found in claims data.¹² We also included information on whether the beneficiary qualified for Medicare because of disability.

The data included two additional insurance variables: whether the beneficiary had Medicaid (was dual-eligible) and/or received a low income subsidy (LIS). These two variables provide information on the beneficiary's income as well as the amount of copayment and premium subsidies they receive. The income of the median dual eligible is 75 percent of the federal poverty level [FPL] although there is some variation across states; while the incomes of the

beneficiaries in the LIS group are below 150% FPL. Thus, the income in the non-LIS group is above 150% FPL. However, since the majority of beneficiaries in the LIS group also have some Medicaid coverage we created three mutually exclusive income categories: duals, non-dual LIS, and non-LIS.

The health status variables included two prospective risk scores: the CMS Hierarchical Condition Category (CMS-HCC) scores and the analogous scores for prescription drugs (CMSRxHCC). These risk scores were calculated using the diagnoses and spending in the year prior to the discharge index date. We calculated the prospective risk scores using prior-year diagnoses, except for the 2.3% of the sample who are new enrollees, for whom we use concurrent risk scores based on age and gender.¹³ Risk scores represent a proxy for health status, with higher scores indicating greater severity of illness and higher expected health care utilization. We included two additional health status indicators: one for a history of prior MI, and the other for institutionalization, defined as 90 days of care in a nursing home. Our sample represents community-residing beneficiaries; less than 0.1% spent over 90 days in nursing home facilities. Because Part D data include drugs used in nursing homes, we did not exclude these individuals.

Finally, the model accounted for ZIP Code level income and education: logarithm of the median household income within the ZIP Code in which the beneficiary lived, and educational level (percentages of residents in the ZIP Code who had not completed high school, had completed high school only, and had attended or completed college).

Nearest neighbor 1:5 matching—We used the nearest neighbor 1 to 5 matching with replacement, restricting the difference in propensity scores to be within 0.001. When using 6-9 month as a window for readmission, we had 7,264 cases and 68,074 potential controls. We were able to match 6,864 cases. Our final sample included these 6,864 cases and 33,726 controls. (We had 404 cases with fewer than 5 controls). When using 9-12 month as the window for readmission, we had 5,377 total cases and 61,500 potential controls. We were able to match 5,184 cases and our final sample includes these cases and 25,843 controls.

Measurement of adherence

We calculated 6-month adherence tracing back from the readmission date for 6 months. Because the control group did not have a readmission date; we traced back from the anchor date, defined above, for 6 months to determine 6 month adherence. In addition, we constrained beneficiaries to be continuously enrolled in stand-alone Part D plan during the 6-month MPR measurement periods. As a result, the total sample size dropped from 40,590 to 40,245 for the 6-9 readmission window and from 31,027 to 30,265 for the 9-12 readmission window.

Two adherence measures were created: one for β -blockers and the other for all three subclasses used to treat MI: β -blockers, statins, and ACEIs/ARBs. We measured adherence for only β -blockers separately because the 6-month persistent use of β -blockers post MI is a Healthcare Effectiveness Data and Information Set (HEDIS) quality measure. We did not measure adherence for aspirins because aspirins are usually purchased without a prescription (over-the-counter) and therefore are not included in Part D claims data.

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Adherence was measured by medication possession ratios (MPR). MPR was defined as the ratio of days of supply of medication the patient had in possession (numerator) over the number of days in the measurement period multiplied by the number of medications prescribed (denominator). Since we include several different medications into one MPR measurement, we only count medications in the denominator after the initial prescription following hospital discharge. For example, suppose a patient filled her first β -blocker prescription on 1/1/08 and her first ACE prescription on 2/1/08. Her MPR would be the number of β -blocker pills in first month divided by 30, while her MPR for the subsequent months would be her number of β -blocker pills plus the number of ACE pills divided by 60. We then defined two indicators for good adherence (first indicator: 1=MPR 0.80; 0=otherwise; second indicator: 1=MPR 0.75; 0=otherwise), two commonly used thresholds.^{11,14} We tested excluding the days in the hospital stay for any reason from the denominator when calculating the MPR because medications used in the hospital cannot be observed in the Part D event data (the results are very similar as not excluding hospital days because we only measure 6-month adherence). Prescriptions filled during the nursing home stay, however, can be observed in Part D data.

Statistical analysis after matching

We tested the distribution of MPR and found that MPR is not normally distributed. Thus, after propensity score matching, we performed two types of regressions: a rate logistic regression and a binary logistic regression. In the rate logistic regression, the dependent variable is 6-month MPR ranging from 0 to 1. In the binary logistic regression, the dependent variable is the indicator for good adherence – we tested separately for MPR 0.8 and MPR 0.75. Robust standard errors were used to adjust for the dependence within matched group.

In both models, the key independent variable is the indicator for being in the case or control group; that is, whether one had a heart-disease related readmission during the time window. We also controlled for all the covariates used in calculating propensity scores. We then applied a doubly robust procedure in estimating covariate effects in the main outcome models (the two types of logistic regression models). The resulting estimators give unbiased estimates of covariate effects when either propensity core or main outcome model is correctly specified, thus allowing the analyst two opportunities for obtaining accurate results (doubly robust). The assumption of no unmeasured confounders is still required.¹⁵

Finally, with this study design, the regression results provide the probability of having good adherence conditional on whether one had a readmission. However, the probability of having a readmission conditional on whether one is a good adherent or not is the core policy relevant variable. Thus, we used Bayesian probability theory to calculate the probabilities of having readmission given whether one was a good adherent or not. We calculated these separately for each time window and adherence measure.

RESULTS

The comparisons of characteristics between the case and control groups before and after propensity score matching are summarized in Table 1 (6-9 months cohort) and Table 2 (9-12

months cohort). Most characteristics are comparable between case and control groups after matching. For the characteristics that are statistically-significantly different between the cases and the controls, the magnitude of the difference is small. In the 6-9 months cohort, about 15% of our sample were younger than 65; 43% were female; and 14% had a history of MI prior to 2008.

Effects of 6-month adherence on the downstream readmission

Both rate (Table 3) and logistic (Table 4) regressions confirm that patients with downstream heart-disease related readmissions had poorer adherence for β -blockers, ACEIs/ARBs, and statins prior to readmission. These results are after adjustment of all the patient-level and ZIP-Code level covariates discussed above. In particular, in the 6-9 month cohort, as shown in Table 3, the rate regressions demonstrate that the MPRs for all MI drugs were lower among those with a down-stream readmission, 0.70 in the case relative to 0.74 in the control after adjustment for all covariates. Adherence to β -blockers was slightly better, with means of 0.75 and 0.78 in the case and control groups. The results from our 9-12 months analyses were similar.

Similarly, logistic regressions shown in Table 4 demonstrate that the odds ratio of having MPR>=0.80 for all MI drugs was 0.78 (95% CI 0.74-0.83) in the case group relative to that in the control group; the analogous odds ratio for β -blockers was 0.84 (95% CI 0.79-0.89) (Table 4). The results were similar when we used MPR>=0.75 as a threshold for good adherence. Results are robust in the sensitivity analysis in the 9-12 month cohort.

Probability of having a heart-disease related readmission conditional on adherence status

The first two columns of Table 5 report the probability of having good adherence conditional on whether one had a readmission or not. These numbers were estimated from the logistic regressions after adjustment of the variables used in the propensity score matching. The last two columns of Table 5 report the probability of having a readmission conditional on whether one was a good adherent or not, converted using Bayes' rule. For example, the probability of having a readmission 6-9 months post-MI discharge was 8.6% for beneficiaries with good adherence (MPR>=0.75) for all MI drugs, whereas the probability was 10.7% for those beneficiaries with MPR<0.75.

DISCUSSION

We found that patients with better adherence for MI drugs had lower downstream heartdisease related readmission rates, after controlling for observed patient-level and ZIP-Code level characteristics. Using the Medicare population who had a recent history of MI, our study demonstrates that medication adherence is an independent factor associated with lower downstream readmission after adjustment for other patient characteristics.

Few studies have examined readmission after 30-day post discharge. One study by Jencks and colleagues noted that among all Medicare fee-for-service beneficiaries in 2003-2004, the accumulative rate of rehospitalizations within 3-month post-discharge regardless of medical conditions was 34.0%; the accumulative rate within 6-month rate was 47.9%; and

12-month post-discharge was 59.4%.¹⁶ Our study shows that better medication adherence can potentially reduce readmission and therefore may save money for Medicare.

Our study has some limitations. First, because there was not random assignment to the case and control groups, we used a propensity score matching method. However, there may have been unobserved variables that were related to both adherence and readmission, which may have biased our estimates. Second, our matching algorithm was not perfect. Even after matching, the case and control groups differed significantly on risk scores, but the magnitude was small. Third, there may be some errors with measuring adherence using claims data; we cannot observe patients who were prescribed a drug but refused to take it. , we cannot observe all contradictions to the studied drugs; e.g. we cannot see measures such as left ventricular ejection fraction (LVEF) and LDL-C, a contradiction to ACEI. We assumed that if we see a prescription filled in the claims for an ACEI, the physician who prescribed the drug had evaluated patient's profile for contraindications. We also cannot distinguish whether an MI is an ST-segment elevation (STEMI) or not. Finally, claims data do not have individual level demographic variables such as education and income, but we used Zip Code level data.

Beginning in 2013, hospitals will receive decreased Medicare payments if they have higherthan-expected 30-day readmission rates for MI, heart failure, and pneumonia. Under ACA, the list of conditions will be expanded. We found that patient compliance to medication treatment is a significant, independent predictor of readmission occurring 6-month after discharge. This implies that patients need to be monitored past the 30-day time period regarding their medication use.

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Take-Away Points

This study demonstrates that patient's good adherence to essential myocardial infarction (MI) medications is a key factor to prevent readmission occurring 6-month to 1-year after discharge and suggests that clinicians need to pay attention to outpatient medication adherence after inpatient discharge.

- The probability of having a preventable readmission 6-12 months post-MI discharge was much lower for beneficiaries with good adherence to all MI drugs, compared to those with poor adherence.
- Outpatient physicians should pay more attention to medication adherence among MI survivors to prevent readmission in the first year after discharge.

Summary of Characteristics in Our Study Cohorts Before and After Propensity Score Matching Among Beneficiaries with the First Readmission 6-9 Months Post Discharge and Their Matched Controls

		Before Matching			After Matching		
		Readmission		P- value	Readmission		P- value
		No	Yes	No	Yes		
N		68,074	7,150		33,381	6,864	
Female, %		45.2	43.1	<.001	42.4	42.7	0.60
	White	81.4	77.1	<.001	78.0	77.5	0.44
	Black	9.0	12.5	<.001	12.0	12.5	0.23
	Hispanic	6.2	6.9	0.02	6.5	6.6	0.90
Race, %	Asian	2.0	2.1	0.83	2.1	2.0	0.74
	Native	0.6	0.7	0.18	0.7	0.7	0.84
	Others	0.7	0.7	0.75	0.7	0.7	0.70
	<35	0.2	0.1	0.22	0.1	0.1	0.93
	35-50	3.4	3.2	0.31	3.0	3.1	0.51
	51-64	10.6	12.4	<.001	12.1	12.3	0.62
Age, %	65-74	31.8	26.6	<.001	25.4	26.6	0.02
	75-84	32.7	33.2	0.41	33.8	33.1	0.26
	>85	21.3	24.4	<.001	25.7	24.8	0.10
Dual eligible		40.7	48.2	<.001	48.4	48.0	0.49
Non-dual LIS, <150% FPL		7.4	7.0	0.32	7.7	7.0	0.06
Disabled, %		14.1	15.7	<.001	15.1	15.5	0.44
Pre MI, %		8.4	13.9	<.001	12.8	13.7	0.02
More than 90 days in SNF, %		0.1	0.1	0.10	0.1	0.1	0.39
	RxHCC	1.1	1.2	<.001	1.2	1.2	0.005
Risk scores	CMS-HCC	2.0	2.4	<.001	2.3	2.4	<.001
	Percent of high school	57.6	57.4	0.24	57.4	57.4	0.97
Zip-Code	Percent of college	21.2	20.6	0.001	20.6	20.6	0.99
Level	Log of median household income	10.6	10.6	<.001	10.6	10.6	0.84

Abbreviations: MI = myocardial infarction; LIS = low-income subsidy; FPL = Federal Poverty Line; RxHCC = Prescription drug Hierarchical Condition Category risk scores, and CMS-HCC = Centers for Medicare & Medicaid Services - Hierarchical Condition Category risk scores.

Summary of Characteristics in Our Study Cohorts Before and After Propensity Score Matching Among Beneficiaries with the First Readmission 9-12 Months Post Discharge and Their Matched Controls

		Before Matching		After Matching			
		Readmission		P-value	Readmission		P- value
		No	Yes		No	Yes	
N		61,500	5,377		25,081	5,184	
Female, %		45.3	44.9	0.54	42.4	44.6	0.003
	White	81.7	78.7	<.001	79.5	79.0	0.40
	Black	8.8	11.1	<.001	10.9	11.0	0.75
	Hispanic	6.1	6.9	0.04	6.5	6.7	0.71
Race, %	Asian	2.1	2.0	0.68	1.9	2.0	0.64
	Native	0.5	0.7	0.23	0.7	0.7	0.92
	Others	0.8	0.7	0.45	0.6	0.7	0.37
	<35	0.1	0.3	0.01	0.2	0.3	0.30
	35-50	3.5	3.4	0.81	3.2	3.3	0.77
	51-64	10.6	10.9	0.51	10.4	10.7	0.49
Age, %	65-74	32.3	28.7	<.001	27.9	28.7	0.21
	75-84	32.8	32.3	0.43	32.4	32.3	0.95
	85	20.7	24.5	<.001	25.9	24.6	0.05
Dual eligibles, %		40.0	45.7	<.001	46.3	45.7	0.42
Non-dual LIS,	150% FPL, %	7.4	7.7	0.42	6.8	7.6	0.03
Disabled, %		14.2	14.6	0.45	13.9	14.3	0.37
Pre MI, %		7.9	13.2	<.001	12.5	13.2	0.07
More than 90 days in SNF, %		0.1	0.1	0.38	0.1	0.1	0.88
	RxHCC	1.1	1.2	<.001	1.2	1.2	0.57
Risk scores	CMS-HCC	2.0	2.3	<.001	2.3	2.3	0.07
	Percent of high school	57.6	57.4	0.09	57.6	57.3	0.07
Zip-Code	Percent of college	21.2	20.7	0.005	20.6	20.7	0.71
Level	Log of median household income	10.6	10.6	0.08	10.6	10.6	0.28

Abbreviations: MI = myocardial infarction; LIS = low-income subsidy; FPL = Federal Poverty Line; RxHCC = Prescription drug Hierarchical Condition Category risk scores, and CMS-HCC = Centers for Medicare & Medicaid Services - Hierarchical Condition Category risk scores.

Comparison of Medication Possession Ratios Between Beneficiaries with and without a Heart-Disease Related Readmission, Results from Rate Regressions

Estimated Medication Possession Ratios Using Results From Rate Regressions

		6-9 Months	9-12 Months
All MI Drugs	With Readmission	0.70	0.70
	Without Readmission	0.74	0.74
B-Blockers	With Readmission	0.75	0.77
	Without Readmission	0.78	0.80

Odds Ratios of Fully Adherent Among Beneficiaries with a Heart-Disease Related Readmission Relative to Those Without a Readmission, Results from Logistic Regressions

	Odds Ratio	Std. Error	95% CI			
First Readmission Occurring During 6-9 Months Post-MI Discharge						
MPR >=0.75 for All MI Drugs	0.79	0.02	(0.75, 0.83)			
MPR >=0.75 for β -Blockers	0.83	0.03	(0.79, 0.89)			
MPR >=0.80 for All MI Drugs	0.78	0.02	(0.74, 0.83)			
MPR >=0.80 for β -Blockers	0.84	0.03	(0.79, 0.89)			
First Readmission Occurring During 9-12 Months Post-MI Discharge						
MPR >=0.75 for All MI Drugs	0.74	0.02	(0.70, 0.79)			
MPR >=0.75 for β -Blockers	0.81	0.03	(0.75, 0.87)			
MPR >=0.80 for All MI Drugs	0.73	0.02	(0.68, 0.77)			
MPR >=0.80 for β -Blockers	0.79	0.03	(0.74, 0.85)			

Notes: The dependent variable is the indicator for good adherence – we tested separately for MPR 0.8 and MPR 0.75. The covariates include individual-level characteristics for demographic, insurance coverage, and health status, as well as ZIP Code level income and education (see the Adjustment Variables section).

Probability of Having a Heart-Disease Related Readmission Conditional on Medication Adherence, Using Bayesian Probability Theory

	Prob. (Good Adherence No Readmission)	Prob. (Good Adherence Readmission)	Prob. (Readmission Good Adherence) ^a	Prob. (Readmission Bad Adherence) ^{<i>a</i>}			
First Readmission Occurring During 6-9 Months Post-MI Discharge							
MPR >=0.75 for All MI Drugs	0.569	0.510	0.086	0.107			
MPR >=0.75 for β -Blockers	0.661	0.619	0.090	0.106			
MPR >=0.80 for All MI Drugs	0.507	0.446	0.085	0.106			
MPR >=0.80 for β -Blockers	0.634	0.593	0.089	0.105			
First Readmission Occurring During 9-12 Months Post-MI Discharge							
MPR >=0.75 for All MI Drugs	0.578	0.505	0.071	0.093			
MPR >=0.75 for β -Blockers	0.694	0.646	0.075	0.092			
MPR >=0.80 for All MI Drugs	0.522	0.442	0.069	0.092			
MPR >=0.80 for β -Blockers	0.674	0.621	0.075	0.092			

 a The probability of having a readmission conditional on whether one was a good adherent or not was calculated using Bayes' rule