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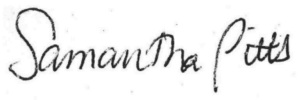
To the Board of the NCPDP Foundation,

It is with great pleasure that I submit this final report for your review. I wish to express my gratitude for the opportunity to conduct the work described in this report and to specifically thank Mr. Charlie Oltman for his support as we overcame challenges.

The NCPDP Foundation support allowed us to deeply examine CancelRx implementation at Johns Hopkins. I strongly believe this will help other institutions in their successful implementation of the technology. I also hope our work will contribute to further enhancements to improve collaboration between prescribers and pharmacy staff to drive medication safety.

Warmly,



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PURPOSE

Adverse Drug Events (ADE) are common and result in an estimated 4.5 million outpatient visits each year.(1) Preventable ADE occur during prescribing, dispensing, and administration despite safety improvements resulting from electronic prescribing and decision support in electronic health records (EHR). Lack of communication between prescribers and pharmacies has been demonstrated to contribute to dispensing errors(2-6); with medications dispensed following intended discontinuation in 1.5 – 5.3% of medication discontinuations, resulting in documented ADE and patient harm.(2, 3)

CancelRx, a functionality of the National Council for Prescription Drug Programs' (NCPDP) SCRIPT standard sends an electronic message from EHRs to pharmacy systems to request discontinuation of a prescription at the pharmacy. While CancelRx has been recommended as a tool to improve medication safety,(7) its impact on medication errors has not been evaluated.

The objectives of this award were as follows:

1. Conduct a controlled before and after study to assess the impact of CancelRx implementation on medication dispensing errors.

2. Assess the usability of CancelRx in pilot implementation and identify areas for improvement.

METHODS

Aim 1

We conducted a pilot pre-post evaluation of CancelRx implementation with prescribers in an outpatient practice and pharmacies affiliated with an academic medical center. We identified medications e-prescribed to one of the outpatient health system pharmacies and subsequently discontinued in the EHR during Jan 16, 2018 – April 15, 2018 (baseline) or Jan 16, 2019 – April 15, 2019 (following CancelRx implementation).

A trained pharmacy analyst queried the Epic Clarity database to identify e-prescriptions discontinued in the EHR and matched these using a unique order identification number to dispensing data from the pharmacy management software, McKesson's EnterpriseRx. We excluded prescription renewals and discontinuations of duplicate prescriptions, as these were configured not to result in a CancelRx message in our EHR. We identified these by either the discontinuation reason or the timing of the subsequent prescription (reordered within one hour in an ambulatory encounter or on the same day in the hospital, without an alternate reason). We compared the timestamp of medication discontinuation in the EHR with the timestamp when the prescription was sold by the pharmacy to identify medications that were sold after discontinuation.

As a proxy for unintended prescription cancellations following CancelRx implementation, we measured the frequency with which discontinued medications were subsequently reordered. For all medications discontinued during our study period, we identified subsequent prescriptions for the same medication and dose/form (e.g., metoprolol 25 mg tablet). We included medication reorders up to 120 days after discontinuation to ensure that the time period was longer than a 90-day prescription but also time limited to reduce the likelihood that the therapy was resumed.

We conducted medical record review of all medications sold after discontinuation in the EHR and, following CancelRx implementation, all medications discontinued reordered within 120 days. A physician reviewed the medical records of patients, including medication lists, visit notes, discharge summaries, and patient instructions to determine if documentation supported the provider intent to discontinue the medication. A pharmacist conducted review of all records for which the primary reviewer concluded that 1) the medication was sold after intended discontinuation or 2) the CancelRx transaction might have resulted in an error. Any discrepancies were resolved by discussion and consensus.

Our primary outcome was the proportion of medications sold by the pharmacy after intended discontinuation by the prescriber. Our secondary outcome was the proportion of discontinued medications which were subsequently reordered within 120 days. We used SAS version 9.4 (SAS Institute Inc, Cary, NC) for all analyses, using a Fisher's exact or Chi-squared test for pre-post comparison of proportions and a binomial distribution for confidence intervals, all with an alpha of 0.05.

Aim 2

A skilled facilitator conducted interviews with prescribers and pharmacists in an outpatient practice which were audio-recorded and transcribed verbatim. Interviews included questions on tasks in the medication discontinuation and e-cancellation process and any challenges completing these tasks. Initial thematic analysis was conducted by the study team to identify key usability issues.

RESULTS

Aim 1

We identified a total of 779 qualifying e-prescriptions that were discontinued in the EHR within our study period, 392 before CancelRx implementation and 387 following implementation (Table 1). Prior to CancelRx implementation, 42/392 (10.7%) e-prescribed medications were sold following discontinuation in the EHR; following CancelRx implementation, no e-prescribed medications (0/387) were sold after discontinuation ($p<0.0001$). The proportion of medications discontinued and subsequently reordered within 120 days was not statistically different before and after CancelRx implementation (10.0% vs 12.7%, $p=0.23$).

In medical record review of medications sold after discontinuation prior to CancelRx implementation, 35.7% (15/42) of the medications had documentation of prescriber intent to discontinue the medication, or 3.8% (15/392, 95% confidence interval, 2.2 – 6.2%) of e-prescriptions prior to CancelRx implementation. Among those intended to be discontinued, reasons for discontinuation were a change to an alternate therapy (7), a change in dose or frequency (5), completion of therapy (2), and an adverse reaction (1). Conversely 38.1% (16/42) medications were intended to be continued, including 9 e-prescriptions discontinued as duplicates, 6 which were resumed and/or reordered, and 1 change in dose using the original prescription. Eleven (26.2%) lacked sufficient documentation of prescriber intent.

Following CancelRx implementation, among medications reordered within 120 days after discontinuation, medical record review identified 10 that were potentially discontinued in error (Table 2), resulting in a positive predictive value of 20.4% (10/49) and an overall rate of error of 2.6% (10/387, 95% confidence interval 1.0 – 4.2%). In four cases, including 2 for the same patient, prescribers discontinued the active prescription and used the "no print" functionality to enter a new order for the medication or to change the directions on an existing prescription without sending a new prescription to the pharmacy. In three cases, providers removed the wrong duplicate prescription, leaving an expired prescription on the patient's medication list. The final three cases appeared to be errors in medication reconciliation.

Table 1: Pharmacy outcomes among prescriptions discontinued in the EHR before and after CancelRx Implementation

	Pre-implementation	Post-implementation	P-value
Qualifying e-prescriptions	392	387	
Sold after discontinuation in the EHR	42 (10.7%)	0 (0.0%)	<0.0001[1]
Reordered within 120 days	39 (10.0%)	49 (12.7%)	0.23[2]

1. Fisher's exact test; 2. Chi-squared test

Table 2: Reason for reorder among prescriptions reordered within 120 days of discontinuation following CancelRx implementation

Reason	**Count (%)**
Resumed	13 (26.5%)
Dose adjustment	11 (22.4%)
Potential error	10 (20.4%)
Reordered	7 (14.3%)
Continued therapy – prior removal of a duplicate	4 (8.2%)
Unclear	4 (8.2%)
Total	49

Aim 2

Interviews with prescribers and pharmacy staff identified several initial key themes.

There was varied awareness and understanding of the functionality of CancelRx. Some prescribers were unaware of the CancelRx functionality, others were aware of the functionality, but sometimes lacked an understanding of when a CancelRx message would be sent, what information pharmacies received, and whether the pharmacy cancelled the prescription as a result of a CancelRx message. It was not intuitive that the reason for discontinuation was only stored in the EHR and not transmitted to the pharmacy. As a result of these uncertainties, some prescribers still made phone calls to pharmacies when they felt communication was important. Limited visibility of the transaction within the EHR and challenges with disseminating information and training large numbers of prescribers in CancelRx use in a complex organization likely contributed to the lack of awareness of the functionality.

Pharmacy staff were uniformly familiar with the CancelRx workflow at the pharmacy. However, they frequently accessed the electronic health record to make determinations about next steps following receipt of a CancelRx. Information sought included the intent of the prescriber (e.g., to change the dose of a medication) and to confirm what medications remained on the patient's active medication list. These elements were used to determine if additional prescription for the same medication should be discontinued (if present). Ready access to the electronic health record is a unique advantage of Johns Hopkins pharmacies when compared to

commercial pharmacies. This need for information in the EHR indicates that the information in the CancelRx is insufficient to meet the needs of pharmacy staff in decision making.

Some pharmacy staff noted that patients would come to the pharmacy expecting to obtain a prescription that had been cancelled. In most cases, pharmacy staff had to direct patient questions back to their provider as they were not able to confidently inform the patient of the reason for cancellation.

IMPLICATIONS

Aim 1

In our pilot evaluation, implementation of CancelRx led to the elimination of the sale of e-prescribed medications following discontinuation in the EHR (10.7% versus 0.0%), including 3.8% which had documented intent to discontinue the medication. There was a 2.7% increase in the proportion of medications reordered within 120 days (10.0% versus 12.7%) which was not statistically significant. Medical record review of the reordered prescriptions following CancelRx implementation found that 10, or 2.6% of discontinued e-prescriptions may have been unintentionally cancelled.

This pilot study is the first to demonstrate the impact of CancelRx on medication errors, specifically on dispensing by pharmacies to patients after intended discontinuation. While confirmation of these findings is needed, these results support the critical importance of CancelRx messages for e-prescribing safety.(7)

In addition to the important reduction in dispensing after intended discontinuation in our pilot, we also identified a risk of unintended cancellation of prescriptions. Our estimated rate of unintended cancellations, 2.6%, is closely matched to the overall increase in the proportion of medications that were reordered within 120 days (2.7%). The primary reasons for unintended cancellations were the use of “no print” functionality to enter medication orders or change directions on prescriptions without sending a new prescription to the pharmacy, errors in medication reconciliation, and removal of the active prescription when discontinuing a duplicate. Further supporting the risk of unintended cancellation of prescriptions, a substantial proportion of e-prescriptions dispensed after discontinuation prior to CancelRx implementation were intended to be continued or lacked documentation of prescriber intent to discontinue the medication.

CancelRx implementation will transform similar failure modes (e.g., errors in medication reconciliation, removal of the active prescription when discontinuing a duplicate prescription) into active errors – patients will not be able to obtain the needed medication from the pharmacy if the medications have been discontinued in error in the EHR. Vulnerabilities in the workflows for medication reconciliation have been identified to have implications for CancelRx.(8) Given the known challenges to accurately complete medication reconciliation, including resource intensity and complexity, it will be important to further evaluate and mitigate this risk.(9) Our intended measure of this risk, reorder within 120 days of

discontinuation had a low positive predictive value (20.4%), but may be further refined to eliminate dose adjustments and reordered medications. However, this measure will only identify unintended cancellations if the error is identified and the prescription is rewritten.

To reduce the risk of unintended cancellations and possible patient harm of CancelRx implementation, safeguards need to be proactively considered, including increased situational awareness for both prescribers and pharmacy staff. We had previously identified the risk of unintended prescription cancellation following CancelRx implementation due to limited visibility of the CancelRx transaction in the EHR and the resulting difficulty users experienced determining whether their action would trigger a CancelRx message.(10) We suppressed CancelRx transactions where we identified risk: medication reorders, discontinuation of duplicates, and with use of the "adjust sig" functionality, which discontinues prescription without generating a new e-prescription, similar to "no print". Health systems should consider whether to require a discontinuation reason if this is used in the logic of CancelRx implementation and whether workflows which intentionally create a discrepancy between the EHR and pharmacy systems are safe.

As prescribers must ultimately determine the appropriateness of a CancelRx message, increased visibility of the CancelRx in the EHR to help providers understand the functionality might reduce unintended cancellations. In addition, EHRs should clearly distinguish between active and expired prescriptions on patient's medication lists to prevent unintended cancellation of the active duplicate prescription. Further, transmission of the reason for discontinuation would provide additional context for pharmacists about the intent of the prescriber; the NCPDP is in the process of adding this data element to the CancelRx standard.

Aim 2

Given our findings that prescribers had limited understanding of the functionality and outcomes of CancelRx and with challenges in disseminating information and training large numbers of prescribers in its use, ideal implementation in the EHR would demonstrate within the system the result of an action. For example, when selecting a reason for discontinuation, the system could indicate if a CancelRx transaction would be sent when this reason is selected. In addition, increased visibility of the outcome of a transaction (e.g., prescription cancellation) would improve the situational awareness of prescribers.

Our findings of the information needs of pharmacy staff, including the importance of the reason for discontinuation, were brought to the NCPDP CancelRx Task Group. As a result, transmission of a standardized cancellation reason to pharmacies will be implemented in the next SCRIPT standard. Our findings also suggest that pharmacy staff would benefit from clear indication whether a single prescription or all prescriptions of a medication should be cancelled. This was also discussed by the Task Group and may be considered in future modifications to the SCRIPT standard.

LIMITATIONS

Our study is limited to a practice and pharmacies associated with an academic medical center. For aim 1, we examined the impact on medication errors in e-prescriptions, as CancelRx currently sends transactions only when medications are e-prescribed within the EHR; we were unable to measure dispensing after discontinuation for medications that were not e-prescribed in our EHR. We were unable to determine the intent of the provider in a significant proportion of discontinued prescriptions nor whether patients took their medications incorrectly or experienced harm. For aim 2, our pharmacy staff have access to the electronic health record, unlike community pharmacy staff. We are continuing to analyze interview transcripts to identify additional themes and inform further recommendations to improve communications between prescribers and pharmacies.

PUBLICATIONS AND PRODUCTS

Pitts S, Chui M, Oltman C, Akinwale T. Implementation of Electronic Prescription Cancellation: A Tale of Two Health Systems, a Retail Pharmacy, and the Evolution of the CancelRx Standard. American Medical Informatics Association Annual Meeting, 2020.

Pitts S, Yang Y, Woodroof T, Mollenkopf N, Wang N, Thomas B, Chen A. The impact of electronic communication of medication discontinuation (CancelRx) on medication safety: a pilot study. Submitted to the Journal of Patient Safety.

NEXT STEPS

A multi-institutional study would provide more generalizable estimates and confirm the results of this analysis. As a single institution, some finding may result from the specific electronic health record and system configurations, practice workflows, and adoption.

Further detailed analysis of interview data will continue to identify opportunities to improve CancelRx workflows and implementation. The support of the NCPDP Foundation will be acknowledged in future publications using data from the interviews conducted in Aim 2.

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