Impact of adherence goal awareness intervention on PDC in various settings: Does awareness help modify medication-taking behavior?

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A B S T R A C T

Background: Interventions to improve medication adherence in chronic conditions have shown limited success or sustainability. Previous data revealed that phone calls to patients regarding adherence goal awareness resulted in significant improvement in proportion of days covered (PDC).

Methods: A prospective, randomized controlled study was conducted with patients who belonged to university-associated health care settings [ambulatory care, chain store, small health plan, and federally qualified health center (FQHC)]. At each site, patients with at least one chronic medication and a calculated PDC < 0.80 were randomized into control (n = 115) and intervention (n = 126) groups. Control groups (C) received usual pharmacy communication while intervention groups (X) were specifically called by a pharmacist to be informed of PDC goals and their commitment to adherence. PDC values were calculated 3 to 12 months for both groups the time of intervention, then compared with each patient's respective baseline/pre-PDC.

Results: Data from a total of 241 patients were pooled to examine change in PDC. There was no significant difference between groups in baseline criteria or PDC. Comparing within groups, there were significant correlations between Pre- and Post-PDCs for the intervention group (X = 0.32 p < 0.05) alone. There were significant improvements from initial PDC to those calculated at the time of Post-intervention PDC within both groups, (C = 0.18 ± 0.28 p < 0.05) and (X = 0.16 ± 0.24 p < 0.05). Approximately 44% of all sampled patients reached their adherence goals (PDC ≥ 0.80) after 3–9 months.

Conclusions: Results suggested that patient adherence behavior may improve after any call made by pharmacy staff. This communication and attention from the pharmacy may be enough for patients to consider their medication-taking habits without the need for discussing specific goals and importance of adherence.

1. Introduction

The World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and research studies have discussed the impact medication adherence may have on individual health outcomes.1–3 Medication adherence has been widely studied in the healthcare field but there has been limited success in determining sustainable effective interventions. Nonadherence to medical therapies in the United States has been responsible for up to half of all treatment failures. In 2018 alone, nonadherence was related to 25% of hospitalizations attributing to approximately 125,000 deaths.4 Nonadherence remains an unsolved problem in healthcare.5

Conversely, increased medication adherence has been shown to coincide with medical or health advice. Previous studies have demonstrated that pharmacists have had a positive influence when promoting adherence in patient groups.6–8 Pharmacists have utilized different approaches in an attempt to impact adherence rates; these include communicating with patients face-to-face, virtually (through computer or telephone), and through focused individualized sessions [e.g., medication therapy management (MTM), chronic care management (CCM)]. Patients reported that receiving information from pharmacists had encouraged their own belief in medication-taking and improved their adherence.9 In a previous pilot study, the authors found that a simple phone call intervention regarding...
adherence at goal of 80%, resulted in significant improvement in proportion of days covered (PDC).

The patients at great risk of being nonadherent include those with chronic illnesses (e.g., hypertension, diabetes, or hyperlipidemia); adherence to long-term therapy is vital to preventing cardiovascular, neurologic, and other delayed complications. Additionally, these patients often have a larger burden of accountability to correctly take several medications at different times within the same 24 h. Hence, this study aimed to evaluate the impact of a designated call about medication adherence and goal levels by pharmacists to patients on chronic medications and at risk of nonadherence. The null hypothesis was that there would be no difference in adherence after patients received the phone-call intervention by pharmacists to make them aware of the 80% PDC goal. An 80% PDC equated to patients taking their medication as prescribed 6 out of 7 days a week.

The objective of the current study was to test this hypothesis again in varied health care settings. PDC was the metric for measuring adherence based on its widespread use in literature, with 80% being an accepted adherence rate. The World Health Organization (WHO) and Centers for Medicare and Medicaid Services (CMS) also support the use of PDC as the most standard measurement tool to assess and report medication adherence.

2. Methods

This multi-site study included a retrospective chart review and prospective cohort design with randomization for group assignment (control (C) or intervention (X)). The CONSORT guidelines were followed to ensure transparent reporting of this study’s results. The site or health plan sent the researchers a list of high risk, nonadherent patients. Patients consented to the study and were blinded to the intervention. They were randomly assigned to intervention or control group by the pharmacist or trained pharmacy intern (using a random number generator). The intervention included a call from the pharmacist or trained pharmacy intern regarding an adherence goal (taking medications at least 80% of the time or 6 out of 7 days and picking them up accordingly from the pharmacy) for their chronic medications. Patients in the control group did not receive a call specific to adherence goals. However, all patients were expected to receive the standard of care phone calls; these may have included live or automated calls regarding mail order requirements for their prescription, notice of a prescription not being covered, the ability to receive 90-day fills or automatic refills, and a notice that a prescription is ready to be picked up at the pharmacy.

A convenience sample of three sites in southern California and an operative system responsible for patient data (through physician partnerships in various California locations) were utilized to collect patient data. These sites included 1) a university ambulatory care center, 2) an FQHC, 3) one regional division of a large community pharmacy chain and 4) capitated medical group. To provide a power of 80% using a two-sided alpha level of 0.05, the minimum number of patients in each group was determined to be approximately 65 for a minimum desired sample size of 130 (10). Inclusion criteria for the patients required at least 18 years of age, at least 1 chronic medication used to treat diabetes, hypertension, or dyslipidemia, and 2 or more documented fills (with at least 1 refill) for the designated medication(s) at the site. Exclusion criteria involved patients who had a pre-intervention PDC of 0.80 or greater. Chronic medications that would have otherwise fit criteria were excluded from data collection if they were not connected to the site recording their medication history or if they were required to be taken more than once daily. This exception was included to prevent the frequency of a medication therapy acting as a confounder when comparing adherence through PDC. A 1:1 randomization was used in all groups except Site 4 (the medical group), which utilized a 2:1 randomization scheme using a random number generator to allocate patients to C or X group.

The baseline average PDC (a.k.a. Pre-intervention PDC) for each recruited patient was provided by their respective sites through their own record systems (not patient-reported). The Post-intervention PDC would be calculated as follows: number of days the prescription medication covered divided by the number of days in the time period. If a medication was observed to be stopped and a different dose of the same medication in its class was continued in the same manner as the previous, the medication was considered for the same purpose and counted towards the PDC calculation. For example, a patient record displayed that atorvastatin 20 mg was stopped in March but simvastatin 40 mg was started in April; these medications treat the same diagnosis of hyperlipidemia, are never indicated as dual therapy, and can be considered continued use versus two separate chronic medications; therefore, the PDC would include these medications in a single calculation for adherence. However, if a patient was taking multiple medications indicated for a condition such as hypertension or diabetes, each chronic medication would have its own calculation for PDC (e.g., metformin and glipizide or lisinopril and metoprolol).

The study was IRB approved and was in accordance with HIPAA regulations. All access to patient data was approved by the health group or pharmacy that maintained the patient records and was utilized solely for research purposes by approved investigators, pharmacists, and rotation student pharmacists. Baseline characteristics were analyzed using descriptive statistics and compared between groups using Chi-Square and independent t-test. The primary outcomes included the average change in PDC from Pre-intervention to Post-intervention between and within C and X. Further analyses identified the secondary outcome of number of sampled patients who were able to reach the goal PDC. Data collection concluded in November 2019, allowing 3–9 months of refills data post-intervention. All statistical analyses were conducted using IBM SPSS v25.

3. Results

A total of 256 patients were recruited from the four sites. Patient refill data were collected from June-November 2019. After reviewing the data, 14 patients were excluded from analyses due to a baseline (pre-intervention) PDC of ≥0.80 (Fig. 1). A total of 241 patients were pooled for analyses. After randomization, the intervention group included 115 patients and the control group included 126 patients (Table 1). There were no significant differences in any of the baseline characteristics between the two groups (Table 1). Due to low sampling of ethnicity, a true comparison between groups in this characteristic was not calculated. Notably, the majority of patient information

Fig. 1. Patient data collection*.
*Only one site was able to collect data regarding patient ethnicity (missing data = 92 and 101 for C and X groups respectively). One patient in the intervention group did not disclose information regarding their sex and was excluded from analyses. One site was not able to provide insurance information for recruited patients (missing data = 80 and 84 for C and X respectively). Another site was not able to provide the number of medications on file per patient (missing data = 13 and 21 for C and X respectively).
came from the medical group, accounting for over 65% in each group. Patients with medication refills 3–9 months after initial records were able to be matched for Post-PDC (n = 89 for C group, n = 97 for X group).

Fig. 2 displays the change in PDC for C and X groups from Pre- to Post-PDC. The mean Pre-PDC and Post-PDC for C groups were 0.52 ± 0.18 and 0.73 ± 0.25 while the mean Pre-PDC and Post-PDC for X groups were 0.53 ± 0.18 and 0.71 ± 0.23 respectively. There was a significant difference from Pre- to Post-PDC for both C (0.18± 0.28, p < 0.05) and X (X = 0.16 + 0.24, p < 0.05) groups. There were no significant differences between C and X groups in any of these analyses. The total number of patients able to reach their adherence goals after the intervention period was 82/186 (44.1% of all patients, 46.1% of C and 42.3% of X).

Paired t-tests compared Pre- and Post-PDC within each group. There was a significant correlation between the Pre- and Post-PDC measures for the intervention group (0.32, p < 0.05), but not within the control group (0.10, p = 0.33). In total (n = 186), the correlation between Pre- and Post-PDC measures was significant (0.214, p < 0.05) and the total paired difference in PDC was significant (0.17 ± 0.26, p < 0.05).

**Table 1**

| Group/Site                        | Control (n = 115) | Intervention (n = 126) |
|-----------------------------------|------------------|------------------------|
| Mean Age ± SD                     | 67.2 ± 13.6      | 67.3 ± 11.9            |
| Sex                               |                  |                        |
| %female                           |                  |                        |
| Ethnicity                         |                  |                        |
| Caucasian                         |                  |                        |
| Hispanic                          |                  |                        |
| African American                  |                  |                        |
| Asian                             |                  |                        |
| Other                             |                  |                        |
| %Medicare                         |                  |                        |
| Private                           |                  |                        |
| Medicare                          |                  |                        |
| MedCal                            |                  |                        |
| Private                           |                  |                        |
| Medical group Database            |                  |                        |
| Total number of medications on file ± SD | 5.74 ± 3.06   | 6.26 ± 3.67            |

**Discussion**

This study was able to show that over time, patients from both groups improved in their medication adherence. The finding that there was no difference between the C and X groups may be explained by the following factors: 1) the style of communication by the pharmacist in each group was not directly documented 2) the intervention may not have been different enough from usual care 3) there may have been some contamination if the same pharmacist communicated with the C and X groups. There was a significant correlation between Pre- and Post-PDC only in the intervention group. The time period was also consistent between groups and could have contributed to improved adherence if patients started to get used to new medications. It was not documented which prescriptions were new fills, just when there were refills in the pharmacy or online system.

This study also presents the idea that specific counseling about an adherence goal may not be necessary in order to approve medication adherence. Future research could include testing different methods of communicating with patients about taking their medications (in person versus telehealth) and through different pharmacist services such as normal counseling, medication therapy management (MTM), chronic care management (CCM), or educational seminars on chronic care.

Former United States Surgeon General C. Everett Coop famously stated, “Drugs don’t work in patients who don’t take them.” It was previously determined that only 17% of patients with chronic medications were close to a “perfect” adherence regimen. Patients ultimately choose whether their medication regimen will be successful; however, patients have in many cases been presented as taking a less than proactive role in their attainment of good adherence. Patient-related factors including their social statuses, health conditions, and access to healthcare have reportedly been partially responsible for their inability to reach the 80% adherence goal. The authors have previously used a personalized approach with the M-DRAW tool to successfully improve medication adherence in a high-risk group. However, utilizing a patient-centered perspective to manage adherence has presented several challenges to implementation in real world settings. In the current study, the authors were unable to distinguish if obstacles in communication or attention may have existed during the study period; for example, a patient might have been more willing to improve their medication adherence if given attention by a pharmacy they were familiar with, regardless of the medication adherence goals being present in the conversation. Secondly, the sites did not provide information in the pharmacy or online system.

**Fig. 2. Change in PDC Over Time***

***Results were not significantly different between groups.
on any potential incentives they may have provided to their patients for taking their medications.

There does not exist a perfect measure of adherence that directly records that a patient is taking their medication exactly as they are meant to, when they are meant to, as instructed by their physician and pharmacist. While the validity of PDC in relation to true patient medication adherence is continually questioned and tested, it remains a popular measure in the healthcare field to infer medication-taking behavior (it has been continually utilized by Centers for Medicare and Medicaid Services (CMS) to rate pharmacy services).\textsuperscript{15,20} While self-reported data can provide an alternative measure, recall bias has been a problematic barrier to adherence data. Studies have shown that patients have been inaccurate documenters of their medication-taking behaviors, and in some cases, significantly overestimated their adherence.\textsuperscript{21,22} Additionally, physicians have not demonstrated an accurate ability to identify non-adherent patients in their own practices.\textsuperscript{23} While not quantitative, the Priming Question (Table 2) has demonstrated its reliability as a measure for patient-reported medication adherence. The utility of the Priming Question may better serve future studies when addressing adherence and potential habits to improve adherence. Until a better measure is found and widely accepted, PDC will likely continue to be used as the quantitative measurement standard for medication adherence in real-life scenarios (e.g., reimbursement and compensation by CMS to pharmacies).

5. Limitations and lessons learned

The study results should be considered in view of its limitations. The specific timing of prescriptions and subsequent refills as well as the insurance limits on how many doses can be dispensed at once could provide an unequal advantage to patients able to receive 90-day supplies on a “ready-fill” system. The PDC may solely show primary adherence, how often medications are filled by the automated system and picked up by patients rather than the intended capture of proper and consistent medication usage. Additionally, only the medical group was able to accurately show all medications being taken by the patients, regardless of where they might pick them up or have them mail ordered. It is unknown if a patient’s Post-PDC was the most accurate method available at these sites to explain their medication adherence; there are several reasons that refills might no longer exist in a pharmacy’s or clinic’s record keeping system. For example, a patient may have stopped picking up the prescription, discontinued the medication per physician instruction or their own choice, or changed pharmacies/mail order that would no longer reflect refill data on these pharmacy record keeping systems. Additionally, pharmacies and insurance plans have the ability to alter refill requirements, thus artificially affecting PDC by changing the quantity allowed per prescription and authorized fill dates. Any reasons for late refills or gap months for medications were unable to be investigated and documented in this study; these reasons may be separate from adherence and due to setting mechanisms of filling, physician ability to refill, patients changing pharmacies, etc. If the adherence goal at 80% was not the sole point of the intervention call, there may be contamination; the control group may have received a call very similar to that of the intervention group. Additionally, this study was unable to account for patient engagement and monitor which patients exhibited two-way dialogue with their pharmacist or if they tended to ask more questions about proper medication techniques. Including data on willingness to take medications and overall activation in addition to a quantitative measure such a PDC may better represent a patient’s adherence to chronic medication.

The generalizability of this study regarding ethnicity, income, and certain medication-taking barriers is unknown. Including demographics and specific adherence factors (e.g., belonging to an ethnic minority, cost of medications, and unemployment) in a future study design may prevent these potential biases and confounders.\textsuperscript{24}

6. Conclusion

This study explored the present roles community pharmacists take to interact with patients that take chronic medications and are at higher risk of consequences from nonadherence. Results of this study suggests that priming patients through a phone call may be sufficient to improve their adherence with chronic medications over at least a three months’ time. Furthermore, the results provided a supporting perspective that pharmacy staff and patients require a communicative relationship to improve adherence.

Credit author statement

Amanda R. Mercadante: Formal analysis, Investigation, Data curation, Writing – Original Draft, Writing – Reviewing & Editing.
Sun Lee: Methodology, Project administration, Writing – Reviewing & Editing, Visualization.
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Previous presentations of this work

Annual American Pharmacists Association Conference, March 2018 via published abstracts with preliminary data and poster presentation, Western States PowerPoint presentation of one site’s data in May 2017.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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