Noninitiation of Discharge Medications After Revascularization

Dominique Medaglio, PharmD, MS; Justin Glasgow, MD, PhD;
Zugui Zhang, PhD; and Daniel Elliott, MD, MSCE

ABSTRACT

BACKGROUND: Timely initiation of medication therapy after a cardiovascular event is vital to achieve optimal patient outcomes, yet there is a lack of insight on the frequency and predictors of discharge medications that are delayed or never initiated.

OBJECTIVES: To (a) describe how frequently patients do not fill newly prescribed discharge medications within 30 days after revascularization and (b) identify predictors of patients who did not fill their new medications.

METHODS: A single-center, retrospective analysis was conducted of patients discharged after percutaneous coronary intervention or coronary artery bypass grafting. Discharge prescriptions were linked to pharmacy claims data to identify medications that were not filled within 30 days of discharge.

RESULTS: 1,206 patients and their 5,253 discharge medications were included for study. More than one third of patients did not fill at least 1 discharge medication within 30 days (466/1,206, 38.6%); nearly 1 in 10 (116/1,206, 9.6%) did not fill any of their discharge prescriptions. Significant predictors of nonadherence included longer length of stay and higher number of prescribed discharge medications (both P values < 0.05). The largest classes of unfilled medications included insulin, factor Xa inhibitors, and narcotic analgesics.

CONCLUSIONS: Noninitiation is a common issue among patients after cardiac revascularization. These patients may be at a higher risk of not filling their medications if they experience longer lengths of stay or are prescribed a higher number of medications at discharge.

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What is already known about this subject

- Medication adherence among the cardiovascular population is poor, with only 66% of patients taking their medications for secondary prevention as prescribed.
- Timely initiation of medications after a cardiac revascularization is important to achieve optimal health outcomes.

What this study adds

- More than one third of patients did not fill all new discharge medications within 30 days after cardiac revascularization; almost 1 in 10 did not fill any of their discharge medications.
- Longer lengths of stay and higher counts of new discharge medications were both associated with lower filling rates.

Effective management of evidence-based medications following a cardiovascular event reduces morbidity, mortality, and excessive health care utilization.^{1,2} However, medication nonadherence has been estimated to be 66% across cardiovascular patients for secondary prevention³ and contributes to poor patient outcomes and overuse of health care resources.^{4,5} As the Centers for Medicare & Medicaid Services continues to develop 90-day voluntary bundled payment programs for coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI),⁶ a focus on the cardiac revascularization population is needed. Timely initiation of medication therapy after a cardiovascular event is critical to achieve optimal patient outcomes.² For example, 30- and 90-day mortality has been shown to decrease when beta blockers are initiated after myocardial infarction.^{7,8}

Medication adherence comprises 3 phases: (1) initiation (the time at which a patient takes the first dose of a prescribed medication), (2) implementation (the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen), and (3) persistence (the time from when a medication is initiated to when it is discontinued).⁹ To date, few studies have focused on the initiation of newly prescribed medications in cardiovascular populations at discharge, either in the United States or in other countries.¹⁰⁻¹² It is important to distinguish this phase of medication adherence from others, as each phase comprises different behaviors and may merit different approaches for intervention. In this study, multipayer aggregate pharmacy claims were linked to discharge prescription data in order to more accurately describe how frequently newly prescribed discharge medications were not filled following cardiac revascularization and possible predictors for noninitiation.

Methods

Population and Study Site

This study was a retrospective analysis of patients discharged from a large academic medical center in Delaware after receiving PCI or CABG from January 2015 to March 2017. If a patient had more than 1 revascularization procedure during this time period, only the first procedure was included.

Exclusion Criteria

Patients were excluded if they were discharged to locations other than home, including but not limited to skilled nursing facilities and intermediate care facilities; the focus of this study was on patients who had more autonomy to fill their

medications. Patients were also excluded if no pharmacy claims data were available for them, including patients who did not have pharmacy benefits at the time of discharge. The date range of any available pharmacy claims data had to include the patient's index visit date. As benefit coverage dates were not available in claims data, the proximity of visible medication fills to the index visit was used as a proxy for active pharmacy benefits. Specifically, patients were excluded if no fills were seen in the 120 days before the index visit (allowing for a 90-day fill with a 30-day cushion) and in the 30 days after discharge. Finally, patients who had a readmission to our system or died within our system within the 30 days after discharge were excluded from the study except if any medications were filled before either of those events. This study was approved by the Christiana Care Health System's Institutional Review Board. Data for all PCI and CABG patients hospitalized during the study period who met eligibility criteria were analyzed.

Data Sources

All pharmacy claims data were collected via a medication history function in the electronic medical record, supported by Surescripts. Surescripts is the largest health information network in the United States, representing more than 258 million insured lives, aggregating data from pharmacy benefit managers, public payers, and pharmacies.¹³ Medication history queries from the medication history function are routinely made at this health system for every hospital admission and also as needed during outpatient clinic visits. The query provides an aggregate report of the past 24 months of all pharmacy claims available for any given patient in the network, regardless of payer or location where the medication was filled. Data in these queries include prescription name, strength, and frequency; fill details; and information on the prescriber and filling pharmacy. Discharge prescriptions and fill information were merged using a unique patient identifier. Noninitiation was defined as a lack of evidence for a medication fill within 30 days of discharge. This methodology is similar to other medication adherence work focusing on initiation behaviors.¹⁴

Data Collection

All discharge prescriptions were collected from the electronic medical record, including those for noncardiovascular medications. Discharge medications were rolled up to the medication class and then were compared with the patient's home medication list, ascertained from the admitting medication reconciliation. Any discharge medication that appeared on the home list or was in the same medication class as a home medication (to account for changes in dose or optimizing within a medication class) was removed. Only medication classes that were new to the patient at discharge were included in this study, as the intent was to look at filling patterns when a patient's medication burden has increased. Furthermore, any medication

available over-the-counter (OTC) or behind-the-counter (BTC), such as vitamins, supplements, and aspirin, were not included in the initiation calculations. Finally, discharge prescriptions were then merged with prescription fill data from Surescripts available in the electronic medical record.

The following demographic and clinical characteristics were extracted from each patient's medical record: age at hospitalization, race and ethnicity, gender, and primary insurer for hospitalization. The Charlson Comorbidity Index score (a weighted index to predict mortality within 1 year of hospitalization) was calculated as a measure of severity.¹⁵ The index visit was characterized by procedure type (PCI or CABG) and length of stay (LOS) in days. Counts of home medications and new discharge medications were determined by the documented inpatient medication reconciliation. Medication-level characteristics were also collected, including transmission method (electronic versus paper), medication class, and whether the medication is recommended for secondary prevention per guidelines (platelet aggregation inhibitors, beta blockers, statins, and renin-angiotensin-aldosterone system inhibitors).²

Outcomes

The outcomes of interest were (a) evidence of patients filling all discharge prescriptions within 30 days, (b) evidence of an individual medication fill within 30 days of prescription, and (c) predictors of patients not filling all new medications within 30 days. The count of discharge medications represents all medications prescribed, including any OTC and BTC medications that were prescribed. However, OTC/BTC medications were not counted in 30-day fill outcome calculations. In this way, patients are not "punished" for not having a claim for an OTC/BTC medication, yet a patient's total discharge medication count accounts for everything prescribed.

Data Analysis

Descriptive statistics were generated for all variables. Patient- and visit-level characteristics were compared between patients who filled all discharge medications within 30 days versus those who did not, using chi-square tests and t-tests as appropriate. The independent association of patient- and visit-level characteristics with initiation of discharge prescriptions as a binary categorical outcome was tested using a logistic regression model, adjusting for age, gender, race, and ethnicity. Medication-level analyses were also conducted, where presence of a 30-day fill was examined for each non-OTC/BTC prescription. Medication characteristics were compared to the 30-day fill outcome through chi-square tests. Analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Of the 2,061 PCI and CABG inpatients treated in the study time frame, 1,206 patients with 5,253 discharge medications

TABLE 1 Patient-Level Demographics and Visit Characteristics by Noninitiation Status

Variable	Total Population N = 1,206	All Medications Filled n = 740	Not All Medications Filled n = 466	P Value ^a
Gender, n (%)				0.85
Male	788 (65.3)	482 (65.1)	306 (65.7)	
Female	418 (34.7)	258 (34.9)	160 (34.3)	
Race, n (%)				0.96
White	961 (79.7)	591 (79.9)	370 (79.4)	
Black/African American	208 (17.3)	127 (17.2)	81 (17.4)	
Other	37 (3.1)	22 (3.0)	15 (3.2)	
Ethnicity, n (%)				0.26
Not Hispanic/Latino	1,139 (94.4)	697 (94.2)	442 (94.9)	
Hispanic/Latino	36 (3.0)	20 (2.7)	16 (3.4)	
Unknown	31 (2.6)	23 (3.1)	8 (1.7)	
Mean age, years $\pm$ SD	65.3 $\pm$ 12.3	64.9 $\pm$ 12.7	66.0 $\pm$ 11.5	0.17
Procedure, n (%)				0.005
PCI	854 (70.8)	546 (73.8)	308 (66.1)	
CABG	352 (29.2)	194 (26.2)	158 (33.9)	
Hospital payer, n (%)				0.05
Medicare	723 (60.0)	428 (57.8)	295 (63.3)	
Private	381 (31.6)	253 (34.2)	128 (27.5)	
Other (Medicaid, self-pay)	102 (8.5)	59 (8.0)	43 (9.2)	
Mean LOS, days $\pm$ SD	4.8 $\pm$ 3.7	4.3 $\pm$ 3.4	5.5 $\pm$ 4.1	<0.0001
Discharge disposition, n (%)				0.02
Home	704 (58.4)	451 (61.0)	253 (54.3)	
Home health services	502 (41.6)	289 (39.1)	213 (45.7)	
Mean count of home medications	5.8 $\pm$ 4.1	5.8 $\pm$ 4.2	5.8 $\pm$ 4.1	0.97
Mean count of new discharge medications	4.6 $\pm$ 2.3	4.3 $\pm$ 2.2	5.2 $\pm$ 2.4	<0.0001
Mean Charlson Comorbidity Index score	4.1 $\pm$ 2.8	4.0 $\pm$ 2.8	4.1 $\pm$ 2.8	0.71

^aChi-square test or t-test.

CABG=coronary artery bypass grafting; LOS=length of stay; PCI=percutaneous coronary intervention; SD=standard deviation.

were ultimately included in the analyses. Of the final 1,206 patients, 740 (61.4%) filled all discharge medications within 30 days of prescription. The remaining 466 (38.6%) did not fill at least 1 of their discharge medications within 30 days, and 116 (9.6%) did not fill any of their discharge prescriptions. Table 1 describes the patient population by filling status and shows results from univariate analyses. Differences in initiation were found by type of procedure (PCI vs. CABG), LOS, receipt of home health services, and count of discharge medications (all *P* values <0.05).

In the multivariable analyses (Table 2), differences in noninitiation were associated with a longer LOS and a higher number of prescribed discharge medications, even after adjustment for other demographic and clinical characteristics (both *P*<0.05).

At the medication level, 986 of 5,253 (18.8%) discharge prescriptions were not filled within 30 days. Of the top 10 most commonly prescribed medications, the medication classes that had the highest proportion of prescriptions not filled within 30 days were insulin (30.4%), factor Xa inhibitors (26.4%), and narcotic analgesics (20.2%). Of the 4,267 medications

that were filled within 30 days, 3,534 (82.8%) were filled on the same day as discharge. More than half of all prescriptions were printed on paper versus e-prescribed; this was not significantly associated with a medication being filled within 30 days. Medications that were categorized as recommended for secondary prevention were more likely to be filled within 30 days (*P*<0.0001).

Discussion

This study found that 38.6% of revascularization patients did not fill all prescribed medications within 30 days of discharge, with 9.6% not filling any of their discharge medications in that time. To our knowledge, this is the first study to estimate 30-day initiation within the cardiac revascularization population in the United States.

Noninitiation is difficult to evaluate due to the types of data necessary to measure the initiation of a therapy. Ideally, initiation would be measured through direct patient monitoring, yet such methods are resource intensive and not appropriate for chronic medications.⁴ To date, noninitiation has not

TABLE 2 Logistic Regression Model Predicting Noninitiation of Any Discharge Medications Within 30 Days^a

Variable	Odds Ratio (95% CI)
CABG procedure	0.90 (0.66-1.24)
Charlson Comorbidity Index	0.99 (0.95-1.04)
LOS, days	1.06 (1.02-1.10)
Age, years	1.01 (0.99-1.02)
Discharge medication count	1.19 (1.12-1.27)
Race	
White	Reference
Black	1.01 (0.72-1.41)
Other	1.13 (0.52-2.44)
Female gender	0.99 (0.76-1.29)
Ethnicity	
Hispanic/Latino	1.06 (0.49-2.32)
Non-Hispanic/Latino	Reference
Unknown	0.69 (0.30-1.58)
Primary payer	
Private	Reference
Medicare	1.26 (0.88-1.81)
Other	1.50 (0.95-2.36)

^aThe C-statistic of the logistic model was 0.648.

CABG=coronary artery bypass grafting; CI=confidence interval; LOS=length of stay.

been consistently evaluated across different clinical settings. Noninitiation rates have ranged from 28% to 34% in the outpatient office setting and from 16% to 28% in the after-discharge setting.^{11,12,14,16} Our study found a higher rate of nonadherence than others with similar after-discharge settings. Two of these studies took place in Canada and one had a cardiovascular focus.^{11,12} Another after-discharge adherence study in the United States focused on a cardiovascular population, yet measured adherence using a validated index score rather than linking prescriptions to claims data.¹⁰ The differences in estimates are likely due to several factors, including varying adherence definitions and measurement methods.¹⁷ Despite these challenges, it is important to study the initiation phase of nonadherence, as it is often left out of overall adherence estimates, leading to potential underestimations.¹⁷

Both a lower number of discharge medications and shorter hospital stays were associated with lower odds of noninitiation. The burden of a high medication count has previously been associated with nonadherence.¹⁸ This is one of the first manuscripts to tie medication burden specifically to noninitiation behaviors. An increasing LOS may be indicative of increased disease severity and complexity of subsequent treatment, both of which have been associated with adherence in other studies.^{18,19}

Of note in the univariate analyses, receiving home health services versus a standard discharge to home was significantly associated with nonadherence. This may be due to 2 things: the complexity of patients who receive home health services and the varying services one could receive through home health

care, which may not consistently focus on medication education and therapy management.²⁰

Of the 5,253 medications prescribed, 18.8% were not filled within 30 days. This figure is similar to those found by other studies focusing on new therapies prescribed in a hospital setting and in a community setting.^{12,16} In the top 10 most-prescribed list, the medication classes with the largest proportions of unfilled medications included insulin, factor Xa inhibitors, and narcotic analgesics. The rising costs of insulin have made national headlines, and it is not surprising to see this class as one that was frequently not filled. From 2002 to 2013, the average price of insulin nearly tripled.²¹ Narcotic analgesics have been previously shown to be subject to high noninitiation rates,¹⁶ which may be due to the national discussion around the opioid epidemic and also to the precedent of mandatory paper prescriptions. During the study time frame, this institution printed all controlled substance prescriptions at discharge, though controlled substance e-prescriptions are now legal in all states.²² Although medications for secondary prevention were significantly more likely to be filled within 30 days, each of the 4 drug classes within this group still had sizable nonfill rates. Given the serious short-term consequences of nonadherence such as in-stent thrombosis, all evidenced-based therapies for the after-revascularization population should be strongly encouraged. During the discharge process and other transitions in care, where risk for medication errors is high,^{23,24} optimizing therapy is especially critical.

Improving the initiation rate for this population is important to achieve successful health outcomes, yet patients who are not filling medications in a timely manner tend to have more complex and severe health conditions with an associated higher medication burden. This study found that nonadherent patients were discharged with nearly double the number of medications they were admitted with, which can have significant implications for therapy management at home. This is an area ripe for pharmacist-driven interventions in transitions of care. “Meds-to-beds” programs or similar programs that connect patients with a system-embedded outpatient pharmacy have demonstrated increases in initiation rates and lower out-of-pocket costs.²⁵ Pharmacist involvement in medication reconciliation, counseling activities, and follow-up phone calls have also shown to improve medication adherence after discharge.^{21,26}

Future directions for this work should include factors that are external to the clinical setting that have been shown to impact medication adherence, including health literacy, socioeconomic factors, and the patient’s support network.²⁷

Limitations

There are several limitations to this study. While the SureScripts network is expansive, it does not capture all pharmacy benefit managers and payers that may have been used by patients. Patients without complete data were removed to more

accurately report on their adherence behavior, yet this may also bias the results against those not represented in the data.

In addition, Surescripts is only able to report claims and does not account for prescriptions paid for without pharmacy benefits. As such, patients who paid for all of their medications without pharmacy benefits were not represented in these data. It is also possible for patients who chose to pay out of pocket for a portion of their medications to be mislabeled as nonadherent. As most OTC and BTC medications are often paid for without insurance, these were removed from the analysis to reduce this potential bias.

Patients who may have received transitions-of-care services or had an office visit within the follow-up period may have received additional support in filling their medications or may have had a change made to their medication regimen; this study was not able to account for these services. The sources of data used in this study did not include other known risk factors for nonadherence, including out-of-pocket costs and health literacy level.

Finally, this study can only report on what was filled at the pharmacy, which may not ultimately reflect what was consumed by the patient. While pharmacy fill data were used as a proxy for adherence, estimating true initiation via timely and appropriate consumption would require other methods of measurement.

Conclusions

Focusing only on adherence behaviors after the first fill can vastly underestimate the population of patients who fail to initiate life-saving medication successfully. This study found that noninitiation of discharge medications is a common issue in the cardiac revascularization population. Longer lengths of stay and higher counts of new medications prescribed at discharge were associated with not filling all discharge medications within 30 days. Further investigation into noninitiation as an opportunity for improving outcomes after discharge is of merit.

Authors

DOMINIQUE MEDAGLIO, PharmD, MS, and ZUGUI ZHANG, PhD, Value Institute, Christiana Care Health System, Newark, Delaware. JUSTIN GLASGOW, MD, PhD, UAB Hospital Medicine, The University of Alabama at Birmingham, and DANIEL ELLIOTT, MD, MSCE, Christiana Care Quality Partners, Christiana Care Health System, Newark, Delaware.

AUTHOR CORRESPONDENCE: Dominique Medaglio, PharmD, MS, Value Institute, Christiana Care Health System, 4755 Ogletown-Stanton Rd., Ste. 8E00, Newark, DE 19718. Tel.: 302.733.5148; E-mail: dominique.m.medaglio@christianacare.org.

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