RESEARCH ARTICLE

Architecting Process of Care: A randomized controlled study evaluating the impact of providing nonadherence information and pharmacist assistance to physicians

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Abstract

Objective: To test the impact of connecting physicians, pharmacists, and patients to address medication nonadherence, and to compare different physician choice architectures.

Data Sources and Study Setting: The study was conducted with 90 physicians and 2602 of their patients on medications treating chronic illness.

Study Design: In this cluster randomized controlled trial, physicians were randomly assigned to an arm where the physician receives notification of patient nonadherence derived from real-time claims data, an arm where they receive this information and a pharmacist may contact patients either by default or by physician choice, and a control group. The primary outcome was resolving nonadherence within 30 days. We also considered physician engagement outcomes including viewing information about nonadherence and utilizing a pharmacist.

Data Collection: Physician engagement was constructed from metadata from the study website; adherence outcomes were constructed from medication claims.

Principal Findings: We see no differences between the treatment arms and control for the primary adherence outcome. The pharmacist intervention was 42 percentage points (95% CI: 28 pp–56 pp) more likely when it was triggered by default.

Conclusions: Access to a pharmacist and real-time nonadherence information did not improve patient adherence. Physician process of care was sensitive to choice architecture.

KEYWORDS

adherence, behavioral economics, choice architecture, defaults, pharmacists, phone-based interventions

1 | INTRODUCTION

Medication nonadherence is a widespread problem with significant financial and health costs.¹ It is responsible for unnecessary hospitalizations^{2,3} and is an important contributing factor to deaths from chronic illnesses. Proper adherence has been estimated to decrease medical

spending by as much as 20 percent.⁴ While the consequences of medication nonadherence are well understood, relatively few interventions have been demonstrated to improve it^{5,6} and there is limited evidence about which components of adherence programs drive impacts.⁷

Several studies of patients' adherence behaviors have evaluated the impact of patient incentives on adherence, with some trials

illustrating encouraging improvements in adherence⁸ and other trials displaying more mixed results.⁹ Since optimizing treatment regimens requires the cooperation of physicians, efforts to change adherence behaviors may be more likely to succeed if they are integrated into health systems. Evidence suggests that incentives to both physicians and patients are more effective than incentives to either patients or physicians alone in encouraging improvements in medication adherence.¹⁰

There are a number of reasons that physicians may not counsel patients to encourage adherence. Physicians may not have accurate and timely information about medication nonadherence,¹¹ may feel that asking patients about whether they are taking their medicine is beyond the scope of their role as a physician, or may feel that they have insufficient time due to competing demands.¹² Given the increasingly limited time they have to spend with patients,^{13,14} engaging other providers such as pharmacists in adherence counseling may be an efficient way to engage patients in conversations about nonadherence. More evidence is needed to understand whether providing time-sensitive information about medication adherence can enable physicians to address nonadherence and the best strategies to integrate pharmacists into care.

Research in behavioral economics has demonstrated the potential for alterations in choice architecture—defined as the intentional use of behavioral tools such as defaults or framing to shape behaviors¹⁵—to alter patient behavior at low cost.^{16–21} Designs that alter the choice architecture of physicians can feasibly be integrated into complex health systems.^{22–30} Changes in default settings of physician electronic systems have been shown to influence decisions about which drugs to prescribe^{22,23} and whether to order tests.^{24,25} Changing physician choice architecture has been shown to influence patient decisions around cancer screening²⁶ and influenza vaccination.²⁷ To our knowledge, no studies to date have tested how physician choice architecture can alter physician's process of care around addressing medication nonadherence. We examined whether defaults have an impact on whether physicians utilize the services of a pharmacist to address patient nonadherence.

We conducted a randomized experiment testing an intervention that connected pharmacy benefit managers (PBMs), primary care doctors, clinical pharmacists, and patients, in real time, to improve medication adherence. The study tested the impact of physician email notification of patient nonadherence, patient contact by a pharmacist, and experimental variations in physicians' choice architecture. The underlying hypothesis of our study is that defaults might be used to direct health care systems toward the utilization of a broader array of health care professionals such as pharmacists.

2 | METHODS

We conducted a randomized experiment in collaboration with a large provider group (the New England Quality Care Alliance, NEQCA), a

large commercial insurer, Express Scripts (ESI), and a pharmacy benefit manager (PBM).

2.1 | Study context

Eligible patients were enrolled in either an HMO or PPO plan. Eligible physicians were part of an alternative quality contract that made them eligible for quality bonuses if their HMO patients met specific quality targets.²⁸ The quality contract did not explicitly incentivize medication adherence. However, medication adherence would have been an important element of a strategy to reach several of the 32 quality targets, including those that provided incentives for control of hypertension, lipids, and diabetes.

2.2 | Intervention

Several intervention components addressed nonadherence: (a) Physicians received a notification when one of their patients was nonadherent; (b) a pharmacist was made available to contact nonadherent patients; and (c) physicians were randomized to two versions of choice architecture with regard to how they engaged the pharmacist. Our design allowed us to answer two distinct research questions. First, we compared the engagement of physicians when pharmacist intervention occurred by default or through the physician's active choice. Second, our design allowed us to examine the impact of each of the elements of the intervention independently in order to understand the relative importance of physicians being aware of patient's nonadherence and having the option for a pharmacist to make a call to address patient nonadherence. Section 2.4 provides more details on the experimental design and randomization.

We tracked adherence in real time using claims data from the PBM. We based all calculations of late refill on medication class, not specific formulations.

To classify potential cases of nonadherence in real time, we defined the depletion date as the latest fill date of any drug in a therapeutically equivalent drug group plus the largest days' supply of all prescriptions of the same drug group for that date. We classified patients as having a nonadherence event if 10 or more days had passed since the depletion date without a refill. Our definition of "nonadherence" was relatively conservative and differed from traditional definitions based on proportion of days covered by medication that are defined retrospectively instead of prospectively. We chose a relatively sensitive definition of nonadherence for this pilot study in order to capture more potential cases of nonadherence. Patients may have been classified as "nonadherent" even if they still had medication on hand for a variety of reasons, including past nonadherence, pill cutting, or paying out of pocket for a medication, but not because they had medication on hand because of previous early refills.

We built a stand-alone study website where physicians could log in to see information about their patient's nonadherence events, including the patient name, medication name, prescribed dose,

scheduled refill date, and number of days since scheduled refill date, and request that a pharmacist contact a nonadherent patient. If a pharmacist call was completed, a summary written by the pharmacist was provided to physicians.

Four pharmacists were contracted by the project to contact patients to counsel them about nonadherence events. Pharmacists were trained, using a Motivational Interviewing model,²⁹ to gather information from patients on the reasons for nonadherence, information about their understanding of their disease, and willingness to comply with prescribed regimen, and to answer any questions about their disease or their medications. The pharmacists prepared a written note to the physician at the end of each patient's phone contact, which was immediately available on the physician's web page and could also be faxed to the physician's office or sent directly to the patient's electronic health record. If the patient communicated any critical time-sensitive health information, the pharmacists were trained to contact the physician immediately. Each physician was assigned only one pharmacist for the duration of the experiment.

Once a nonadherence event was identified for an eligible patient, the study sent a personalized initial alert email to the patient's physician to notify the physician of the nonadherence event. Email alerts stated.^a

You have a PHARxMOS^b non-adherence message to be viewed. Please click here to be connected to the secure website.

For physicians who were eligible for assistance from a pharmacist, the pharmacist called patients using a web-based calling platform. To eliminate redundant call attempts, pharmacists combined adherence counseling for more than one medication into a single conversation. Pharmacists were trained to call landlines before cell lines, make the first call during evening hours, and attempt to reach patients up to five times. If a new event appeared for a patient who was reached recently

for a prior event, pharmacists waited two weeks before attempting to call the patient again to reduce patient annoyance. If patients requested that the pharmacists not call them again, the patient was removed from the contact list.

2.3 | Study population and recruitment

We recruited physicians from NEQCA, a provider network in MA. Physicians were eligible if they were primary care physicians in a practice affiliated with NEQCA and had a patient panel that included adults and treated patients covered by the insurer we partnered with for this study (a northeastern health care insurer with a mixed geographic population).

From a list of 389 eligible physicians, we recruited physicians through a series of recruitment presentations at regular gatherings of physicians. Among 205 physicians who attended these events, 113 physicians consented to participate in the study. At the time of physician randomization, 91 physicians remained willing to participate in the study (the most common reason for study withdrawal was leaving the network). One physician assigned to the information-only treatment dropped out after physician randomization but prior to the period where any of their patients were randomly assigned to a treatment arm. The final sample for analysis included the patients of 90 physicians.

Patients were eligible if they were (a) being treated for hypertension, hypercholesterolemia, or diabetes, as indicated by a past fill for at least one prescription in the past six months for at least one of the study medications, (b) 18 years of age or older, (c) covered by our commercial insurer partner, (d) and not on the insurer's "do not contact" list. For HMO patients, we used the primary care provider identified by the plan. For patients covered under a PPO insurance model without one primary physician, the insurer used an algorithm to identify their primary physician.^c To consent

FIGURE 1 Patient and physician flow through enrollment, randomization and follow-up

eligible patients, we sent a note card explaining that their physician was participating in a study. The card indicated that if they wanted to “opt out” of the study, they should send the card back in or contact the study team. At the time the study launched, 2602 had consented. Of those, 1474 had a valid medication claim during the study period that we adjudicated as nonadherent (details in Figure 1).

2.4 | Experimental design and randomization

We randomized at both physician and patient levels. The trial was unblinded. There were three physician treatment arms. In an “Info only” (information) group, physicians received information on patient nonadherence via email or fax notification but did not have access to trained pharmacists. In the “Default” treatment arm, for eligible patients, the pharmacist contacted the patient as the default option unless the physician canceled the intervention. To cancel, the physician had to log in to the study website and actively chose to cancel the pharmacist intervention. If they did not cancel the pharmacist call within five days of physician notification, the system automatically requested that the pharmacist call the patient. In the “Choice” treatment arm, the pharmacist contacted the patient only if the doctor logged into the study website and clicked on a button to actively request that the pharmacist contact the patient. Supplemental Figure 1 provides screenshots of the choices and information available to physicians in the “Default” and “Choice” versions of the choice architecture. Prior to the launch of the study, physicians were randomized into one of these three treatments with equal probability and informed of their treatment assignment by the study biostatistician. Physician randomization was stratified by practice.

At their first nonadherence event, patients of physicians assigned to the pharmacist intervention were randomized to pharmacist intervention (either Default or Choice depending on their physician’s random assignment), information-only (Info only) or control groups, with 50 percent of patients randomized to intervention (choice or default), 25 percent to Info only, and 25 percent to control by the study’s biostatistician. Patients of physicians assigned to the “Info only” physician arm were randomly assigned to “Info only” or control groups with equal probability. This design yields four possible treatment categories for patients (“Choice” pharmacist intervention, “Default” pharmacist intervention, “Information only,” and control). This multilevel experimental design is summarized in Figure 2. For control patients, physicians received no notification or information about patients’ nonadherence. For Info only patients, physicians received only an email or fax notification about the nonadherence event with information on the fill due date and the medication type but no opportunity to engage the pharmacist to call the patient. If assigned to the intervention arm, patients received either the Default or Choice pharmacist intervention, according to their doctor’s treatment assignment. Final allocations of physicians and patients are shown in Figure 1 (see technical Appendix S1 for CONSORT checklist).

The intervention ran between February 2013 and August 2013. The study received IRB approval from Brown University and Tufts University Medical Center and was registered after the end of data collection at ClinicalTrials.gov NCT02306122.

2.5 | Sample size determination and outcome measures

The study sample size and complex multilevel experimental design were chosen to ensure statistical power to identify two central research questions: (a) whether providing nonadherence information to physicians improved adherence, and whether engaging a pharmacist improved it further; and (b) whether the default choice architecture resulted in more physician engagement than the choice option. Power calculations were conducted accounting for the clustered nature of the randomized trial.

We measured patients’ adherence using real-time data obtained for participating patients through their PBM. The electronic pharmacy data capture all refills that take place at pharmacies and are linked to claims data. Our primary outcome for the first study question was binary—whether the nonadherence event was resolved within 30 days or not. We considered a nonadherence event “resolved” if a patient picked up their medication within 30 days of the calculated depletion date. This was chosen as the primary outcome because of its implications for health outcomes and because it could be observed for all study participants. We also considered a continuous variable which indicated how many days late a fill occurred. This value was not observed for 724 claims that were never filled during the intervention period.

For the second set of study questions, we measured physicians’ engagement with the medication adherence system using metadata from the study website. The website tracked all physician logins to the system and anytime a physician clicked to make a choice. Because information about each nonadherence event was on a separate web page, we could track whether a physician viewed nonadherence event information for each patient in the study. We constructed a binary outcome indicating whether a physician ever logged into the online system and viewed a nonadherence event claim. We also constructed a binary variable indicating whether a pharmacist intervention was triggered. For Default arm physicians, this happened by default after five days as long as the physician did not log in to the system and explicitly choose to cancel the pharmacist intervention. For Choice arm physicians, this happened when the physician logged into the system and requested the pharmacist intervention.

2.6 | Analysis

We provide summary statistics and orthogonality checks for patient and physician randomization. We check orthogonality across the final patient assignment (either control, information only, default

FIGURE 2 Experimental design [Color figure can be viewed at wileyonlinelibrary.com]

pharmacist, or choice pharmacist) and across the initial physician random assignment (excluding the one physician that dropped out prior to the start to engaging with the study). We report *P*-values from chi-squared tests from multinomial logit regressions of each covariate on an outcome that includes the four patient random assignment categories (control, information only, default pharmacist, and choice pharmacist) with robust standard errors clustered at the physician level.

We analyzed the data using the intent-to-treat principle with our primary analyses focusing on the four possible final patient assignments. For binary outcomes, we tested for differences across treatment arms using a linear probability model to allow us to interpret parameters as probability differences. Specifically, we estimated a generalized linear model for a binomial outcome with an identity link function. For the continuous outcome of the duration of the nonadherence event, we used ordinary least-squares estimation. In analyzing physician effort, we excluded the control group and considered only claims where physicians assigned to a treatment arm would have been notified by email of nonadherence. For the analysis of whether the pharmacist was engaged by the physician, we considered only claims for patients who had been randomly assigned to intervention arms where the pharmacist was available. Robust standard errors were clustered at the physician level to account for the physician-level randomization.

We also analyzed how patterns of adherence differ based on physicians' response to choice architecture. We constructed the cumulative distribution function for the number of days late a prescription was filled within the subsample of claims eligible for the pharmacist intervention. We compared the distribution for each arm by physician behavior, comparing claims where physicians

requested pharmacist action to those that did not in the Choice arm, and comparing claims where physicians canceled the pharmacist intervention to claims where they took no action in the Default arm. Within each arm, we compared the distribution of days late across the two possible physician behaviors using the Kolmogorov-Smirnov (KS) equality of distribution test. Claims that were never filled were excluded from this exploratory analysis (21.46 percent of claims).

We present robustness checks in supplemental appendices including versions of all main estimates adjusting for baseline characteristics presented in summary table 1 (Table S1), estimates of the impact of physicians' treatment arm assignment on study outcomes (Table S2), and estimates that consider only the patient's first nonadherence event (Table S3).

3 | RESULTS

3.1 | Characteristics of the sample

The average age of patients was 56, and 65 percent of patients were male (Table 1). Seventy four percent of patients were part of an HMO insurance plan with incentives compatible with prioritizing medication adherence for these conditions. Seventy eight percent of patients were on a medication for hypertension, 72 percent were on a medication for hypercholesterolemia, and 22 percent were on a medication for diabetes. The sample was balanced across treatment arms for most patient characteristics with the exception of the proportion of patients on any medication for

TABLE 1 Characteristics of study participants and balance across treatment arms

Patient characteristics: N patients = 1474						
	Control	Info	Choice	Default	Full sample	P-value
Age (mean)	56.58 (0.47)	55.99 (0.51)	56.29 (0.68)	56.80 (0.49)	56.37 (0.36)	.63
Share male	0.66 (0.03)	0.65 (0.03)	0.61 (0.04)	0.68 (0.03)	0.65 (0.02)	.58
Share in HMO insurance plan ^a	0.72 (0.03)	0.76 (0.02)	0.72 (0.03)	0.78 (0.03)	0.74 (0.02)	.36
Share on diabetes medication	0.24 (0.02)	0.22 (0.02)	0.16 (0.02)	0.21 (0.03)	0.22 (0.01)	.01
Share on hypertension medication	0.77 (0.02)	0.80 (0.02)	0.76 (0.03)	0.82 (0.02)	0.78 (0.02)	.37
Share on lipid medication	0.73 (0.02)	0.71 (0.02)	0.77 (0.03)	0.71 (0.03)	0.72 (0.01)	.54
Rate of nonadherence event before study (mean)	0.30 (0.02)	0.32 (0.02)	0.32 (0.02)	0.35 (0.02)	0.32 (0.01)	.39
Share left study prior to conclusion	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.01 (0.01)	0.00 (0.00)	.11
Physician characteristics: N physicians = 90						
	No Intervention	Choice	Default	Full sample	P-value	
Number of patients in study (mean)	26.82 (5.09)	30.26 (3.92)	29.06 (3.88)	28.78 (2.45)	.85	
Age (mean)	53.86 (1.67)	56.87 (1.53)	56.16 (1.78)	55.69 (0.96)	.42	
Share male	0.46 (0.10)	0.65 (0.09)	0.61 (0.09)	0.58 (0.05)	.34	
Rate of nonadherence event before study (mean)	0.75 (0.04)	0.70 (0.04)	0.71 (0.04)	0.72 (0.02)	.62	
Rate of study patients in HMO insurance ^a (mean)	0.24 (0.03)	0.17 (0.03)	0.25 (0.03)	0.22 (0.02)	.15	
Rate of patients on diabetes medication (mean)	0.77 (0.03)	0.81 (0.03)	0.85 (0.02)	0.81 (0.02)	.09	
Rate of patients on hypertension medication (mean)	0.73 (0.03)	0.70 (0.03)	0.69 (0.03)	0.70 (0.02)	.53	
Rate of patients on lipid medication (mean)	0.27 (0.03)	0.22 (0.01)	0.24 (0.02)	0.24 (0.01)	.22	
Share left study prior to conclusion	0.07 (0.05)	0.10 (0.05)	0.13 (0.06)	0.10 (0.03)	.77	

Note: Numbers represent means or proportions for binary variables. Standard errors are provided in parentheses. P-values are from chi-squared tests of multinomial logit regressions of covariate on treatment assignment. Patient orthogonality checks are clustered at the physician level.

^aPatients not enrolled in HMO insurance plans are enrolled in PPO insurance plans.

diabetes, where the rate is lower for patients in the choice treatment. There was some differential attrition, with patients in the default treatment significantly more likely to drop out of the study than patients in the information-only treatment. Overall, rates of dropout were low with 1 percent of patients dropping out of the study in the default treatment. The physician randomization was balanced across all physician characteristics. There was not statistically significant differential attrition across the sample of physicians, though the rate of dropout for physicians was higher in the Default arm compared to the Control arm.

3.2 | Intent-to-treat analysis of impact on study outcomes

Over the course of the study, more than 3374 claims indicated a nonadherence event, of which 2299 nonadherence events were eligible for physicians to receive an email alert and information about the claim and 1166 were eligible for intervention by a pharmacist. We considered the impact of the intervention on key outcomes in Table 2. In column 1, we did not find differences across arms in the probability that a physician engages with the system to view

TABLE 2 Patient treatment assignment impact on key outcomes

Outcome	Physician viewed nonadherence event info	Pharmacist action triggered	Probability of nonadherence event resolving within 30 d	Duration of nonadherence event in days
Regression type	GLM	GLM	GLM	OLS
Sample	Sample of claims eligible for receiving email notification	Sample of claims eligible for receiving pharmacist intervention	All claims	All claims
	(1)	(2)	(3)	(4)
Default arm	-0.043 (0.068)	0.420*** (0.071)	-0.015 (0.034)	-0.128 (2.523)
Choice arm	0.060 (0.063)		-0.015 (0.041)	-1.582 (2.997)
Info only arm			0.012 (0.029)	0.308 (2.380)
Mean of dependent variable	0.331	0.395	0.443	40.836
Number of claims	2299	1166	3374	2650
Number of patients	995	518	1474	1210
Number of physicians	90	62	90	90

Note: Estimates for regressions 1-3 represent estimates from GLM of percentage point changes; estimates for regression 4 represent the coefficient of an ordinary least-squares regression. Treatment assignment represents patients' treatment assignment. Standard errors (in parentheses) are clustered at the physician level. Comparison category for regression (1) is information-only patients. Comparison category for regression (2) is patients whose physicians were assigned to the "choice" condition. Comparison category for regression (3) and (4) is control patients who received no intervention.

*** $P < .01$

Patient adherence by physician action and treatment arm

FIGURE 3 Physician responses [Color figure can be viewed at wileyonlinelibrary.com]

information about patients' nonadherence after receiving an alert about a nonadherence event. In column 2, we find that the likelihood of engaging the pharmacist in the Default arm was 42 percentage points (95% CI: 28 percentage points - 56 percentage points) greater

than in the Choice arm. In Table 2 columns 3 and 4, we demonstrate that patient treatment assignment did not have a statistically significant impact on adherence outcomes. We present robustness checks in Tables S1-S3, all displaying similar results.

3.3 | Engagement with the adherence tracking system

Thirty-seven percent of physicians (33 of 90) never logged in to the system to see a patient's claim over the course of the study. Physicians observed details of the nonadherence event for only 33 percent of the events where they received a notification (33 percent of nonadherence events: 760/2299). When a nonadherence event was eligible for pharmacist intervention, the pharmacist was requested to contact a patient in only 36 percent of cases (418/1166). This is partly because physicians did not engage the pharmacists, though pharmacist intervention did not always occur even in the Default arm if the physician took no action. For example, the pharmacist intervention was canceled if patients filled a prescription within the window between when the claim was declared nonadherent (after 10 days) and when the pharmacist's action would have been automatically triggered in the Default arm (after 15 days). When pharmacists did attempt to contact patients (82 percent of cases where they were requested: 341/418), they were able to have a conversation with the patient less than a third of the time (36 percent of cases: 123/341). These conversations happened a median of 9 days after when the patient was classified as nonadherent. When pharmacists were able to have a conversation with a patient, the most common reason for nonadherence reported by patients was that they already had drugs on hand or had already filled their prescription (82 percent of cases: 101/123).

3.4 | Heterogeneity of physician engagement with pharmacist intervention

In Figure 3, we consider whether patient outcomes were associated with physicians' behaviors. In the Choice arm, we found that patients of physicians who did and did not choose to utilize the pharmacist experienced similar patterns of nonadherence. After this point, adherence outcomes were better when physicians chose to engage the pharmacist though the difference is not statistically significant (P -value from KS test statistic = 0.19, P -value = .24). In the Default arm, outcomes for claims where the physician canceled the pharmacist intervention were uniformly better than for claims where the physician took no action (P -value from KS test statistic = 0.46, P -value < .01).

4 | DISCUSSION

We find that physicians' choice architecture has a significant impact on physicians' process of care in handling patient's nonadherence when the assistance of a pharmacist is available. In a Default arm where pharmacists contacted patients when physicians took no action, the rate of patient contact increased more than threefold compared to a Choice arm, even though the only difference between the arms was that the Choice arm required the physician to log in to a

website and click on a link. Our finding that a simple change in choice architecture can significantly impact physician behaviors is consistent with prior studies.^{25-27,30} Recent evidence that policy makers fail to understand the impact of defaults³¹ highlights the importance of understanding how choice architecture may influence physician behavior in the design of health care delivery systems.

Despite the impact of choice architecture on the implementation of the pharmacist intervention, we saw little impact of any of the intervention elements on the primary outcome of resolving nonadherence within 30 days. Even though we saw significantly higher engagement of the pharmacist in the Default arm compared to the Choice arm, the confidence intervals indicate that patients' nonadherence in the Default arm was estimated to last no more than five days less than the control group of patients whose physicians never learned that their patient had experienced nonadherence. In addition to finding no evidence that the intervention improved adherence, we see very limited physician engagement with the intervention system, despite the fact that all physicians had actively consented to participate in the study. Future research should examine the degree to which physicians perceive value in the engagement of pharmacists in addressing patients' nonadherence.

Our findings highlight several potential challenges for interventions that engage pharmacists to call patients. First, there are challenges to providing physicians and pharmacists with information that is timely enough to be actionable in resolving cases of nonadherence. Many of the potential incidents of nonadherence identified by our real-time tracking system were resolved by patients prior to the pharmacist contact or corresponded to situations where patients may have still had medication on hand. Second, we found challenges with interventions that use phone calls as primary points of contact with patients. Some recent studies have shown that interventions that utilize pharmacists to improve medication adherence using intensive in-person counseling including comprehensive medication review and teaching can improve adherence,³²⁻³⁵ yet others found no effects.³⁶ Phone-based interventions face the same challenges that have been extensively documented in phone-based survey research over the past decade.³⁷ A systematic review of evidence on interventions to improve adherence to antidiabetic medications found that multifaceted interventions were more effective than interventions using just one touch point.³⁸ Finally, an important challenge for insurance-based interventions to track adherence is that each insurer can only provide information about a subset of physician's patients. If this information is not integrated into physician's overall workflow, as in the case of the external web portal used in this study, physicians' engagement may be poor.

We found that over-riding the system (whether by canceling pharmacist in the Default arm or choosing to have a pharmacist engage in the Choice arm) was associated with quicker resolution of nonadherence events. The finding that patients do better when physicians do not stick with the default highlights one potential downside of designing with defaults. Recent findings highlight that physicians increasingly spend a significant portion of their time on

paperwork and electronic systems.³⁹ Default systems that shift effort away from physicians may present an attractive solution to this problem but will not necessarily improve patient outcomes if they depress essential physician engagement with patients or if the systems that substitute for physicians' engagement with other health care providers are less effective.

Our results cannot determine whether physicians in the Choice arm did not engage the pharmacist because they perceived the pharmacist contacting the patient to be low value or because it required extra effort on their part. Prior evidence has suggested that pharmacist-driven interventions to improve medication adherence can be particularly effective when pharmacists provide comprehensive education,⁴⁰ which may be challenging over the phone without in-person contact. Other evidence suggests that pharmacist-led interventions have been effective when they identify patients at high risk for nonadherence and more intensively target adherence within these populations.³³

Our study has some important limitations. Because this was a pilot study with limited resources, we only track pharmacist interaction with patients; we do not know whether and how physicians engage with patients themselves. Furthermore, our study partnered with only one insurer and pharmacy benefit manager and therefore only provides information on adherence for a subset of any physician's patients. We only have information on medications that were part of the study and not the patient's entire suite of medications, making it difficult to paint a complete picture of the patient's adherence. We can only track patient outcomes related to adherence so we do not know the potential health implications of our findings, though the null results for adherence suggest we are unlikely to see difference in health outcomes. Another limitation is that despite a nontrivial overall sample size, relatively few patients actually received the pharmacist intervention. In part, this is due to the relatively high rate of adherence. We expect that participants in our study were likely to simultaneously experience other efforts to improve adherence, whether phone calls from pharmacies or efforts from physicians as part of other quality improvement programs that were ongoing in Massachusetts at the time of our study.²⁹ A related and surprising finding is the relatively high share of patients who choose to opt out of the research (29 percent of patients returned an opt-out card to leave the study), compared to findings in previous similar research designs.⁴¹ While the potential for opt-out to transform participation in trials has been highlighted,⁴² our finding of relatively high rates of opting out suggests that the potential of opt-out may differ significantly by study setting. Our setting featured a relatively engaged patient population who tended to be older on average, which could be associated with greater attention to reading the mail. Finally, our multilevel experimental design, with randomization occurring at both patient and physician levels, is relatively complex. We demonstrate similar results when considering just the physician-level randomization and considering only the first claim of the study, suggesting that our findings are robust to this concern.

5 | CONCLUSION

We see no evidence that access to a pharmacist to assist with addressing medication nonadherence improved adherence outcomes. Choice architecture has a significant impact on physician behavior. However, in some cases patients may fare better when physicians actively engage with decisions around their care than they do in systems where interventions are triggered by default without physician engagement.

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ENDNOTES

^a In another experimental randomization, for half of nonadherence events, we added an additional sentence to the email alert that informed physicians whether the patient was covered by HMO or PPO insurance. The impact of this additional experimental treatment was analyzed in a separate manuscript.

^b Stands for "Pharmacy home adherence reporting and monitoring outcome study".

^c We cross-checked the physician identified by the insurer's algorithm with the physician on record with the pharmacy benefit manager for a subsample of 37 patients and found 100% agreement with the algorithm.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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