An Evidence-Based Approach to Understanding the

Benefits of Pharmaceutical Point-of-Care Awareness & Adherence Messaging



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INTRODUCTION

Prescription drugs are increasingly important in the treatment of illnesses in the United States. They are crucial to the management of chronic diseases, prevention of disease progression, and promotion of overall health. The findings from a 2022 Kaiser Family Foundation poll found that **62% of American adults are taking at least one prescription medication, and 25% take four or more (Figure 1).**¹

For each and every one of these millions of patients - and for their health care providers (HCPs) - awareness and adherence are vital issues. In many respects, better adherence starts with more complete awareness, and today's point-of-care (POC) awareness communications can reach key stakeholders before, during, and after the patient encounter. These targeted messages help educate patients on disease state, brand effectiveness and safety, and affordability programs. Additionally, they help physicians and pharmacists stay fully informed with proactive messaging both at the point of prescribing and the point of dispensing. In the end, these POC messages help get the right prescription written for the right drug and the right patient and dispensed correctly at the right pharmacy.

But getting the prescription written and dispensed is just the first step. Optimal adherence is paramount, especially for the treatment of chronic illnesses.² Adherence can wane for many reasons, including cost, forgetfulness, depression, lack of medical literacy, and more. Not surprisingly, medication nonadherence is a significant problem in today's marketplace. A study by Kleinsinger in The Permanente Journal reports that nonadherence for patients with chronic diseases is extremely common, affecting as many as 40% to 50% of patients who are prescribed medications for management of chronic conditions such as diabetes or hypertension.³

This report illustrates several issues germane to POC messaging. The report reviews published articles, largely from peer-reviewed journals, which provide clear evidence that poor adherence increases avoidable costs and worsens health outcomes, while higher adherence improves health and reduces overall medical costs. Then the report reviews the origins of pharmaceutical messaging and uses additional published studies to show how POC messaging to HCPs changes prescribing behavior and POC messaging to patients increases uptake and adherence. The paper wraps up by assessing the future of academic and governmental "nudging."

Figure 1. Six in 10 adults report currently taking at least 1 presciption medicine; one-quarter say they take 4 or more

Percent who say they take the following number of prescription drugs:



Source: KFF Health Tracking Poll Sept 23-Oct 4, 2021

Poor Medication Adherence Increases Avoidable Costs and Worsens Health Outcomes

Nonadherence to prescribed treatment is estimated to cause hundreds of billions of dollars in preventable medical costs per year. A study published in *Annals of Pharmacotherapy* revealed that in 2016, \$528.4 billion — or 16% of total health expenditure — was spent because of poor adherence. The plausible range is \$495.3 billion to \$672.7 billion.⁴

For example, heart disease is the leading cause of mortality in the United States, responsible for approximately 695,000 deaths annually — 20% of all deaths.⁵ Therefore, adherence to medications used to treat heart disease, such as statins, is crucial. A recent study in JAMA *Cardiology* examined the correlations between statin adherence and mortality in patients with atherosclerotic cardiovascular disease (ASCVD), a form of heart disease.⁶

Adherence was measured by the medication possession ratio (MPR), describing the ratio of the number of days a patient is *stocked* for their medication to the number of days a patient should be stocked for their medication. In this study, to be classified as adherent a patient would need an MPR of 80% or greater. A total of 347,104 patients were included in the study. Patients with an MPR of <50% experienced an 8.8% mortality rate, whereas patients with an MPR ≥90% had just a 5.7% mortality rate (P <.001). Patients with the lowest level of adherence had a hazard risk for mortality of 1.36 (95% confidence interval (CI), 1.34-1.38) times that of the most adherent patients. In conclusion, the study found a graded, inverse association between long-term statin adherence and all-cause mortality.

Patients with the lowest level of adherence had a hazard risk for mortality of

1.36x the most adherent patients



Higher Medication Adherence Improves Health and Reduces Overall Medical Costs

While low adherence increases avoidable costs and worsens health outcomes, research shows that higher adherence improves health and reduces overall medical costs. A 2020 retrospective analysis published in the Journal of Managed Care and Specialty Pharmacy examined the reduction in costs that was associated with adherence to statin medications.⁷ David Axon and colleagues analyzed data from a cohort of 77,174 patients using the Pharmacy Quality Alliance (PQA) Statin Adherence Measure along with low-density lipoprotein (LDL) laboratory values from IBM MarketScan Medicare Supplemental Research Databases (2009-2015). The

authors found that adherence to statins doubled the likelihood that a patient had a controlled disease state compared to non-adherers. Moreover, adherers had 9.9% lower outpatient costs and 28.3% lower inpatient costs than non-adherers. Adherent patients also had fewer overall outpatient and inpatient visits. Additionally, adherers experienced 14.7% lower total healthcare costs.

All things considered, it's clear that adherence to medication is essential to ensure that the prescribed treatment is effective. After all, medications can only work if taken consistently and as directed. What's more, proper adherence can reduce the need for hospitalizations and reduce costs.

Origins of Pharmaceutical Messaging

New drugs are constantly in development and receiving FDA approval (not to mention updates to in-market drug indications, other changes in prescribing information, and formulary adjustments), making it hard for overworked prescribers to stay up to date. In such a rapidly changing marketplace, it is important that drug makers work to build prescriber awareness. Indeed, one of the first steps toward enjoying the benefits of robust adherence is making prescribers aware of a drug's availability, prescribing guidelines, and the access support available. Pharmaceutical

messaging programs play an extremely important role in creating this brand awareness.

With that background, let's take a moment to review the origins of pharmaceutical messaging. In many respects, it started with the discovery of penicillin by Alexander Fleming in 1929, which accelerated the development of therapeutic drugs available only via prescription. As a percentage of total drug product revenue (including over the counter), the share attributed to prescription drugs exploded from just 32% in 1929 to 83% in 1969. This growth was aided by increased state funding of science, the growing prevalence of large research universities, and the World War



Figure 2. Percent of US office-based physicians using an EHR

II military-industrial complex.8

As the Rx pharmaceutical industry grew, so did pharmaceutical marketing. And while direct-to-consumer advertising may be what immediately comes to mind when discussing drug advertising, in the early years of the industry most marketing messaging was directed toward prescribers. Drug companies hired fleets of fieldbased sales representatives to speak directly to clinicians — a practice called "detailing." Detailing was the dominant drug marketing channel for many years. In 2021 there were over 150,000 pharmaceutical sales representatives in the United States.⁹ They meet directly with health care providers, delivering the "details" of a drug's efficacy and safety profile, offering drug samples and/or copay support programs, and distributing educational materials like pamphlets and posters. Annually, \$5.6 billion is spent by pharmaceutical companies on detailing visits.¹⁰

While detailing is still a major part of the marketing mix, the landscape began to shift as technological advances

increased the opportunities to interact with prescribers electronically. The most important technological advance may well be the advent of electronic health records (EHRs). EHRs were developed with the rise of computer technology in the 1970s and became widely used at academic medical facilities by the early 1990s. EHRs facilitate the processes of viewing a patient's medical history and lab/test results, updating diagnoses, creating treatment plans, prescribing medications, and authorizing tests.

As hardware and software became more affordable, more powerful, and easier to navigate, EHRs began to gain popularity outside of academia. Approximately 20% of office-based physicians utilized EHRs by the early 2000s and by 2010 this number rose to 50%.¹¹ Adoption increased more rapidly after 2010 thanks to the Affordable Care Act, which mandated that practices convert medical charts into digital format. As of 2021, approximately 90% of all office-based physicians in the United States utilized EHRs (Figure 2).¹²

EHRs have become a crucial component of physicians' daily workflow. One study found that physicians spend an average of 4.5 hour daily working in their EHR system.¹³ Furthermore, physicians who used EHRs spent an average of 1.84 hours using the system outside of the office each day.¹⁴

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Because EHRs are an established technology that providers use throughout each workday, they are a perfect channel for the delivery of key drug marketing messages. Indeed, Indegene's 2019 annual healthcare provider survey indicated that, for the first time, digital communications were preferred over in-person sales representatives.¹⁵

Messaging to HCPs Changes Prescribing Behavior

It should come as no surprise that messaging to HCPs changes prescribing behavior.

By connecting pharmaceutical messaging with clinicians at the point of prescribing in the EHR, information about available drugs is delivered without requiring HCPs to search through the literature on their own. Providers get access to pertinent pharma messaging in workflow, allowing them to stay up to date on important drug information and adjust their prescribing accordingly. Given that most patients consider doctors and nurses to be trusted sources of health information, the ability to have the key facts immediately available helps maintain the relationship between providers and their patients. Above all, increasing awareness is the first step in increasing adherence.

Internal data from ConnectiveRx confirms the effectiveness of in-EHR messaging to prescribers. An analysis of recent messaging programs showed that prescribers respond to in-workflow messages that include current formulary information. A study of 8 programs in which the messages included formulary information yielded an average 11.9% script lift.¹⁶ Additionally, having information about copay coupons available *before writing a script* gives providers confidence *that they* can prescribe the most appropriate medication without worrying about whether the patient can afford it. A study of 27 programs that featured brand messages plus patient savings offers resulted in an average 11.5% script lift.¹⁶

It is not just ConnectiveRx internal data that proves the point. In-EHR messaging has also been shown in the academic literature to change prescribing behavior. A 2022 study by Srinath Adusumalli and colleagues found that in-EHR clinician nudges (subtle, non-coercive interventions designed to influence the behavior and decisionmaking of HCPs) had a positive effect on prescribing.¹⁷ The authors examined the prescription of statin medications to eligible patients during primary care visits. The researchers compared the rates of initiation when patients, clinicians, or both were provided with information about statin medication for patients with elevated levels of low density lipoprotein. The clinician nudge was delivered as an interactive in-EHR prompt displayed during the patient visit. There was a significant increase in statin prescriptions when clinicians were messaged (5.5 percentage points; 95% CI, 3.9 to 7.8 percentage points; P < 0.001). However, an even greater increase in prescribing occurred when both clinicians and patients were messaged (7.2 percentage points; 95% CI, 5.1 to 9.1 percentage points; P = 0.001). The initiation of a statin

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prescription during the visit increased by 10.8 percentage points from preintervention to intervention and by 7.2 percentage points more than usual care. The study concludes that a two-pronged approach to messaging, including nudges to both the clinician and the patient, yield the best outcomes for statin prescribing.

Non-EHR HCP messaging tactics have also been shown to increase the prescribing of necessary medications. For example, a study in JAMA Network Open revealed the impact of email messages regarding statin prescriptions to clinicians in the University of Pennsylvania Health System.¹⁸ Given that heart disease is a pressing health challenge and that statins are not prescribed for approximately 50% of patients who could benefit from them, finding ways to increase prescribing is important. The study included a control group and two intervention groups. In the first intervention (called active choice), clinicians were emailed a dashboard with a list of patients who met American Heart Association guidelines for statin prescription. The PCPs were asked to review the list of patients within one week and use the dashboard to select whether to prescribe each patient a statin. In the second intervention (active choice with peer comparison), clinicians were emailed the same dashboard,

but were also informed of their statin prescription rate in comparison to their peers. The clinicians below the median were informed of how they compared with the median (for example, "your statin prescribing rate is 50%, while the average of your peers at Penn is 64%"). Clinicians above the median but below 90% were compared with the "top performers" in the 90th percentile. The study found that the percentage of patients prescribed a statin was 2.6% in the control arm but 6.7% in the active choice arm. In the active choice with peer comparison arm, there was a further increase in prescribing, at a statistically significant 8.0%.

In the end, the data is clear: Messaging to physicians can indeed have a significant impact on their prescribing behavior. That's why pharmaceutical companies, healthcare organizations, and other stakeholders often use various forms of messaging to influence physicians' decisions regarding medication choices. But strategic messaging campaigns reach beyond just prescribers. Direct-to-patient messaging also delivers valuable benefits.

Patient savings offers resulted in an

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Point-of-Care Messaging to Patients Increases Uptake and Adherence

Aside from contact with prescribers, increased awareness and adherence can be achieved by communicating directly with patients. In one example, ZS Pharma reported that 68% of patients requested a pharma brand they had been exposed to in POC marketing.¹⁹ And 65% of patients indicated a willingness to switch brands after seeing POC messaging. Furthermore, patients are 84% more likely to ask clinicians about a drug they were exposed to through POC messaging. Even more impressively, POC marketing decreases prescription abandonment and increases persistence, with patients being 31% more likely to fill

their prescription.

Direct-to-patient mobile communication shows particular promise as an adherence booster. A report in JAMA Internal Medicine summarized the findings of 16 randomized clinical trials that studied adult patients with chronic disease.²⁰ In each trial, patients received a mobile telephone text message intervention designed to promote medication adherence. In the pooled analysis of 2742 patients (median age, 39 years and 50.3% female), text messaging significantly improved medication adherence (odds ratio, 2.11; 95% CI, 1.52-2.93; P < .001). The authors conclude that, "mobile telephone text messaging increased adherence to

taking medications among middleaged patients with chronic disease. The ease of use, instantaneous relay of information, and boundless reach make it an attractive tool for public health."

In another recent study of patientdirected texting, Benjamin Horne and colleagues studied the impact of text message nudges to patients taking statins.²¹ In this study, the experimental population received nudges in the form of text messages (78.4%), email (13.4%), and interactive voice response (8.2%). For most study participants, the nudge was delivered once a week. Twelve months after the primary trial ended, the mean statin adherence was greater for the nudge group (PDC = 0.742 ± 0.318) than for the control group control (PDC = 0.639 ± 0.358); P = 0.042. This results in an absolute 0.103 higher statin PDC for nudges.

As shown in Figure 3, at 3 months, adherence was 73.0% for the nudge group and 68.8% (P = 0.63); at 6 months it was 67.4% vs 58.1% (P = 0.22); and at 9 months it was 65.2% vs 55.9% (P = 0.23), respectively. Importantly, the results



Figure 3. Statins: Percent adherent

show an increasing gap at 12 months, when 66.3% of nudge group patients were adherent vs. just 50.5% of control-group patients (P = 0.036). Notice in Figure 3 the accelerating adherence fall-off in the control group at 12 months. Furthermore, these gains in adherence correlated with a reduced incidence of major adverse cardiac (MACE) events. MACE events at 12 months were just 6.7% for nudge recipients but 10.8% for control patients (P = 0.44; odds ratio = 0.60, 95% CI = 0.21, 1.72).

Another study, from a group of researchers published in BMC Endocrine Disorders, analyzed nine randomized controlled trials from countries around the world, evaluating the potential of patient messaging as a solution to nonadherence globally.²² Their metaanalysis included 1,121 participants and indicated a positive impact of text messaging on medication adherence in patients with type two diabetes mellitus (T2DM). They concluded that text messaging combined with standard medical care can produce significant improvements in prescription adherence: "Mobile phone text messaging interventions had a favorable effect on medication adherence in patients with T2DM, with significant improvement in medication adherence by 0.36% when

nine studies were pooled together in a meta-analysis."

Finally, let's note the promise of patientdirected mobile messaging strategies focused on increasing refills. A 2021 paper described the outcome of a pilot study utilizing EHR pharmacy data to target patients with gaps in prescription refills, then sending those patients automated text message reminders.²³ Participants who received messages had higher rates of prescription refills than the control group (30.6% vs 18.0%). While this study is limited in scope and does not seek to assess exploratory endpoints, it does demonstrate the promising future of messaging for increasing adherence. These automated messages can be generated based on the status of a prescription and delivered to patients in the form of a text message, email, or phone call. This technology is widely used in the United States and has real potential to reduce medication nonadherence if adoption is widespread.²⁴

In aggregate, the data shows that directto-patient messaging programs decrease prescription abandonment, boost adherence and persistence, and improve prescription refill rates.

The Future of Academic and Governmental Nudging

It's not just drug makers that recognize the value of stakeholder messaging. Hospital systems and governments are highly invested in the potential of nudging to revolutionize healthcare. The Penn Medicine Nudge Unit was established in 2016 to optimize clinician behavior and improve patient care. Since its founding, the Nudge Unit has worked on over 100 projects, including 25+ randomized trials yielding over 75 publications.²⁵ Moreover, in 2010, the Cabinet Office of the United Kingdom established the Behavioral Insights team, and in 2015,

the Social and Behavioral Sciences Team was established in the U.S. White House. Both organizations use the principles of nudging to improve public policy, including health policy. Successful nudges require targeted individuals to notice the intervention and interpret it appropriately. Then they must decide to react in the desired manner and follow through with that behavior.²⁶ Given the positive impact nudging has had on health outcomes, continuing to research and develop effective nudges should be given priority.

CONCLUSION

In the long history of pharmaceutical marketing, brand teams have always looked for the most efficient way to communicate with prescribers and patients. And while nonadherence remains a major challenge that impacts treatment outcomes, directto-physician and direct-to-patient messaging have repeatedly shown positive outcomes.

Messaging to prescribers is vital to increasing brand awareness and prescribing. Tailoring HCP messaging strategies to our present technological environment, including EHRs, is crucial to achieving a good return on investment. Reaching clinicians in the EHR via short textTailoring HCP messaging strategies to our present technological environment, including EHRs, is crucial to achieving a good ROI.

based messages or active choice prompts has been shown to have a positive impact on prescribing. And reaching patients via text, email, and phone has resulted in improvements in uptake and adherence.

By leveraging technology to deliver timely and relevant information to key stakeholders, pharmaceutical messaging solutions can play a key role in enhancing patient care and achieving better health outcomes.

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