Adherence and persistence associated with an appointment-based medication synchronization program

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Abstract

Objective: To assess the impact of an appointment-based medication synchronization (ABMS) program on medication adherence and persistence with chronic medications.

Design: Quasiexperimental study in which study patients were matched with control patients.

Setting: Rural pharmacies in the Midwestern United States between June 30, 2011, and October 31, 2012.

Patients: Individuals receiving at least two refills for one of six categories of medications to treat chronic diseases (i.e., angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta blockers, dihydropyridine calcium channel blockers, thiazide diuretics, metformin, statins).

Intervention: Patients in the ABMS program were compared with control patients receiving usual care.

Main outcome measures: 1-year adherence rates using proportion of days covered (PDC) and 1-year nonpersistence rates.

Results: Depending on the drug class, patients enrolled in the medication synchronization program (n = 47–81) had adherences rates of 66.1% to 75.5% during 1 year versus 37.0% to 40.8% among control patients. Program patients had 3.4 to 6.1 times greater odds of adherence compared with control patients. Control patients were 52% to 73% more likely to stop taking their chronic medications over 1 year.

Conclusion: An ABMS program in community pharmacies was associated with improved patient adherence and reduced likelihood of nonpersistence.

Keywords: Community pharmacy services, medication adherence, chronic disease, pharmacies

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Medications are valuable in preventing and treating chronic medical conditions, but their effectiveness in the community is limited by patient nonadherence and nonpersistence with recommended therapeutic plans. Nonadherence can lead to serious consequences, resulting in considerable morbidity, hospitalizations, and mortality.[1–3] Estimates indicate that nonadherence costs the U.S. health care system $100 billon[4] to $289 billion[5] annually.

Adherence to physician prescriptions varies depending on the intervention, setting, patient population, and study, but evidence consistently indicates that adherence needs to be improved. A 50-year review of all physician medication and nonmedication therapies found that patients follow physician recommendations only 25% of the time.[6] For chronic medication prescriptions, studies have found adherence rates to vary widely, with most assessments reporting approximately 50% adherence.[4,7–10]

The reasons why patients do not take their medications are complex and varied. The World Health Organization classifies the causes for medication nonadherence into five categories.[11] The first category of causes refers to individual characteristics of the patient such as physical impairments (e.g., vision or dexterity problems), cognitive problems, and age-related concerns. The second addresses difficulties associated with the patient's medical condition (e.g., asymptomatic) and comorbidities (e.g., depression). Third is the health system itself, and it includes causes such as poor continuity of care, lack of health care access, and poor provider–patient communications. Fourth is the complexity of therapeutic regimens and the various associated adverse effects. Last are socioeconomic causes, including affordability barriers, low reading literacy, low health literacy, and lack of social support for individuals.

Each patient's nonadherence typically is the result of multiple interrelated causes.[11–13] Resolution of these interrelated factors is needed for improvement to occur. In addition, the causes of nonadherence continually change for each patient as their medical conditions progress, new therapies are added to the regimen, socioeconomic situations change, and other circumstances arise. This suggests a need for interventions that can be continuously modified as the situation changes.

Because of the multifactorial nature of medication nonadherence, the most effective interventions typically are individualized to the unique needs of patients. Successful interventions combine diverse strategies that enhance patient access and convenience to medications, offer education and reminders, provide self-monitoring and feedback, engage in mutual problem solving, and offer a range of other approaches.[11–13] Community pharmacists have been offering variations of these approaches to their patients for many years.[14–16]

Indeed, a systematic review of the adherence literature found that five of six pharmacist-directed interventions in community pharmacies were effective in improving adherence by 7% to 27%.[14] Compared with other approaches, interventions delivered by pharmacists in a pharmacy were 83% successful compared with electronic interventions without a human involved (67%), phone calls (38%), and clinic programs (38%). When supported by electronic messaging or phone calls, additional evidence of the impact of face-to-face pharmacist services on improving medication adherence has been promising.[15,16]

The complexity of a patient's therapy influences medication adherence,[17,18] and it has been suggested that standardizing medication schedules can improve medication adherence and health outcomes.[19–22] Consequently, several programs that simplify patient medication regimens currently are being offered in community pharmacies. Known by various names (e.g., Patient Centric Model, Med Sync, Sync Your Meds), the programs involve pharmacists working with patients to synchronize their chronic refill medications to come due on a single day of the month. By streamlining the refill process and by working together to resolve medication-related issues, it is hypothesized that patients will have better adherence with their prescribed medications.

At a Glance

Synopsis: This study described how patient adherence and persistence with chronic medications can be improved by allowing patients to meet with a pharmacist to solve medication-related problems and synchronize prescriptions to be dispensed on a single day of the month. Compared with control patients, those in the appointment-based medication synchronization (ABMS) group had 3.4 to 6.1 times greater odds of adherence compared with control patients. Control patients were 52% to 73% more likely to stop taking their chronic medications over 1 year.

Analysis: *Although medication synchronization can help remind patients, provide updates on their progress, simplify the process, and make refilling a prescription more convenient, the monthly appointment allows pharmacists to educate, engage, and solve problems. In contrast to the typical prescription-filling process, during which pharmacists react to patients' needs, the ABMS program allows pharmacists to proactively manage patients' medication-related needs. The appointment provides an opportunity for pharmacists and patients to engage in mutual problem solving about issues such as physical impairments, lack of affordability, low literacy, and lack of social support. In addition, synchronization can free pharmacists to provide medication therapy management and additional clinical services.*

Objective

The purpose of this study was to assess the impact of an appointment-based medication synchronization (ABMS) program in community pharmacies on medication adherence and persistence. Prescription records for program patients for six medication categories (i.e., angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin receptor blockers, beta blockers, dihydropyridine calcium channel blockers [DCCBs], thiazide diuretics, metformin, statins) were matched to nonprogram patients to compare the likelihood of adherence and persistence. It was hypothesized that individuals who (1) make an appointment with a pharmacist to resolve medication-related issues and (2) synchronize their chronic medications to be refilled on a single day of the month will be more likely to take their medications as directed.

Methods

The study was conducted on patients served by Thrifty White Pharmacy, a chain of employee-owned community pharmacies located in several rural Midwestern U.S. states (Minnesota, Iowa, Montana, North Dakota, South Dakota, and Wisconsin). A quasiexperimental research design with participant matching was used to assess medication use of pharmacy patients from June 30, 2011, to October 31, 2012. The study was approved by the Institutional Review Board of Virginia Commonwealth University.

Promotion and enrollment into the ABMS program was conducted at the individual store level. Patients were contacted by a clerk, technician, or pharmacist about the availability of the program. Contacts were made verbally or via printouts stapled to prescription bags. Interested patients were scheduled for a synchronization appointment immediately or at a later date. The synchronization appointment consisted of the following steps:

- Printing a list of the patient's medications
- Establishing the first appointment date or "sync date" (i.e., date agreed upon by patient and pharmacist on which all medications would come due at the same time)
- Establishing which medications the patient would like enrolled in the ABMS program
- Identifying medications that required partial fills in order for them to sync at the scheduled date
- Establishing the dispensed quantity desired by the patient or third party (e.g., 30 days, 90 days)
- Scheduling a monthly call to the patient from an automated call service to review the patient's current medications and identify any needed changes
- Developing a monthly prescription cost estimate and planning for either a single monthly payment or a payment interspersed throughout the month
- Addressing any patient questions related to the program or medication-related problems
- Having the patient sign an enrollment agreement form

Although synchronization appointments with pharmacists were individualized to patients' needs, each involved a one-on-one conversation seeking to clarify, modify, and enhance patient therapy when needed. Review of patient medications was integral to the appointment process. The review provided an opportunity to critically assess current therapy and discuss specific patient needs and problems that might lead to nonadherence. Depending on the needs of patients, pharmacists might suggest adding other adherence options to the synchronization program, such as HealthyPackRX, which is Thrifty White's proprietary compliance packaging system in which all medications are organized into individual packets labeled with the medication, day, date, and time to be taken. Clinical services such as medication therapy management (MTM) and immunizations also could be promoted.

In addition, the appointment was an opportunity to tailor the program to patient preferences for delivery, payment, and methods of contact. Of the options for medication delivery, approximately 80% of patients picked up their maintenance medications at the pharmacy and the rest received them via mail or courier. Patients also were offered a choice of paying for all monthly medications in a single payment or spreading payments throughout the month. Finally, all patients were required to provide preferred cell or home phone numbers to receive automated calls in preparation for the monthly medication delivery. This number was updated periodically to ensure the ability of the pharmacist to contact the patient when necessary.

To synchronize medications, the pharmacist identified an anchor medication around which the first sync date was established. Pill counts were used to determine how many pills patients had remaining for each of their prescriptions and ensure an accurate first-time sync date. Physicians were contacted by patients or pharmacists regarding enrollment in the ABMS program.

Patients were identified in the patient record as being in the ABMS program. This allowed specialized software to track patient progress, schedule automatic reviews of prescription records, and send automated communications before pharmacy visits. If the patient indicated changes in the prescription or had questions, a patient care center serving all pharmacies at a centralized location addressed them before patients visited the pharmacy.

A centralized refill center filled prescriptions approximately 7 days before the sync date. All problems related to therapy or insurance coverage (e.g., drug use review rejects) were addressed before the prescription was filled and delivered to the dispensing pharmacy.

Three days before the sync date, a pickup reminder call was made. Depending on patient preference, the medication could be picked up, delivered, or mailed. Pharmacists followed up with patients who were late picking up their medications.

Individuals receiving at least two refills for one of six types of chronic disease medication (i.e., ACEIs or ARBs, beta blockers, DCCBs, thiazide diuretics, metformin, statins) were identified from patient records. The first fill within 30 days of enrollment was considered the start date for the medication being evaluated. Patients with start dates after November 1, 2011, and prescriptions of less than 30 days' supply were excluded. Originally, sulfonylureas were included in the analysis, but they were eventually excluded because of low sample sizes after matching (n = 22 in control patients and n = 22 among study patients).

A pool of control patients was developed by identifying all individuals not in the ABMS program who had at least two fills for one of the chronic drugs within the time period of enrollment. These patients received the usual care provided by community pharmacies within the Thrifty White Chain. From that pool, patients were matched to study patients based on drug class, age, gender, region according to ZIP Code, and start date (±15 days).

The outcomes of interest in this study were adherence and nonpersistence. Adherence was defined as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen"[23] and was measured using proportion of days covered (PDC). PDC was calculated by the ratio of number of days covered by the prescription fills divided by the time between the first fill of the medication and the end of study period.[24] The PDC ratio ranges from 0 to 1, with larger proportions equaling greater adherence. Persistence was defined as "the duration of time from initiation to discontinuation of therapy."[23] Nonpersistence was calculated by identifying the date at which a patient stopped taking a medication within the chronic medication category for 30 days or more. At that point, they were labeled nonpersistent.

Data analysis

PDC and persistence data for study patients enrolled in the ABMS program were compared with data for control patients. Up to three control patients per study patient were used depending on the availability of matching control patients. Patients with a PDC of at least 0.80 were considered adherent.[24] Overlapping days were credited toward the PDC.

Adherence between groups was compared in two ways. First, the value of the PDC was compared between groups. To account for the paired nature of the matched comparisons and the nonnormality of the PDC, the Friedman test was used. Second, adherence was assessed by comparing the proportion of patients who were considered adherent (i.e., PDC of at least 0.80). Accounting for the matched sample design, a univariate conditional logistic regression was used to evaluate the odds of adherence by group. A univariate conditional Cox proportional hazards regression was performed to identify the time at which patients discontinued their chronic medication, in order to model time to nonpersistence. Using an intent-to-treat principle, it was assumed that patients continued in the program regardless of whether they did. This was done because it was not possible to track the exact dates at which point patients dropped out of the program. $P < 0.05$ was considered statistically significant. The data analysis was conducted using SAS software (version 9.2; SAS Institute, Cary, NC).

Results

Table 1 provides descriptive data about patients enrolled in the ABMS program prior to matching. Before matching, the average patient was female, enrolled in a commercial insurance plan, and older than 65 years. After matching, inclusion, and exclusion, the demographics of the ABMS and control patients were similar, and the final sample sizes for control and study patients varied from 47 to 564 (Table 2).

Mean PDC scores for study patients were significantly greater than those for control patients in each of the drug classes (Table 2). Mean PDCs for the control group ranged from 0.58 to 0.63, while those for patients in the ABMS program ranged from 0.80 to 0.87. The difference was statistically significant for each drug class.

The percentage of patients who were considered adherent (i.e., PDC ≥0.8) also was significantly greater for study patients compared with control patients (Table 3). In the control group, approximately 37% to 41% were considered adherent depending on the drug class. In contrast, the percent of adherent patients in the ABMS program ranged from 66% to 79%. When evaluating the odds of adherence, patients enrolled in the program had 3.4 to 6.1 times greater odds of adherence (depending on drug class) compared with control patients.

The percent considered nonpersistent according to group and hazard ratios are displayed in Table 4. In the control group, approximately 67% to 74% became nonpersistent within 1 year after starting, while 34% to 48% became nonpersistent in the synchronization group. Compared with patients in the program, patients who were not enrolled in the ABMS program had a 52% to 73% greater hazard of nonpersistence, depending on drug class.

Discussion

This study describes how patient adherence and persistence with chronic medications can be improved by

Table 1. Description of patients eligible for and enrolled in the ABMS program prior to matching

Variable	ACEIs/ARBs	Beta blockers	DCCBs	Thiazide diuretics	Metformin	Statins
n						
ABMS	1,263	1,022	606	447	411	1,281
Eligible control patients	22,126	18,636	10,471	7,078	5,832	18,361
Age (years), mean ± SD	68.4 ± 16.1	70.4 ± 16.2	72.4 ± 15.7	68.2 ± 16.4	63.3 ± 15.5	68.4 ± 14.4
Female gender (%)	53.2	57.1	60.3	60.7	50.1	51.5
Plan type (%)						
Cash	4.3	3.9	2.8	4.3	3.8	2.4
Commercial	79.9	77.6	79.6	80.6	81.2	81.7
Private	12.5	15.1	15.3	12.0	9.3	12.8
Welfare	3.3	3.4	2.3	3.1	5.7	3.1

Abbreviations used: ABMS, appointment-based medication synchronization; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker.

Table 2. Proportion of days covered by drug class

Drug class	Control patients Mean ± SD (n)	Study patients Mean ± SD (n)	*P*
ACEIs/ARBs	0.61 ± 0.318 (537)	0.87 ± 0.216 (278)	<0.0001
Beta blockers	0.61 ± 0.312 (415)	0.84 ± 0.227 (202)	<0.0001
DCCBs	0.63 ± 0.306 (196)	0.82 ± 0.255 (106)	<0.0001
Thiazide diuretics	0.58 ± 0.328 (100)	0.80 ± 0.269 (59)	0.001
Metformin	0.62 ± 0.295 (87)	0.86 ± 0.233 (47)	0.001
Statins	0.62 ± 0.289 (564)	0.84 ± 0.248 (281)	<0.0001

Abbreviations used: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker.

Table 3. Percent of patients adherent and ORs from univariate logistic regression

	Adherent (%)			
Drug class	Control	Treatment	OR (95% CI)	*P*
ACEIs/ARBs	40.8	79.5	6.1 (4.2–9.0)	<0.0001
Beta blockers	38.3	71.8	4.7 (3.1–7.1)	<0.0001
DCCBs	40.3	68.9	3.8 (2.2–6.7)	<0.0001
Thiazide diuretics	37.0	66.1	3.4 (1.6–7.5)	0.0017
Metformin	40.2	76.6	4.8 (2.0–11.5)	0.0003
Statins	37.4	76.2	5.8 (4.0–8.4)	<0.0001

Abbreviations used: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker; OR, odds ratio.

Table 4. Rates of nonpersistence and hazard ratios

	Nonpersistent (%)			
Drug class	Control	Treatment	HR	*P*
ACEIs/ARBs	70.0	33.8	0.27 (0.20–0.35)	<0.0001
Beta blockers	71.6	38.1	0.30 (0.22–0.41)	<0.0001
DCCBs	67.4	43.4	0.48 (0.32–0.71)	0.0003
Thiazide diuretics	74.0	47.5	0.38 (0.22–0.66)	0.0006
Metformin	73.6	34.0	0.37 (0.20–0.68)	0.0013
Statins	72.5	41.6	0.39 (0.31–0.50)	<0.0001

Abbreviations used: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker; HR, hazard ratio. HRs were obtained from univariate conditional Cox proportional hazard regression models. HRs represent the ratio of hazard rates of nonpersistence for study patients compared with that of control patients. An HR <1 favors the treatment group.

allowing patients to meet with a pharmacist to solve medication-related problems and synchronize prescriptions to be dispensed on a single day of the month. Synchronizing patient refills has been suggested as a solution to nonadherence caused by therapeutic complexity.[25] Evidence also indicates that medication adherence can improve if patients consolidate the number of visits to a pharmacy for medication refills and they visit fewer pharmacies for their medication-related needs.[26] To our knowledge, however, this is the first study to examine the impact of an ABMS system.

This study found significant improvements in medication adherence and persistence with the ABMS program. For every 100 patients in the study, approximately 29 to 38 additional individuals were adherent in the ABMS group than in the control group depending on the drug class. In addition, approximately 24 to 39 fewer individuals per 100 were nonpersistent in the ABMS group. These results indicate that an ABMS program can improve patient medication-taking behavior significantly.

Focusing on the synchronization portion of the system might be tempting, but the importance of patients meeting with pharmacists also should be emphasized. Medication nonadherence has many causes, and it is unlikely that synchronization alone was the reason for the program's positive impact. Although synchronization can help remind patients, provide updates on their progress, simplify the process, and make refilling a prescription more convenient, the monthly appointment allows pharmacists to educate, engage, and solve problems. Overemphasizing synchronization can miss a key ingredient of the program's value.

The ABMS program should be seen as blending technology with face-to-face contact with pharmacists to address the causes of nonadherence. In contrast to the typical prescription-filling process, during which pharmacists react to patients' needs, the ABMS program allows pharmacists to proactively manage patients' medication-related needs. The appointment with the pharmacist provides an opportunity without distractions for the pharmacist to engage in mutual problem solving about issues related to physical impairments, lack of affordability, low literacy, and lack of social support. The centralized reminder and refill process can address the problems of simple forgetfulness, poor continuity of care, poor provider–patient communications, and insurance, thereby allowing these and other issues to be resolved before patients arrive at the pharmacy. Synchronizing the medications to a single day of the month can improve access to care for patients with limited transportation options and help simplify therapeutic regimens. Synchronization can free pharmacists to provide MTM and additional clinical services.

Future research

This research highlights benefits of a synchronization and appointment-based program that have not been explored previously. Currently, the impact of synchronization has been shown only in relation to medication adherence. The effect of synchronization as it relates to patient health outcomes (e.g., cardiovascular events) or intermediaries of those outcomes (e.g., blood pressure control) has not been reported. Although better adherence is associated with improved health, the impact of ABMS on outcomes is unclear. Positive nonmedical benefits to patients, such as the impact on patient satisfaction and patronage of pharmacies, also would be worth exploring.

Another important question to answer is the relative impact of various components of the ABMS program and the degree to which the components might interact to influence adherence and persistence. The ABMS program described in this article has multiple elements, including face-to-face interviews, electronic reminders, telephonic interventions, and additional services. Future research might seek to identify how each component contributes to patient adherence and determine the extent to which the sum of the components of the ABMS program might be greater than its individual parts. This might require itemizing the various elements of the program and systematically varying them in much larger patient populations than that present in the current work.

Research also should assess the benefits of the program to pharmacy operations. Synchronizing medication refills to a single day of the week may allow pharmacists to manage their workflow better and improve service to patients. More predictable patient demand might reduce medication inventory and personnel costs. Better adherence to medications could increase store revenue by capturing lost refill revenue. In addition, the ABMS program might influence up-front sales of OTC medications and merchandise. Although fewer visits to the pharmacy could lead to less up-front sales, it is also possible that increased patient loyalty to a pharmacy that uses the ABMS program could lead to greater sales.

Finally, research should be conducted to assess ways in which ABMS might reduce primary medication nonadherence. Primary nonadherence occurs when a patient never takes a newly prescribed drug, while secondary nonadherence occurs when a medication is taken but not as prescribed. This study focuses on secondary medication adherence because inclusion in the data set was conditional on filling a prescription. Because primary nonadherence averages approximately 15% of patients seeing physicians,[29,30] understanding how ABMS might help prescriptions from being left at the pharmacy would be useful.

Limitations

This research involved several limitations. The findings of the current work may not be duplicated in other settings. Research has shown that pharmacists can influence medication adherence,[14,27] but significant variability exists in pharmacy effects on medication adherence.[28] Thrifty White Pharmacy is a medium-sized chain of owner-operated pharmacies. Other pharmacies may not be able to offer the same convenience, reminders, education, self-monitoring, reinforcement, support, and mutual problem solving.

Another limitation is that the study design established association between the program and adherence, not causality. A convenience sample was used to select participants in the ABMS program, making it possible that patients in the ABMS group differed from the control group before the start of the program, even after matching. Unlike the control group, individuals in the ABMS program were recruited, consented, and enrolled in the program. Compared with nonparticipants, ABMS participants may have been more motivated or likely to adhere to their medications without the program.

The analysis also did not control for all factors affecting adherence to medications. Factors not addressed in the study design included patient insurance status, complexity of medication regimens, severity of conditions, and level of patient motivation and engagement in their health care. Another limitation is that patients may have been incorrectly labeled as adherent or nonpersistent. Adherent patients may have obtained their prescriptions but not taken them as directed. Nonpersistent patients may have been directed by the physician to discontinue therapy, or they may have simply switched pharmacies. The ability to address these limitations was outside the scope of this study.

Conclusion

This is the first study to assess the impact of ABMS in community pharmacies. The results indicated that the ABMS program was associated with improved patient adherence and that it reduced the likelihood of nonpersistence. Although more research is needed to fully understand the program's impact on other outcomes and in different settings, the ABMS program shows promise as a strategy for pharmacists to use in serving the needs of patients.

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