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## Predictors of medication adherence post-discharge: the impact of patient age, insurance status and prior adherence

**Marya J. Cohen, MD, MPH,**

Massachusetts General Hospital, Harvard Medical School

**Shimon Shaykevich, MS,**

Brigham and Women's Hospital

**Courtney Cawthon, MPH,**

Vanderbilt Center for Health Services Research

**Sunil Kripalani, MD, M.Sc.,**

Section of Hospital Medicine, Division of General Internal Medicine and Public Health, Department of Medicine, Vanderbilt University; Vanderbilt Center for Health Services Research

**Michael K. Paasche-Orlow, MD, MA, MPH, and**

Boston Medical Center, Boston University School of Medicine

**Jeffrey L. Schnipper, MD, MPH**

BWH Hospitalist Service and Division of General Medicine, Brigham and Women's Hospital, Harvard Medical School

### Abstract

**Background**—Optimizing post-discharge medication adherence is a target for avoiding adverse events. Nevertheless, few studies have focused on predictors of post-discharge medication adherence.

**Methods**—The Pharmacist Intervention for Low Literacy in Cardiovascular Disease (PILL-CVD) study used counseling and follow-up to improve post-discharge medication safety. In this secondary data analysis, we analyzed predictors of self-reported medication adherence after discharge. Based on an interview at 30 days post-discharge, an adherence score was calculated as the mean adherence in the previous week of all regularly scheduled medications. Multivariable linear regression was used to determine the independent predictors of post-discharge adherence.

**Results**—The mean age of the 646 included patients was 61.2 years, and they were prescribed an average of 8 daily medications. The mean post-discharge adherence score was 95% (SD = 10.2%). For every 10 year increase in age, there was a 1% absolute increase in post-discharge adherence (95% CI 0.4% –2.0%). Compared to patients with private insurance, patients with Medicaid were 4.5% less adherent (95% CI –7.6% to –1.4%). For every 1-point increase in baseline medication adherence score, as measured by the 4-item Morisky score, there was a 1.6% absolute increase in post-discharge medication adherence (95% CI 0.8% to 2.4%). Surprisingly, health literacy was not an independent predictor of post-discharge adherence.

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Corresponding Author: Marya J. Cohen, MD, MPH<sup>1,2</sup>, General Medicine Unit, Massachusetts General Hospital, 50 Staniford St., 9<sup>th</sup> Floor, Boston, MA 02114, mjcohen@partners.org, 617-869-7935 phone, 617-889-8579 fax.

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**Conclusions**—In patients hospitalized for cardiovascular disease, predictors of lower medication adherence post-discharge included younger age, Medicaid insurance, and baseline non-adherence. These factors can help predict patients who may benefit from further interventions.

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## Background

In the outpatient setting, medication adherence (defined as percentage of prescribed medication doses taken by a patient during a specific time period) ranges between 40 and 80 percent for chronic conditions.<sup>1</sup> During acute care hospitalization, changes are often made to patients' medication regimens, which can be confusing and contribute to non-adherence, medication errors, and harmful adverse events.<sup>2</sup> Indeed it is estimated that almost half of patients encounter a medication error after discharge, and approximately 12–17% experience an adverse drug event after returning home.<sup>3–6</sup> It is likely that some of these adverse events may be the result of medication non-adherence.<sup>7</sup> Improved patient-provider communication, systems to reconcile pre- and post-hospitalization medications, as well as development of mechanisms to enhance adherence may prevent many of these errors and have become new targets for quality improvement.<sup>4, 8</sup> Although post-discharge medication adherence is a crucial target for avoiding adverse events and re-hospitalization, few studies have focused on understanding its incidence and predictors, in particular patient demographic factors such as age and insurance status.<sup>9–11</sup>

In addition, few studies have looked at general and post-hospital adherence in a population where health literacy is measured, an important area because medication changes during hospitalization may be particularly confusing for patients with low health literacy.<sup>11, 12</sup> Health literacy is defined as “the degree to which an individual has the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.”<sup>13</sup> Prior outpatient research shows that low health literacy is associated with poor patient understanding of the medication regimen and instructions for medication use, which may contribute to post-discharge medication non-adherence.<sup>14, 15</sup> Understanding the factors associated with post-discharge medication adherence could help refine interventions that are oriented toward improving transitions in care, patient safety, and reducing unnecessary re-hospitalization.

We report here on factors associated with post-discharge medication adherence using data from the Pharmacist Intervention for Low Literacy in Cardiovascular Disease (PILL-CVD) study.<sup>16</sup>

## Methods

### Study and Participants

PILL-CVD was a federally-funded, two-site randomized controlled trial using pharmacist-assisted medication reconciliation, inpatient pharmacist counseling, low-literacy adherence aids, and telephone follow-up that aimed to decrease rates of serious medication errors after hospital discharge.<sup>16</sup> The study targeted patients with cardiovascular disease (hospitalized on cardiology or general medical or geriatric services for acute coronary syndromes [ACS] or acute decompensated heart failure [ADHF]) at two large academic hospitals, Brigham and Women's Hospital (BWH) and Vanderbilt University Hospital (VUH).

Subjects were eligible for enrollment if they met criteria for ACS or ADHF, were likely to be discharged to home as determined by the primary medical team at the time of study enrollment, and took primary responsibility for administering their medications prior to admission (caregivers could be involved in medication management after discharge).

Exclusion criteria included severe visual or hearing impairment, inability to communicate in English or Spanish, active psychiatric illness, dementia, delirium, illness too severe to participate, lack of a home phone number, being in police custody, or participation in another intensive medication adherence program (e.g., due to renal transplant).

Out of 6416 patients originally screened for possible enrollment, 862 were randomly assigned to receive usual care or usual care plus the intervention, and 851 remained in the study.<sup>16</sup> Both the main study and this secondary data analysis were approved by the Institutional Review Boards of each site.

### Baseline measures

Following informed consent and study enrollment, a variety of baseline data were collected on study participants from medical records and patient interview, including primary language, demographic information (age, race, insurance status, income, and education level), cognition (through administration of the 0–5 point MiniCog scale)<sup>17</sup> and level of health literacy (through use of the 0–36 point short form of the Test of Functional Health Literacy in Adults, s-TOFHLA scale).<sup>18</sup> Baseline information was also collected on medication use, including number of preadmission medications, measurement of self-reported adherence prior to admission (using the Morisky scale, a validated 0–4 point questionnaire shown to correlate with disease control and indicative of general patterns of adherence),<sup>19</sup> and a medication understanding score, adapted from other instruments, which quantifies understanding of the indication, dose, and frequency of up to 5 randomly selected preadmission medications on a 0–3 point scale.<sup>16,20, 21</sup>

### Outcome measures

Outcomes were collected 30 days post-discharge through a structured questionnaire, administered by telephone. Only patients who completed this call are included in the present analysis. Post-discharge medication adherence was assessed by asking patients to report the number of days out of the previous week they had taken each medication from their post-discharge regimen exactly as prescribed.<sup>22</sup> A score was calculated for each medication as the proportion of adherent days (e.g., if a patient reported missing 2 days of a medication in the previous week, then adherence would be 5/7 or 71%). A global post-discharge adherence score was then derived for each patient by averaging the adherence score for all regularly-scheduled medications. This quantitative measure focused on adherence to medications patients knew they should be taking and did not measure medication discrepancies (sometimes termed “unintentional non-adherence”).

### Analysis

Patient characteristics were summarized and reported using simple descriptive statistics. Candidate predictors of post-discharge medication adherence were chosen *a priori* from patient characteristics assessed during hospital admission. These included patient age, gender, race, ethnicity, marital status, insurance, years of education, presence of PCP, study site, number of preadmission medications, medication understanding, baseline adherence, cognition, and health literacy. Unadjusted results were calculated using univariable linear regression with each patient’s adherence score as the dependent variable and each predictor as the independent variable. Adjusted results were then derived using multivariable linear regression with all the candidate predictors in the model.

Lastly, because of missing data for some predictors, in particular baseline adherence and medication understanding, multiple imputation techniques were used to impute missing data and increase statistical power.<sup>23</sup> We used the Markov Chain Monte Carlo (MCMC) method for multiple imputation, which generally assumes that the data came from a normal

distribution and that the missing data are missing at random. Because of the essentially normal distribution of the data, and because the amount of missing data was so small (<1% for almost all variables, 5% for baseline adherence, and 8% for medication understanding), we expected little bias and present the complete case analysis, which maximized statistical power.

Two-sided  $p$  values < 0.05 were considered significant, and SAS version 9.2 (Cary, NC) was used for all analyses.

## Results

Table 1 shows descriptive baseline patient characteristics of study sample (responders) as well as non-responders at 30 days. For the responders, the mean age of the 646 patients was 61.2 years, 94.7% were insured, and 19.3% had inadequate or marginal health literacy. Patients were prescribed an average of 8 preadmission medications. Most patients (92.3%) had a regular primary care physician prior to admission. Non-responders had non-significant trends towards having lower health literacy, medication understanding, and baseline medication adherence.

The average post-discharge adherence score was 95% (SD = 10.2%), and less than 10% of patients had an adherence score of less than 85%; overall the distribution was left-skewed. Table 2 illustrates crude and adjusted parameter estimates for variables in the model. Table 3 shows significant findings in the fully adjusted model, which used multiple imputation techniques to account for missing data.

Intervention arm was of borderline statistical significance in predicting post-discharge adherence ( $p=0.052$ ), and so was removed from the final model. Study site, age, insurance, and baseline adherence were the only significant independent predictors of post-discharge adherence in the fully adjusted model (Table 3). For example, for every 10 year increase in age, patients had, on average, an adjusted 1% absolute increase in their adherence score (95% CI 0.4% to 2.0%). For every 1-point increase in baseline medication adherence (based on the Morisky scale), there was a 1.6% absolute increase in medication adherence (95% CI 0.8% to 2.4%). In unadjusted analyses, patients with Medicaid were less adherent with medications after discharge than were patients with private insurance. This difference became non-significant in adjusted analyses, but when analyses were repeated using multiple imputation techniques, the results again became statistically significant – Medicaid insurance was associated with a 4.5% absolute decrease in post-discharge adherence compared with private insurance (95% CI -7.6% to -1.4%). Study site (specifically, Brigham and Women's Hospital) was also a significant predictor of greater post-discharge medication adherence. Years of education was a significant predictor of adherence in unadjusted analyses but was not an independent predictor when adjusted for other factors. When baseline adherence was removed from the multiple imputation model, there were no changes in which factors were significant predictors of adherence.

## Discussion

In this study, we found that low baseline adherence, younger age, Medicaid insurance, and study site were significant predictors of lower 30-day medication adherence. Of particular interest is our finding regarding baseline adherence, a simple measure to obtain on hospitalized patients. It is notable that in our study, education was not an independent significant predictor of post-discharge adherence, even when baseline adherence was removed from the model. The same is true for medication understanding, cognitive function, and health literacy.

Older patients appeared more adherent with medications in the month after hospital discharge, perhaps reflecting increased interaction with the healthcare system (appointments, number of physician interactions), a greater belief in the importance of chronic medication management, or a higher level of experience with managing medications. A similar relationship between age and adherence has been shown in outpatient studies of patients with hypertension, diabetes, and other chronic diseases.<sup>24–27</sup>

Medicaid patients may be less likely to remain adherent because of the plan's limited coverage of medications relative to patients' ability to pay. For example, Medicaid in Tennessee covers the first 5 generic medications at no cost to the patient but has copayments for additional medications and for brand name drugs. Medicaid in Massachusetts has copayments of \$1 to \$3 for each medication. Alternatively, Medicaid insurance may be a marker for other patient characteristics associated with low adherence for which we were not fully able to adjust.

Site differences were also notable in this study; these differences could have been due to differences in insurance coverage in Tennessee vs. Massachusetts (which has near-universal coverage), differences in types of insurance (e.g., fewer patients at Brigham and Women's Hospital had Medicaid than at Vanderbilt), cultural and geographic differences between the two locations, or other differences in transitional care between the two sites.

This study corroborates previous literature on medication adherence (specifically unintentional non-adherence) in the outpatient setting,<sup>4, 8–11</sup> for example on the association of younger age with low adherence in certain populations. On the other hand, it may contrast with previous literature which has sometimes shown a relationship between patient education or health literacy and medication adherence.<sup>14, 15, 28–35</sup> However, previous studies have not focused on the transition from inpatient to outpatient settings. Perhaps intensive medication education in the hospital, even under usual care, mitigates the effects of these factors on post-discharge adherence. Finally, baseline adherence seems to correlate with post-discharge adherence, a finding which makes intuitive sense and has been previously reported for specific medications.<sup>36</sup>

There are several limitations to this study. Although large, the study was performed at only two clinical sites where most patients were white and fairly well-educated, perhaps because patients admitted to a tertiary care center with ACS or ADHF are more affluent than general medical inpatients as a whole; this may limit generalizability. Post-discharge medication adherence might have been higher than in other patient populations given the nature of the population, possible loss-to-follow-up bias, and the fact that half of the subjects received an intervention designed to improve medication management after discharge; such low rates of non-adherence in our study may have reduced our ability to detect important predictors in our models. In addition, the period of follow-up was 30 days, thus limiting our findings to short-term post-discharge medication adherence. Post-discharge medication adherence was based on patient self-report, which not only assumed that the patient was still managing his/her own medications after discharge, but may also be susceptible to both recall and social acceptability bias, which might overestimate our adherence scores, again limiting our ability to detect important predictors of non-adherence. However, other studies have shown a good correlation between self-reported medication adherence and other more objective measures<sup>37, 38</sup> and recall was only for 7 days, a measure used previously in the literature<sup>39, 40</sup> and one designed to reduce recall bias. Systematic under-reporting in certain patient populations is less likely but possible.

In the future, research should focus on targeting patients who have low baseline adherence to evaluate the effects of various interventions on post-discharge medication outcomes.

Repeating the study in a population with a high prevalence of low health literacy might be illuminating given that previous studies have shown that patients with low health literacy have less ability to identify their medications and have less refill adherence.<sup>29, 30</sup>

In conclusion, in patients hospitalized with cardiovascular disease, predictors of lower post-discharge adherence include younger age, Medicaid insurance, and low baseline adherence. It may be prudent to assess baseline adherence and insurance type in hospitalized patients in order to identify those who may benefit from additional assistance to improve medication adherence and medication safety during transitions in care.

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Table 1

## Baseline characteristics

Characteristic	Total N, 30 day respondents	Value	Total N, nonrespondents	Value
Age, mean in years (SD)	646	61.2 (13.5)	45	55.4 (14.3)
Gender, N (percentage)	646		45	
- Female		272 (42.1)		18 (40.0)
- Male		374 (57.9)		27 (60.0)
Race, N (percentage)	643		45	
- White		511 (79.5)		32 (71.1)
- Black		104 (16.2)		11 (24.4)
- Other		28 (4.4)		2 (4.4)
Ethnicity, N (percentage)	639		45	
- Hispanic		24 (3.8)		1 (2.2)
- Not Hispanic		615 (96.2)		44 (97.8)
Marital status, N (percentage)	646		45	
- Married/cohabitate		382 (59.1)		20 (44.4)
- Separated/divorced		118 (18.3)		11 (24.4)
- Widowed		81 (12.5)		5 (11.1)
- Never married		65 (10.1)		9 (2.0)
Insurance type, N (percentage)	646		45	
- Medicaid		53 (8.2)		5 (11.1)
- Medicare		270 (41.8)		13 (28.9)
- Private		289 (44.7)		19 (42.2)
- Self-pay		34 (5.3)		8 (17.8)
Years of education, mean in years (SD)	643	14.0 (3.1)	45	13.3 (2.7)
Presence of PCP prior to admission, N (percentage)	646		45	
- Yes		596 (92.3)		38 (84.4)
- No		50 (7.74)		7 (15.6)
Site, N (percentage)	646		45	
- Site 1		358 (55.4)		8 (17.8)
- Site 2		288 (44.6)		37 (82.2)
Number of preadmission medications, mean number (SD)	641	7.8 (4.8)	45	7.7 (5.4)
Medication Understanding Score, mean (SD) *	597	2.4 (0.5)	40	2.2 (0.62)
Health Literacy (STOFHLA) score, mean (SD) †	642	29.1 (8.9)	45	26.0 (12.0)
Baseline adherence (SD) ‡	613	2.7 (1.1)	45	2.4 (1.2)

Characteristic	Total N, 30 day respondents	Value	Total N, nonrespondents	Value
Minicog score, N (percentage) <sup>//</sup>	646		45	
- Demented		63 (9.8)		5 (11.1)
- Not demented		583 (90.2)		40 (88.9)

\* 0–3, with 3 indicating better understanding

<sup>†</sup> 0–36, with higher scores indicating higher health literacy

<sup>‡</sup> 0–4, with 4 indicating higher baseline adherence

<sup>//</sup> 0–5, with higher scores indicating better cognition. A score < 3 indicates dementia

Table 2

## Crude and Adjusted Measurements

Predictor	Crude parameter estimate (beta) with 95% confidence intervals	P value	Adjusted parameter estimate (beta) with 95% confidence intervals	P value
Age per 10 years	0.010 (0.007–0.020)	<0.0001	0.010 (0.002, 0.020)	0.018
Male gender	0.012 (–0.004, 0.028)	0.137	0.003 (–0.014, 0.020)	0.727
Race/ethnicity				
- White	0.011 (–0.009, 0.031)	0.266	Ref	Ref
- Black	–0.017 (–0.038, 0.005)	0.13	0.006 (–0.017, 0.030)	0.598
- Other	0.010 (–0.029, 0.049)	0.599	0.017 (–0.027, 0.062)	0.446
Hispanic/Latino	0.005 (–0.037, 0.047)	0.803	0.036 (–0.013, 0.085)	0.149
Marital status				
- Married/cohabitate	0.006 (–0.011, 0.022)	0.500	Ref	Ref
- Separated/divorced	–0.005 (–0.025, 0.016)	0.664	0.009 (–0.014, 0.031)	0.446
- Widowed	0.001 (–0.023, 0.025)	0.922	–0.013 (–0.039, 0.013)	0.338
- Never married	–0.009 (–0.035, 0.018)	0.515	–0.004 (–0.033, 0.025)	0.784
Insurance type				
- Private	0.008 (–0.008, 0.024)	0.347	Ref	Ref
- Medicaid	–0.046 (–0.075, –0.018)	0.002	–0.026 (–0.058, 0.007)	0.121
- Medicare	0.012 (–0.004, 0.028)	0.138	–0.002 (–0.023, 0.018)	0.844
- Self-pay	–0.027 (–0.062, 0.008)	0.135	–0.029 (–0.073, 0.015)	0.202
Years of education	0.003 (0.0003, 0.005)	0.028	0.0001 (–0.003, 0.003)	0.949
Presence of PCP prior to admission	0.007 (–0.022, 0.037)	0.630	0.002 (–0.032, 0.036)	0.888
Site	–0.050 (–0.065, –0.034)	<0.0001	–0.038 (–0.056, –0.021)	<0.0001
Number of preadmission medications	–0.0003 (–0.002, 0.001)	0.684	–0.0001 (–0.002, 0.002)	0.918
Med understanding score per point	0.007 (–0.009, 0.023)	0.390	0.006 (–0.011, 0.023)	0.513
Health literacy (STOFHLA) score per 10 points	0.0006 (–0.008, 0.01)	0.897	0.003 (–0.008, 0.01)	0.644
Baseline adherence per point	0.023 (0.016, 0.031)	<0.0001	0.017 (0.009, 0.024)	<0.0001
Cognitive function	0.004 (–0.022, 0.031)	0.757	0.008 (–0.019, 0.036)	0.549

- For crude estimates, value is category versus absence of parameter in bivariate testing
- For adjusted estimates of categorical variables, value is each category compared to referent category
- Beta-coefficient represents absolute change in adherence (e.g., 0.010 for age means a 1% absolute increase in adherence for every 10 year increase in patient age)

**Table 3**

Significant results in adjusted analyses with multiple imputation

Predictor	Parameter estimate (beta) with 95% confidence intervals	P value
Age per 10 years	0.010 (0.004, 0.020)	0.004
Insurance type		
- Private	Ref	Ref
- Medicaid	-0.045 (-0.076, -0.014)	0.005
- Medicare	-0.010 (-0.030, 0.010)	0.333
- Self-pay	-0.013 (-0.050, 0.025)	0.512
Site	-0.036 (-0.053, -0.019)	<0.0001
Baseline adherence per point	0.016 (0.008, 0.024)	<0.0001

- Total observations 646; 67 with missing values

- All variables adjusted for gender, race, cognitive function, number of preadmission medications, marital status, health literacy score, medication understanding score, presence of PCP, years of school, Hispanic/Latino ethnicity.