Title

Impact of a Pharmacist-led Adherence Intervention Program on Primary Medication Non-Adherence Among Four Chronic Disease States in One Regional Division of a Large Community Pharmacy Chain

Authors

Danya Horchi Wilson, PharmD
Kroger Health
University of Tennessee Health Science Center
Leanne Rein, PharmD
Kroger Health
Michele Fountain, PharmD
Kroger Health
Andrea Brookhart, PharmD
Kroger Health
Daniel Atchley, PharmD
Kroger Health
Kenneth Hohmeier, PharmD
University of Tennessee Health Science Center

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Introduction

Medication non-adherence is a consistent barrier to better outcomes for patients—resulting in more than $100 billion spent on avoidable hospitalizations each year.[1-2] There are two subsets that contribute to the public health issue of non-adherence, primary and secondary medication nonadherence.

Primary medication non-adherence (PMN) is the failure to fill an *initial* prescription within an appropriate time frame, while secondary non-adherence is the failure to *refill* prescriptions within an appropriate time frame.[3] Secondary non-adherence has been a key measure in quality improvement of medication non-adherence; as such, it has been adopted as a measure into the Centers for Medicare and Medicaid Services (CMS) Star Ratings Program. With the focus of non-adherence research on its counterpart, PMN has been identified as a major gap in research.[4-6]

The Pharmacy Quality Alliance (PQA) has standardized the definition of PMN in order to capture more meaningful data on the measurement and to guide research to better understand the true occurrence of primary non-adherence rates.[7] By standardizing the definition of PMN, we not only are able to better track the rates of occurrence, but we are also able to track the effectiveness of interventions aimed at reducing PMN among patients. Using the PQA measure for PMN, there is a 12.2% rate of primary medication non-adherence (PMN) among community pharmacies.[7]

Multiple studies have found that medications prescribed for chronic diseases are among some of the highest rates of PMN.[8-10] Because of this, and because of the priorities outlined in the National Quality Strategy, PQA has given priority to medications used to treat diabetes, hypertension, dyslipidemia, and chronic obstructive pulmonary disease (COPD).[7] Research has also revealed why patients may not pick up newly prescribed medications. Individual patient and

medication factors, health system and socioeconomic effects, and provider-patient communication are all contributing aspects to PMN.[11]

Objectives

The objectives of this study are **(1)** to determine the impact of a pharmacist-led, evidence-based adherence intervention program on primary medication non-adherence (PMN) rates among four chronic disease states (diabetes, hypertension, hyperlipidemia, chronic obstructive pulmonary disease) and **(2)** to identify and characterize factors associated with PMN

Methods

The study used electronic prescription and internal patient record data to determine the impact of a pharmacist-led, evidence-based adherence intervention program on PMN rates among medications used to treat four chronic disease states. The PQA-PMN measure was used to define PMN. This intervention was implemented across a select number of regional pharmacies of a large community chain over a 4-month period.

An a-priori sample size power analysis of 88 patients in both the control and intervention group was calculated. At 2.5 months into the study, it was determined that the rate of enrollment was not enough to meet power by the end of the planned implementation period, so more stores were added into the study. This study was exempted by the University of Tennessee Health Science Center Institutional Review Board.

Pharmacy dispensing software was used to identify *newly initiated* prescriptions within certain therapeutic classes **(table 1)** *at risk* of primary medication non-adherence for patients 18 years of age or older. A newly initiated prescription is defined as the same drug, or its generic equivalent, not being filled during the preceding 180 days.[14-15] A patient is considered "at risk" of PMN if they had not obtained the newly initiated prescription within 7 days of it being filled. A prescription is considered PMN if the patient does not obtain the newly initiated medication, or an appropriate alternative, within 30 days after it was prescribed. [14-15] Prescriptions were included in the study if they were filled anytime during the 30 days after being prescribed, (i.e., if the newly initiated medication was not filled until 14 days into the 30-day period, it was still included giving us less time to contact patient).

If a patient was at risk of PMN, they were randomized into a control or intervention group. The intervention group was contacted by a pharmacist who used an evidence-based protocol to support pharmacist-patient communication in order to identify barriers and create solutions to overcome potential PMN.[12] The protocol was adapted from the DRAW Tool and from the conversation flowchart used in P. Chancy et al.[12-13] This evidence-based tool walks pharmacy staff through screening patients for PMN and creating a conversation about addressing and educating patients on potential PMN.

When the intervention implementation period was over, the rate of PMN was assessed between the control and intervention group using a chi-square test.

Table 1: Therapeutic Classes Included in PQA-PMN Measure[7,14-15]

Therapeutic Classes
Angiotensin-converting enzyme (ACE) inhibitors, plus combination products
Angiotensin II receptor blockers (ARBs), plus combination products
Biguanides, plus combination products
Chronic obstructive pulmonary disease (COPD) medications
Direct renin inhibitors, plus combination products
Dipeptidyl peptidase 4 (DPP-IV) inhibitors, plus combination products
Hydroxymethlglutaryl-CoA (HMG-CoA) reductase inhibitors, plus combination products
Incretin mimetic agents
Inhaled corticosteroids
Meglitinides, plus combination products
Sulfonylureas, plus combination products
Thiazolidinediones, plus combination products
Sodium-glucose co-transporter type 2 (SGLT2) inhibitors

Results

During the 4-month intervention period (November 30th, 2020 through March 30th, 2021), 203 prescriptions were included in the study with 94 in the intervention group and 109 in the control group. There was a 9% difference (p=0.193) in PMN between the intervention group (44 patients, 47%) and the control group (61 patients, 56%). The therapeutic classes most at risk of PMN include statins (34%), ACE inhibitors (19%), and COPD inhalers (15%). Cost (26%) and confusion/miscommunication (15%) were the most common reasons for PMN within the intervention group. Among the four chronic disease states studied, the intervention had the largest impact on hypertension (table 4).

Table 2: Patient Characteristics

Characteristic	**All Patients (n= 203)**	**Intervention (n= 94)**		**Control (n= 109)**	
		All	PMN (n=44)	All	PMN (n=61)
Age					
18-24	5 (2%)	2 (2%)	1 (2%)	3 (3%)	3 (4.9%)
25-39	24 (12%)	11 (12%)	3 (7%)	13 (12%)	6 (9.8%)
40-49	47 (23%)	28 (30%)	11 (25%)	19 (17%)	11 (18%)
50-64	81 (40%)	32 (34%)	15 (34%)	49 (45%)	29 (47.6%)
65+	46 (23%)	21 (22%)	14 (32%)	25 (23%)	12 (19.7%)
Sex					
Male	112 (55%)	54 (57%)	29 (66%)	58 (53%)	34 (56%)
Female	91 (45%)	40 (43%)	15 (34%)	51 (47%)	27 (44%)

Table 3: Rate of Primary Medication Non-Adherence (PMN)

Intervention (n= 94)	Control (n= 109)	*P* Value
44/94 (47%)	61/109 (56%)	0.193

Table 4: Intervention Subgroup Analysis by Disease State

Disease State	Intervention All (n= 94)	Intervention Adherent (n=44)	Intervention PMN (n=50)
COPD	10	5	5
Diabetes	26	12	14
Hyperlipidemia	33	16	17
Hypertension	25	17	8

Table 5: Intervention Subgroup Analysis by Drug Class

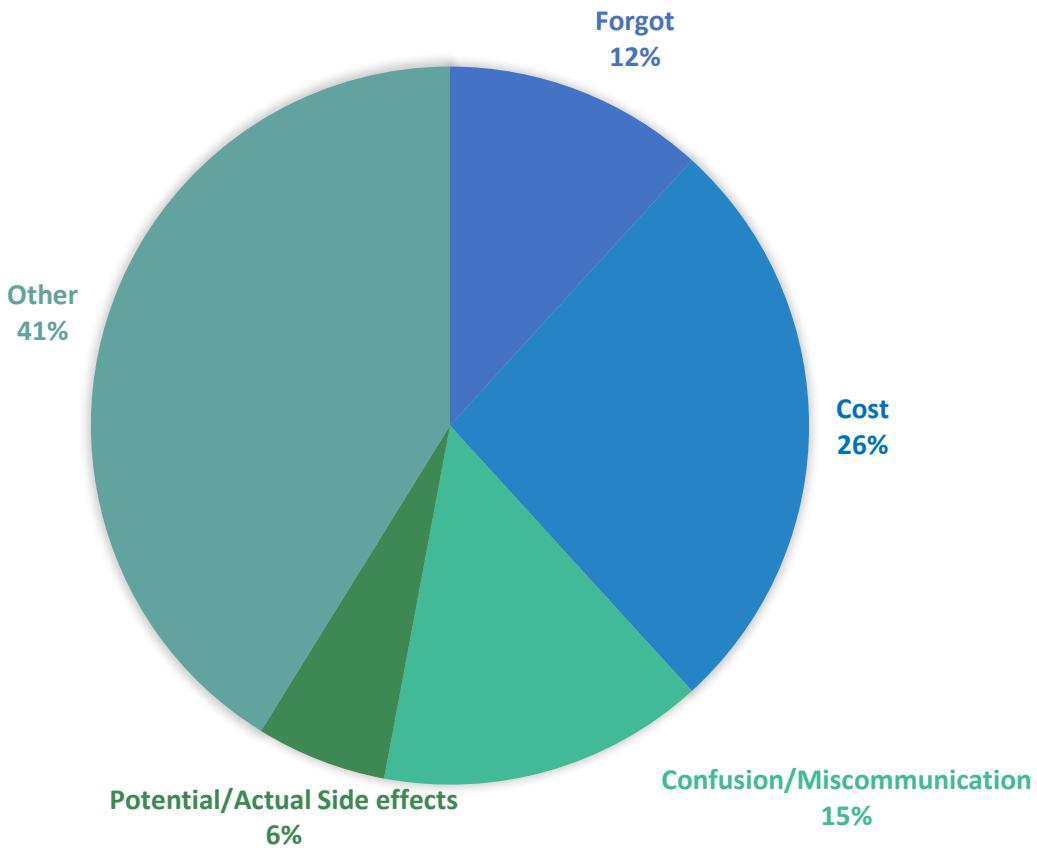
Medication Class	Intervention Adherent (n=44)	Intervention Non-Adherent (n=50)	Intervention All (n=94)
ACE Inhibitor + Combos	11%	5%	16%
ARB + Combos	7%	3%	11%
Biguanides	0%	2%	2%
Biguanides + Combos	5%	4%	10%
COPD Inhalers	5%	5%	11%
DPP-4 Inhibitors	2%	2%	4%
Incretin Mimetic Agents	1%	3%	4%
Meglitinides	2%	0%	2%
SGLT2 Inhibitors	0%	3%	3%
Statin Medications	17%	18%	35%
Sulfonylureas	2%	0%	2%

Table 6: Drug Classes Associated with PMN Risk*

Medication Class	n=203
ACE Inhibitor + Combos	39 (19%)
ARB + Combos	21 (10%)
Biguanides	20 (10%)
Biguanides + Combos	2 (1%)
COPD Inhalers	30 (15%)
DPP-4 Inhibitors	4 (2%)
DPP-4 inhibitor/SGLT-2 inhibitor	1 (1%)
Incretin Mimetic Agents	6 (3%)
Meglitinides	2 (1%)
SGLT2 Inhibitors	5 (2%)
Statin Medications	68 (34%)
Sulfonylureas	5 (2%)

*risk is defined as newly prescribed prescriptions not obtained by patient within 7 days of fill date

Chart 1: Factors Associated with PMN in Intervention Group*



*11 patients were unreachable

Discussion

During this study, there was a non-significant increase in adherence rates after the implementation of a PMN intervention. The intervention that was implemented could be better improved by creating more targeted conversations with patients. During this study, it was found that patients had a hard time articulating why they had not yet picked up their newly prescribed medication, which may explain the large percentage of "other" factors associated with PMN. Barriers to adherence may be better addressed by creating a survey that targets common factors associated with PMN and having a pharmacy staff member use the survey to better guide conversation. This is a similar approach to the DRAW Tool, a resource used to address secondary non-adherence. Another way to improve this intervention would be to better integrate it into pharmacy workflow by automating identification of patients at risk of PMN. This enhanced integration into workflow would not only decrease the time it takes to manually identify patients but would also allow a better platform of documentation meaning more pharmacy staff members could be involved in the intervention to improve patient engagement.

The intervention had the largest impact on prescriptions for medications used for hypertension (ACEI/ARB) which is a similar finding to another study, Fischer et. al.[16] This result may be explained by patient perception of the implications of hypertension and the medications used to treat it. When improving the intervention to create more targeted conversations, it may be important to assess patient perceptions of the other types of medications and disease states included in this study.

There are important limitations to consider when reading the results of this study. Patients were called from a centralized location using a mobile-based program that assured patients saw their local pharmacies phone number on their caller identification instead of an unknown number. Even with this feature, 27 out of 94 (29%) patients were unreachable within the intervention group. This can be explained by certain barriers that present due to cold calling. First, while this mobile-based program was helpful to assure the patients saw a potentially familiar number, it also meant voicemails could not be left since there was not a good call-back number to leave. Second, even with caller identification feature, patients may not recognize their local pharmacies number and be unwilling to answer. An additional limitation was that claims data from only one large community pharmacy chain was used. This means that patients could have been filling a medication at another pharmacy and switched to one the pharmacies included in the study, making their prescription look like a newly prescribed medication when it truly was not. The PQA-PMN measure includes medications classes that are typically used for four certain chronic diseases, but certain medications included in the study can be used for diseases other than the included four (i.e., metformin for polycystic ovary syndrome [PCOS]). The PQA-PMN measure directs the user to only include electronically prescribed prescriptions; however, this study did not differentiate between electronically prescribed and written prescriptions due to the nature of the pharmacy dispensing software and the way the prescriptions were screened for inclusion. Ultimately, it is not believed that this made a large impact on the study overall.

Conclusion

In conclusion, while there was an increase in adherence rates after the implementation of a pharmacist led, PMN intervention, it was found to be not significant. Factors such as more targeted conversations and enhanced integration of protocol into workflow should be further investigated as facilitators to improving PMN via a pharmacy-based intervention.

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