

E-Prescribing With Decision Support Is Associated With Improvements in Medication Adherence

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Pharmacy benefit managers (PBMs) are critical stakeholders in the healthcare industry, responsible for administering prescription benefit programs for the vast majority of insured Americans. Prescription drug spending represents 10% of total healthcare expenditures, or roughly 1.8% of US gross domestic product.¹ Importantly, prescription drugs are first- or second-line treatments for many chronic diseases associated with an outsized portion of healthcare spend.^{2,3} Appropriate and persistent use of prescription drugs to treat chronic diseases has also been demonstrated to reduce downstream medical expenditures,⁴ achieving substantial cost savings.^{5,6} In addition, pharmacies are the most frequently utilized healthcare service, with the average patient filling nearly 4 times as many prescriptions as the number of their visits to office-based physicians.^{7,8} Given these facts and additional demographic context—an aging population with increasing prescription drug use on a per capita basis^{9,10}—it becomes clear that PBMs can play a significant role in the current healthcare reform landscape.^{11,12}

PBMs are adopting benefit design strategies that reflect the broader healthcare trend of aligning payment to value and outcomes. A common theme among the evolving strategies is an effort to address and improve patient adherence to medication. Due to their position of processing prescription claims, PBMs are in a unique position to have the most comprehensive view of a patient's prescription treatment regimen. PBMs can leverage claims, eligibility, pharmacy data, and provider data to understand prescribing patterns and patient behavior by identifying gaps in care and suboptimal adherence, and potentially to effect positive behavior change relating to medication adherence through the timely delivery of information to providers, patients, and pharmacies.

Surescripts is a health information network that connects PBMs, pharmacies, and providers using electronic health records (EHRs) for the purpose of enabling real-time electronic prescribing. Through Surescripts, PBMs can electronically deliver prescription formulary, eligibility, and co-pay information to providers using a certified EHR. MedImpact

ABSTRACT

Objectives: To evaluate whether provider adoption and use of the formulary decision support element of e-prescribing were directly associated with significant prescriber and patient behavior change.

Study Design: Retrospective, observational prepost study comparing a treatment group with a control group.

Methods: Pharmacy fill information and provider enrollment records from January 2009 to December 2011 were used to compare fill volumes—primary fill and subsequent refill volume by retail and mail order fulfillment channels—of prescribers who had adopted e-prescribing (treatment group) with those who had not (control group). Propensity scores were used to match treatment and control groups by baseline prescribing patterns. Primary outcomes of interest were prepost differences for 90-day retail fills, initial fills (primary adherence), and subsequent refills.

Results: E-prescribers demonstrated significantly higher average increases in 90-day retail fills (+2.8 fills per provider, $P < .001$), primary adherence (+12.0 fills per provider, $P < .001$), and subsequent adherence (second fill: +4.5 fills per provider, $P < .001$; and third fill: +2.4 fills per provider, $P < .001$) compared with non-e-prescribers.

Conclusions: Provider adoption and use of e-prescribing applications with formulary decision support were associated with significant prescriber and patient behavior change in a large, nationally representative population. E-prescribing adoption was positively associated with prescribers' selection of longer supply prescriptions and improvements in adherence. E-prescribing infrastructure may allow for additional provider messaging opportunities designed to improve quality of care and patient outcomes.

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PRACTICAL IMPLICATIONS

Adoption of e-prescribing is associated with increased 90-day supply prescriptions and increased adherence, as measured by primary, secondary, and tertiary fill rates.

- We found greater increases in initial fill rates, refill rates, and 90-day supply prescribing among prescribers adopting technology compared with prescribers not adopting e-prescribing.
- Real-time electronic access to formulary decision support and electronic prescription routing increase primary and subsequent medication adherence levels.
- E-prescribing infrastructure may allow for additional provider messaging opportunities designed to improve quality of care and patient outcomes.

Healthcare Systems, Inc, is one such PBM, managing pharmacy benefits for more than 47 million individuals nationwide, connected to the Surescripts network. Provider use of the benefit information through Surescripts is associated with increased levels of preferred brand and generic prescribing, resulting in lower co-pays that are in turn linked to improved adherence.^{13,14} Surescripts also provides PBM-supplied decision support information about availability of retail 90-day supply and mail-order benefits, both of which have been linked to improved adherence.^{15,16} The ability of providers to route prescriptions electronically provides an auditable trail between what the provider prescribed and whether the patient filled the prescription at the pharmacy, addressing a current challenge with quality measures relating to primary adherence.^{17,18} Additionally, provider use of electronic prescribing (e-prescribing) is a core measure in the EHR Incentive Program, a federal incentive program to promote provider adoption and meaningful use of EHRs.¹⁹ The e-prescribing core measure requirement is currently limited to the routing component of e-prescribing; however, e-prescribing infrastructure allows numerous opportunities for formulary decision support and clinical messaging.

Current widely used methods of measuring medication adherence (such as proportion of days covered or medication possession ratio) rely on the presence of a claim for the first prescription fill, which is available only if the patient successfully picked up the initial prescription from the pharmacy. A challenge with these methods is that as many as 28% of first-fill prescriptions are abandoned before they reach the pharmacy, and therefore, such measures may be overstating true levels of medication adherence.²⁰

Our study is novel in that we sought to understand whether provider adoption and use of the formulary decision support element of e-prescribing was directly associated with improved medication adherence as indicated by increases in the number of claims for 90 days' supply, first fill, and subsequent refills. We did this by pairing data from Surescripts' provider network and MedImpact's pharmacy information. We investigated 3 core questions: first, we assessed whether e-prescribing resulted in prescribing behavior change, as indicated by selection of 90-day prescriptions; second, whether e-prescribing is associated with an increase in primary adherence, as indicated by the number of claims for first-fill prescriptions; and third, whether there was a discernible subsequent impact on second and third medication fills.

METHODS

Study Design

A prepost, retrospective analysis was performed by linking summary prescriber-level fill information from MedImpact and prescriber enrollment data from Surescripts. MedImpact's pharmacy fill information from January 2009 to December 2011 was summarized to monthly prescriber-level data. More than 75 variables were aggregated by prescriber, using National Provider Identifier (NPI) codes, to the following levels: a) fulfillment channel and days' supply amount: retail 30-day supply, retail 90-day supply, and mail 90-day supply; and b) adherence defined as the number of prescriptions filled for members' first, second, and third fills. We measured the raw volume of these claims associated with each prescriber (treatment and control) for 1-year pre- and post e-prescribing adoption. Total prescription claims was defined as the sum of retail 30-day supply, retail 90-day supply, and mail pharmacy claims for primary and subsequent fills. For the purpose of this analysis, comparisons of prescribing behavior were conducted based on a treatment versus control group research design. Prescribers adopting e-prescribing were included in the treatment group. Prescribers not using e-prescribing technology were included in the control group. The preperiod was defined as the 12 months prior to a provider's first use of the e-prescribing formulary decision support element, and the subsequent 12 months was defined as the post period. Differences among provider-level variables over the pre- and post periods were assessed to measure the impact of electronic prescribing on the study population. The primary outcomes of interest were prepost differences in claims for 90-day retail fills, initial fill (primary adherence), and subsequent refills.



Study Cohort Selection

A 2-stage matching algorithm was employed to enhance statistical rigor and to include adjustments for baseline differences in prescribing behavior between treatment and control groups. The goal of the 2-stage matching approach was to improve the comparability of the treatment and control groups while limiting potential confounding.²¹ Robust matching procedures combined simulation-based adjustments (1-stage matched methods), and propensity score matching (2-stage matched methods) was used to minimize the effect of bias that may have occurred in the absence of such advanced statistical techniques. Both 1- and 2-stage matched results are presented to describe the impact of advanced matching methods between e-prescribers and non-e-prescribers, and to validate findings of 1-stage matching methods.

1-Stage Matched Methods

First, an adoption month and year were randomly assigned to each control group prescriber to simulate the introduction of e-prescribing into the population and to control for rapid changes in adoption of e-prescribing during the study period. This approach was used to avoid measuring pre- and post prescribing rates for a control prescriber in January 2010 to a treatment prescriber in December 2010. Random assignment of proxy exposure dates to unexposed populations is a research design used to identify the onset of risk for exposure to the unexposed control group.²² Frequency distributions were calculated based on eligibility transaction dates from providers in the treatment group. Each control group prescriber was assigned a proxy eligibility date to replicate the observed distribution of the treatment group. Establishing this proxy or simulated eligibility transaction date in the control group created a basis for comparison over the study period between the treatment and control groups.

2-Stage Matched Methods

Second, propensity score methods were used to balance treatment and control groups by baseline prescribing patterns.²³ Propensity scores were based on estimated probabilities from a multivariable logistic regression model used to predict the probability of prescribers' membership in the treatment group. Covariates placed in the generalized linear model with logit link function included baseline prescribing patterns for retail 90-day, retail 30-day, mail 90-day, first fill, second fill, and third fill. A 1-to-1 matching algorithm was performed using the nearest available neighbor without replacement method to match control group prescribers to prescribers in the treatment group based on the propensity scores of the treatment group.²⁴

Statistical Analysis

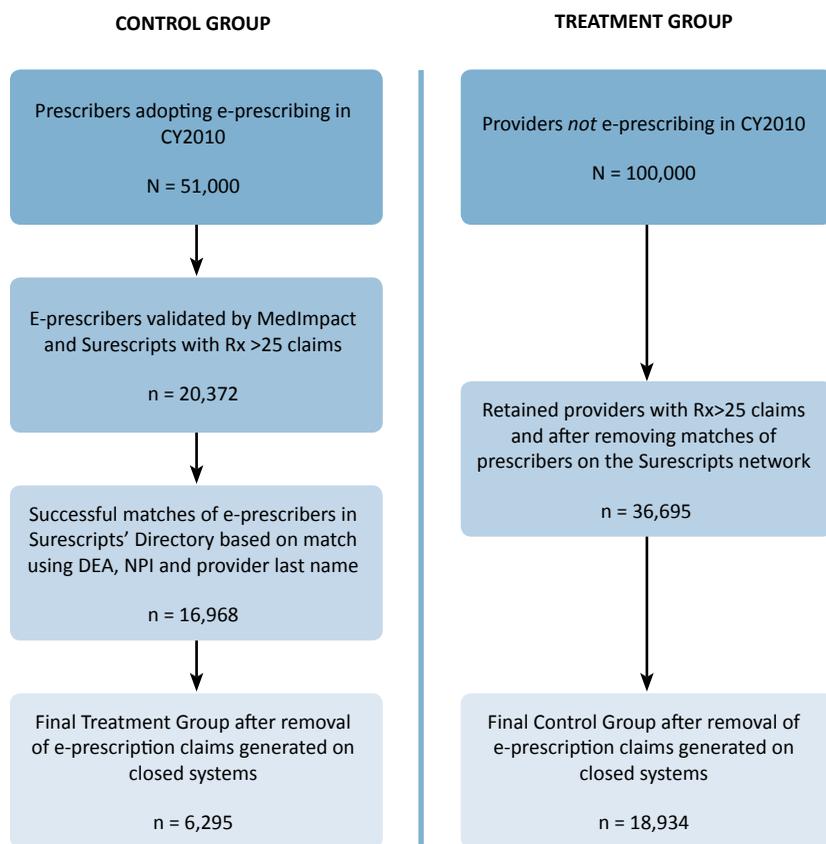
Outcomes were calculated for both 1-stage and 2-stage matching scenarios. The treatment group was compared with 1- and 2-stage matched control groups. Changes for each outcome, day supply, and adherence were calculated to determine the relative percent difference in claim volume for each group, and the absolute difference of percent differences between treatment and control groups. Relative percent difference for each group was determined as $\% \blacktriangle = (\text{Post} - \text{Pre}) / \text{Pre}$. For example, the treatment group was measured as follows: $\% \blacktriangle_T = (\text{Post}_{\text{Treatment}} - \text{Pre}_{\text{Treatment}}) / \text{Pre}_{\text{Treatment}}$. Absolute percent differences between treatment and control groups were defined as e-prescribing value_n = $\% \blacktriangle_T - \% \blacktriangle_{\text{Cn}}$, where n = 1 for 1-stage matching and n = 2 for 2-stage matching. E-prescribing value serves as a proxy to measure the impact of e-prescribing on each measure, as the differences among the treatment and control groups were estimated to be attributed to e-prescribing. Postperiod data were compared with baseline results by group using parametric *t* tests. Statistical significance was determined at *P* < .05 level. All analyses were conducted with SAS version 9.4 (SAS Institute, Inc, Cary, North Carolina).

RESULTS

Derivation of Study Cohorts

Selection of the treatment (e-prescribers) and control (non-e-prescribers) groups included a multistep exclusion process (Figure 1). Approximately 20,372 prescribers who had adopted e-prescribing during the 2010 calendar year were identified using the Surescripts provider network. E-prescribing adoption was evidenced by a prescriber's registration, activation, and first e-prescribing transaction. To be selected, prescribers must have completed at least 1 eligibility transaction with MedImpact through the Surescripts network. An eligibility transaction is a request for drug coverage and formulary information generated at the point of care and routed electronically to the corresponding PBM through the Surescripts network. The eligible provider must have been successfully matched in the Surescripts directory and must have had at least 25 claims, decreasing the sample by 3404 providers. Eligibility transactions dates were divided into 2 periods: the 12 months prior to the first eligibility transaction date (pre-period), and the 12 months following the first eligibility transaction date (post period). Prescribers with claim totals of 0 in either the pre- or post periods (426) were excluded. As both treatment and control groups were expected to have no e-prescription claims in the pre-period, such providers were removed from the population. Omitting e-prescription claims derived from integrated healthcare delivery systems led to an additional

Figure 1. Selection of Study Population



CY2010 indicates calendar year 2010; DEA, U.S. Drug Enforcement Administration; NPI, National Provider Identifier.

reduction in prescriber count by 10,247 providers. The final treatment group consisted of 6295 providers.

The control group was selected from providers who had not adopted e-prescribing prior to and during the study period by using the nationwide Surescripts provider directory. 63,305 prescribers were removed in the exclusion process using a combination of the provider's Drug Enforcement Administration number, NPI code, and last name to remove all prescribers registered on the Surescripts network, in addition to removing prescribers with fewer than 25 claims. This resulted in retaining only the providers who had not adopted e-prescribing during the study period, with more than 25 claims. The final control group consisted of 18,934 providers after removing 810 providers due to 0 total claims in the pre- or post period, and 16,591 providers due to affiliations with integrated healthcare systems.

Prepost Fill Volume

Average prepost volume of retail 90-day fills increased by 3.3 fills per provider (R_x /provider) in the treatment

group versus 0.5 R_x /provider in the 1-stage matched control group, an absolute difference of +2.8 R_x /provider ($P < .001$) (Table). The absolute difference between treatment and 2-stage matched control group was +3.2 R_x /provider ($P < .001$). Increases in retail 30-day fills were greater in the treatment group. The overall absolute difference in retail 30-day fills indicated greater increases among e-prescribers, 16.4 R_x /provider ($P < .001$) for 1-stage matched comparisons and a 21.2 R_x /provider ($P < .001$) change for 2-stage matched comparisons.

As shown in Figure 2, estimated e-prescribing value, as measured by differences in retail 90-day fills, ranged from 17.2% to 29.9%, indicating that prepost differences were substantially higher for the treatment group compared with both control groups. This trend was consistent for both mail 90-day and retail 30-day measures as well. Although the absolute difference from pre- to post periods was not statistically significant and indicated a decrease in mail 90-day fills of 0.1 R_x /provider ($P < .846$) for the treatment group, significant differences using 2-stage matched methods showed

an overall absolute increase for the treatment group in mail 90-day fills of +1.8 R_x /provider ($P < .001$). Calculations of percent difference for mail 90-day indicated a decrease of 10.0% for the treatment group, a decrease of 23.4% for the control group 1-stage, and a decrease of 29.1% for control group 2-stage. Decreases in mail fills for the treatment group were significantly less than decreases for the control groups (1- and 2-stage), yielding estimated e-prescribing values ranging from 13.4% to 19.1% for 1- and 2-stage matched results, respectively. E-prescribing value for retail 30-day ranged from 6.2% to 17.4%, indicating greater increases in retail for the treatment group compared with both control groups (1- and 2-stage).

Adherence

E-prescribing providers experienced significantly higher increases in both primary and subsequent fills compared with the 1-stage and 2-stage control groups (Table). For primary adherence, prepost differences between treatment and control groups were 12.0 R_x /provider ($P < .001$)



Table. Prepost Prescribing Behavior (claims per provider) for Treatment and Control Groups

| 1-Stage Matching | Treatment N = 6295 | | Control N = 18,934 | | Difference (T _{post} - T _{pre}) - (C _{post} - C _{pre}) |
|------------------|-----------------------|-------------------|-----------------------|-------------------|---|
| | Pre mean (SD) | Post mean (SD) | Pre mean (SD) | Post mean (SD) | |
| Total claims | 135.1 (189.1) | 178.9 (207.0) | 89.5 (123.8) | 113.8 (141.8) | 19.5 ^a |
| Claim type | | | | | |
| Retail 90-day | 10.6 (37.2) | 13.9 (46.1) | 3.6 (16.7) | 4.1 (21.8) | 2.8 ^a |
| Mail 90-day | 12.0 (42.4) | 10.8 (41.8) | 4.7 (21.5) | 3.6 (20.1) | (0.1) ^b |
| Retail 30-day | 111.8 (154.2) | 153.0 (170.8) | 80.9 (111.2) | 105.7 (131.5) | 16.4 ^a |
| Adherence | | | | | |
| First fill | 67.9 (104.3) | 88.8 (107.7) | 53.9 (85.6) | 62.8 (85.0) | 12.0 ^a |
| Second fill | 20.2 (33.9) | 27.0 (37.3) | 10.1 (20.3) | 12.4 (21.5) | 4.5 ^a |
| Third fill | 12.6 (22.5) | 16.7 (24.5) | 6.0 (12.9) | 7.6 (14.1) | 2.4 ^a |

| 2-Stage Matching | Treatment N = 6295 | | Control N = 6295 | | Difference (T _{post} - T _{pre}) - (C _{post} - C _{pre}) |
|------------------|-----------------------|-------------------|---------------------|-------------------|---|
| | Pre mean (SD) | Post mean (SD) | Pre mean (SD) | Post mean (SD) | |
| Total claims | 135.1 (189.1) | 178.9 (207.0) | 121.8 (168.6) | 139.2 (176.7) | 26.5 ^a |
| Claim type | | | | | |
| Retail 90-day | 10.6 (37.2) | 13.9 (46.1) | 8.0 (27.4) | 8.1 (35.1) | 3.2 ^a |
| Mail 90-day | 12.0 (42.4) | 10.8 (41.8) | 10.3 (34.5) | 7.3 (31.7) | 1.8 ^a |
| Retail 30-day | 111.8 (154.2) | 153.0 (170.8) | 103.0 (144.6) | 123.0 (156.1) | 21.2 ^a |
| Adherence | | | | | |
| First fill | 67.9 (104.3) | 88.8 (107.7) | 58.6 (92.9) | 64.6 (86.4) | 14.9 ^a |
| Second fill | 20.2 (33.9) | 27.0 (37.3) | 18.7 (31.3) | 19.7 (30.7) | 5.8 ^a |
| Third fill | 12.6 (22.5) | 16.7 (24.5) | 11.5 (20.1) | 12.5 (20.5) | 3.0 ^a |

C indicates control group; pre, 1-year period prior to e-prescribing adoption; post, 1-year period following e-prescribing adoption; T, treatment group.

^a*P* < .001.

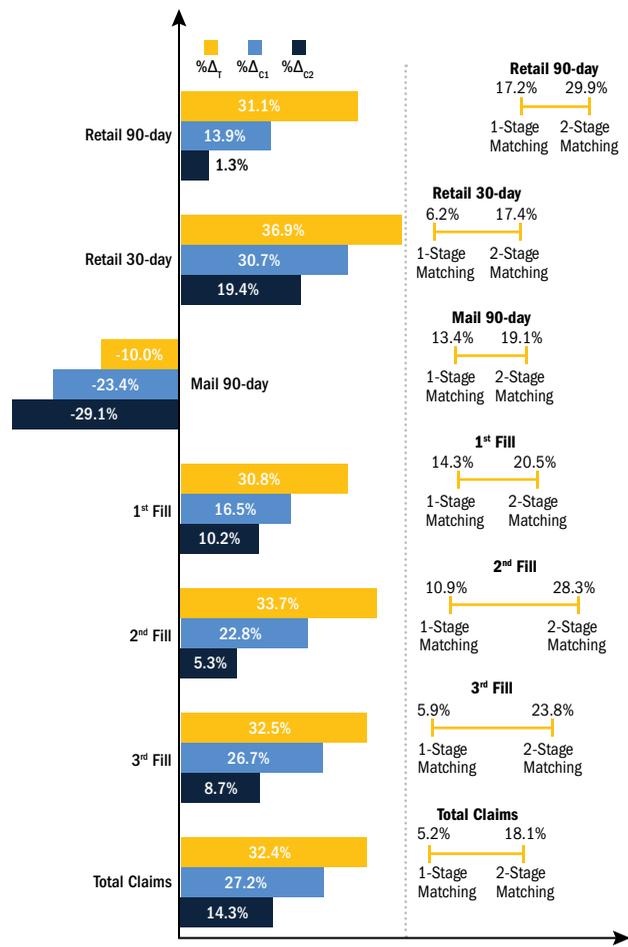
^b*P* > .846.

and 14.9 R_x/provider (*P* < .001), respectively, for 1-stage and 2-stage matched groups. This was observed for subsequent (second and third) fills as well. The treatment group exceeded the 1-stage control group in second fills by 4.5 R_x/provider (*P* < .001) and by 5.8 R_x/provider (*P* < .001) for 2-stage matched groups. For third fills, increases in the treatment group were significantly higher than in the control groups. Differences between treatment group and 1-stage matched groups were 2.4 R_x/provider (*P* < .001) and greater differences occurred for 2-stage matched groups (3.0 R_x/provider *P* < .001). Overall, the estimated value of e-prescribing on primary adherence ranged from 14.3% to 20.5%, indicating greater increases in primary fills for e-prescribers (Figure 2). E-prescribing value on subsequent fills ranged from 10.9% to 28.3% for second fill and 5.9% to 23.8% for third fills, indicating significantly greater results for the treatment group when compared with the control groups.

DISCUSSION

Nonadherence to medications results in substantial downstream medical costs, and therefore warrants the significant attention and accompanying investments that payers and care providers have created with programs and resources to improve patient adherence. Our findings suggest that provider adoption and use of e-prescribing applications with formulary decision support were associated with improvements in medication adherence in a nationally representative population. Specifically, we found that e-prescribing adoption was positively associated with providers' selection of longer-supply prescriptions, which in turn has been linked to increased medication adherence, and improvements in adherence to first fill, as well as subsequent fills. Considering the growth in e-prescribing adoption in 2013, with close to 640,000 prescribers routing roughly half of all prescriptions electronically,

Figure 2. Relative Differences in Prescribing Patterns by Group



E-prescribing Value
 C1 indicates 1-stage matched control group; C2, 2-stage matched control group; T, treatment group.
 $\% \Delta_T = (\text{Post}_{\text{treatment}} - \text{Pre}_{\text{treatment}}) / \text{Pre}_{\text{treatment}}$
 $\% \Delta_{C1} = (\text{Post}_{\text{Control1-stage}} - \text{Pre}_{\text{Control1-stage}}) / \text{Pre}_{\text{Control1-stage}}$
 $\% \Delta_{C2} = (\text{Post}_{\text{Control2-stage}} - \text{Pre}_{\text{Control2-stage}}) / \text{Pre}_{\text{Control2-stage}}$

the potential improvements in medication adherence and health outcomes are significant.

We observed a marked increase among e-prescribers in the selection of 90-day supply prescriptions when compared with the control group. Importantly, the increase in 90-day supply prescriptions—both to mail (+13.4% to +19.1%) and retail pharmacies (+17.2% to +29.9%)—among e-prescribers was comparatively greater than that of 30-day supply prescriptions. When providers adopt EHRs and are made aware of 90-day channel (mail and at retail) benefit information conveyed through e-prescribing, they may be more likely to: a) pay attention to this information when presented, and b) shift their overall prescribing habits and choose 90-day rather than 30-day prescriptions for maintenance medications.

Our findings show that providers who adopted e-prescribing during the study period saw a substantial increase in primary medication adherence (+14.3% to +20.5% in first fills), suggesting that electronically routed prescriptions increased the likelihood of patients starting therapy. This finding is consistent with other studies observing that between 22% and 31% of paper prescriptions (ie, those printed out and handed to patients) do not make it to the pharmacy.^{20,26,27} E-prescription routing addresses this issue of “leakage,” which is a contributing factor to the increase in primary adherence. Many pharmacies have developed outreach programs to remind patients that their prescriptions are ready, programs that are likely benefited by the increase in prescriptions submitted electronically. We suspect that prescriber use of the benefit information from e-prescribing, and patient knowledge that the prescription is likely to have lower co-pays (due to increased use of generic prescriptions and 90-day supply prescriptions), were also factors in the improved primary adherence numbers. We observed a positive spillover adherence effect, as subsequent increases in second fills (+10.9% to +28.3%) and third fills (+5.9% to +23.8%) were also higher among patients whose providers e-prescribed. This spillover effect makes intuitive sense, as any significant increase in primary adherence is likely to result in increases in longer-term adherence, which is consistent with discontinuation patterns of medication adherence.^{28,29}

E-prescribing increases the number of prescriptions making it to the pharmacy. Providing greater visibility into the prescription fulfillment process, in particular the discrepancy between what is prescribed versus what is picked up by the patient, has the paradoxical effect of revealing higher abandonment rates for primary, or first fill, prescriptions. Quality organizations should consider the policy implications of advocating for adherence measures that may inadvertently harm or reduce performance scores from e-prescribers. This issue is becoming more salient given 3 additional trends: First, that roughly three-quarters of all office-based prescribers now actively e-prescribe, and this proportion is likely to continue increasing given federal incentive programs to stimulate meaningful use of EHRs^{30,31}; second, that e-prescribing use is increasing among those who have adopted it; and third, that many payer organizations, including Medicare, are instituting pay-for-performance programs that rely on adherence quality measures.³²

In a period of significant change within the healthcare system, stakeholders—including the federal government, private health insurers, providers, pharmacies, patients, and PBMs—are all investing in health information technology. EHRs can be leveraged to connect providers in new



ways with richer information that can facilitate improved care coordination and enable population health management. PBMs and providers are leveraging these connections through e-prescribing to enhance prescribed pharmacotherapy. The ability to connect providers and PBMs to enable real-time electronic messaging via the e-prescribing channel could be leveraged to improve prior authorization processes and medication adherence interventions.

Further investigation on how PBMs and providers can better use e-prescribing communication channels is critical. Our results present additional questions worthy of further investigation, including: a) whether some EHR systems are inherently more functional than others, and therefore may drive better outcomes; b) whether other advanced functionalities within e-prescribing, such as medication history or electronic prior authorization, are associated with positive clinical outcomes; and c) whether previous findings of e-prescribing reducing costs can be substantiated, given that e-prescribing adoption has reached maturity.

Limitations

First, the prepost study design used in this analysis assumes that prescribers in the treatment and control groups would have demonstrated similar prescribing behavior in the absence of electronic prescribing. To address this assumption, our approach used simulation-based adjustments and propensity scoring methods to produce comparable pre-period comparison groups; however, we acknowledge residual confounding due to selection bias may have remained. Second, although covariates derived from a combination of provider demographics are often used to match comparison groups, such demographic data were unavailable in this study. However, baseline utilization and prescriber patterns were used to maximize matching of providers between groups. Third, we recognize that patients' actual medication adherence may differ from estimated rates using pharmacy claims data; however, adherence estimates by way of pharmacy claims has been well validated in integrated health systems.^{33,34}

CONCLUSIONS

We linked nationally representative prescription information from a PBM with an e-prescribing network to examine changes in prescribing patterns and patient adherence after e-prescribing adoption. We found greater increases in initial fill rates, refill rates, and 90-day supply prescribing among prescribers adopting technology, compared with prescribers not adopting e-prescribing. E-prescribing infrastructure allows for additional provider

messaging opportunities intended to increase efficiencies and improve patient outcomes.

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Authorship Information: Concept and design (RSL, BVP, CK, MS, JYS, SBJ); acquisition of data (RSL, BVP, CK, MS, SBJ); analysis and interpretation of data (RSL, BVP, CK, JYS); drafting of the manuscript (MS, JYS, SBJ); critical revision of the manuscript for important intellectual content (RSL, BVP, MS, JYS, SBJ); statistical analysis (JYS); provision of patients or study materials (RSL, BVP, CK); administrative, technical, or logistic support (MS, SBJ); and supervision (RSL, BVP, MS, SBJ).

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