JAMIA Open, 2024, **7(1)**, ooae003
https://doi.org/10.1093/jamiaopen/ooae003
Research and Applications

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Design and evaluation of an electronic prospective medication order review system for medication orders in the inpatient setting

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Abstract

Objectives: Since the 1970s, a plethora of tools have been introduced to support the medication use process. However, automation initiatives to assist pharmacists in prospectively reviewing medication orders are lacking. The review of many medications may be protocolized and implemented in an algorithmic fashion utilizing discrete data from the electronic health record (EHR). This research serves as a proof of concept to evaluate the capability and effectiveness of an electronic prospective medication order review (EPMOR) system compared to pharmacists' review.

Materials and methods: A subset of the most frequently verified medication orders were identified for inclusion. A team of clinical pharmacist experts developed best-practice EPMOR criteria. The established criteria were incorporated into conditional logic built within the EHR. Verification outcomes from the pharmacist (human) and EPMOR (automation) were compared.

Results: Overall, 13 404 medication orders were included. Of those orders, 13 133 passed pharmacist review, 7388 of which passed EPMOR. A total of 271 medication orders failed pharmacist review due to order modification or discontinuation, 105 of which passed EPMOR. Of the 105 orders, 19 were duplicate orders correctly caught by both EPMOR and pharmacists, but the opposite duplicate order was rejected, 51 orders failed due to scheduling changes.

Discussion: This simulation was capable of effectively discriminating and triaging orders. Protocolization and automation of the prospective medication order review process in the EHR appear possible using clinically driven algorithms.

Conclusion: Further research is necessary to refine such algorithms to maximize value, improve efficiency, and minimize safety risks in preparation for the implementation of fully automated systems.

Lay Summary

Pharmacists prospectively evaluate most medication orders placed in the hospital. While this review serves an important function, the current system gives equal significance to all orders. This system creates opportunity costs where the pharmacist reviews routine medication orders instead of performing other more valuable clinical activities that may produce greater patient benefits and outcomes. It may be possible for the review of routine medication orders to be protocolized and performed consistently and efficiently by an electronic system. This investigation aimed to evaluate the opportunity to develop a protocol for medication order review and implement an electronic system to mimic this activity. A team of clinical pharmacists and informaticists created a best-practice framework of what should be checked when reviewing medication orders. They then designed an electronic prospective medication order review (EPMOR) system to run in the background of the electronic health record (EHR). A comparative review of the EPMOR system versus the human-driven order verification process was performed. During a 5-day period, 13 404 medication orders were studied. Of the 13 133 orders reviewed by a pharmacist, 7388 passed the EPMOR. Further research is necessary to evaluate the safety and use of enhanced automation including artificial intelligence for verifying medication orders.

Key words: informatics; pharmacists; automation; electronic prospective medication order review; prospective medication order review.

Background and significance

Pharmacist prospective medication order review (PMOR) is performed for nearly all medications in a hospital-based setting. PMOR occurs following a prescriber's signed order but prior to dispensing and administration.[1–4] Pharmacist PMOR is assisted by clinical decision support (CDS) tools including drug interactions, dosage alerts, duplicate checking, lab warnings, age warnings, and more. The presumed value of PMOR is influenced by the known patient safety and efficacy benefits a pharmacist provides in determining the appropriateness of a medication order.[5] While professional societies, accreditation bodies, and regulatory groups have outlined a subset of criteria for PMOR, it is neither inclusive nor standardized, giving the pharmacist latitude to exercise their

Received: April 6, 2023; **Revised:** August 21, 2023; **Editorial Decision:** January 4, 2024; **Accepted:** January 5, 2024

professional judgment during the process. Thus, the cognitive processes and time spent performing an individual medication order review can vary dramatically. Some medication orders have a few factors that impact their overall appropriateness for use. Such medication orders may be part of an institutionally approved order set that utilizes CDS tools to consider patient factors upfront, limiting the amount of time and cognitive effort required to evaluate. Other medication orders are of greater complexity and require a more thorough review to ensure the patient's status and context of use are appropriate before verification.

Despite significant advancements in implementing proven medication safety practices and technologies, the regulatory requirements surrounding PMOR have remained relatively unchanged. As a consequence, PMOR is rarely discussed as a potential candidate for automation in the inpatient setting.[6,7] In 2009, Flynn recognized the evolving use of systems and technologies as well as the growing demand and missed opportunities for pharmacists to improve medication therapy outcomes.[8] He suggested that requiring pharmacists to acknowledge almost every medication order is pharmacist time lost to a potentially more valuable opportunity, particularly for low-risk, highly standardized medication orders that require little cognitive effort, yet contribute markedly to clerical and administrative burden. This contention suggested that by leveraging evolving systems, pharmacists could shift their efforts from low-complexity medication orders to higher-value activities that yield greater overall value to the patient and organization. Dakwa et al. studied the impact of drug order complexity on PMOR and verification time.[5] Although unable to establish that verification time increases as medication orders become more complex, there were time differences between the different low, medium, and high complexity categories. Their data also suggest that 4.1-7.6 s of pharmacist time per medication order could be reallocated if the low complexity medication orders in their study were no longer verified by pharmacist. Dakwa et al. suggest that further research investigating the appropriateness of verification performed along with validated standards for medications of differing complexity is warranted. The successful deployment of highly sophisticated electronic health records (EHR), tightly integrated medication management and CDS systems, institutionally derived electronic order sets and protocolized medication orders has produced additional safety features and a platform to further explore the opportunity for automation within the PMOR framework.

The purpose of this proof-of-concept study was to develop and validate a real-time background simulated electronic prospective medication order review (EPMOR) system for a subset of high-volume medication orders in the inpatient setting across a large academic health system to determine if the current technical infrastructure within EHRs can support process automation and iterative system refinement. Secondarily, this study aimed to establish a framework to evaluate the outcomes and safety of these automated systems in a real-world setting.

Methods

Study design and patient selection

A retrospective cohort study was conducted across all Mayo Clinic inpatient care facilities, which includes sites in Rochester, MN, Jacksonville, FL, Phoenix, AZ, Southern Minnesota, and Western Wisconsin. Study approval was obtained from the Mayo Clinic Investigational Review Board (IRB 21-009668). Included individuals were hospitalized adults aged 18 or older with medication orders verified between April 5, 2022 and April 10, 2022. A short timeframe was selected because verification volumes at the facilities studied were high and sufficient order generation would likely occur within 1 day to achieve sufficient power. To be included for evaluation, patients must have had an order placed for a medication of interest that was reviewed in the verification queue by a pharmacist.

Operational design

To determine the medications of interest for this study, the pharmacy informatics team pulled the top 20 most frequently verified medications in the inpatient setting. From that list, a core team of 6 clinical pharmacist subject matter experts (SMEs) identified a list of 10 medications that were thought to be the most impactful for evaluation. The selection of medications was done based on those that would provide meaningful time to the pharmacists and were thought to have straightforward criteria available in the EHR to evaluate against. The group considered it important to involve some higher-risk medications from a safety standpoint to test the limits of the system. The medications selected included acetaminophen, bisacodyl, diphenhydramine, haloperidol, naloxone, ondansetron, pantoprazole, polyethylene glycol, potassium chloride, and senna docusate.

Without established criteria for PMOR of the medications, clinical expertise was required to develop the EPMOR production rules. We developed a series of parameters based on The Joint Commission standards MM01.01.01 1 and MM.05.01.01 4 and ASHP's recommendation of what should be reviewed in the patient's profile.[9,10] Criteria to exclude high risk patients (eg, age, weight) and other assessment parameters were determined. These parameters included dosage form, route, dose, frequency, allergies, lab values, therapeutic duplications, drug interactions, and other contraindications. To determine the safety parameters for each medication, Lexicomp, Micromedex, package inserts, and institutional practice standards were utilized. The conditional logic for each medication, including appropriate laboratory values, was defined by the SMEs. The medication-specific parameters were sent to medication knowledge management pharmacists and experts from multiple disciplines to provide consensus on medication-specific criteria that would be evaluated by EPMOR. Once consensus was achieved between all stakeholders for medication-specific criteria, the production rules were developed. The clinical logic informing the rules used by the EPMOR system is provided in Table S1.

Medication order-specific conditional logic was built in the EHR by the pharmacy informatics team. The production rules were then attached to 10 background CDS alerts to store the pass/fail outcomes of the rule evaluation without displaying to the end-user. We leveraged CDS alerts because they provided the opportunity to mimic real-world EPMOR production rule evaluation, without needing to implement EPMOR on medication orders. This allowed our study to remain within the legal bounds of pharmacy regulation and provided a secondary benefit by allowing us to measure EPMOR outcomes for the same medication orders under identical conditions to those reviewed by a pharmacist. This design permitted head-to-head comparison between

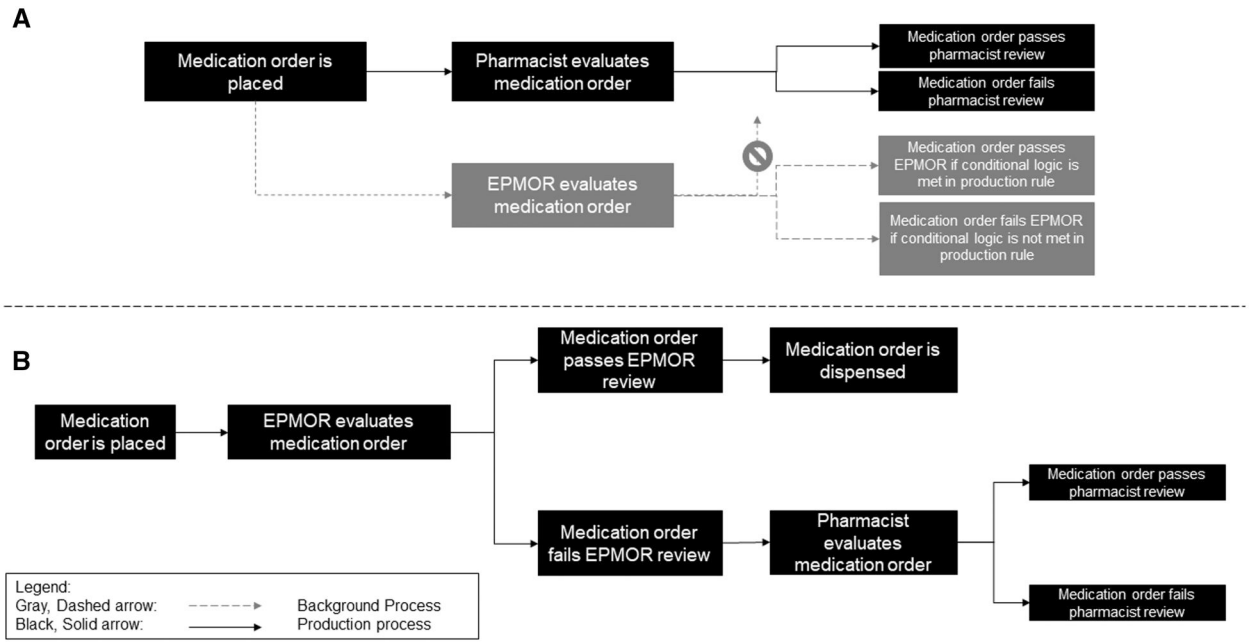

Figure 1. (A) Current state: medication orders are verified by the pharmacist and evaluated in parallel by the EPMOR system running in the background. The pharmacist does not see the EPMOR outcome. (B) Future state: EPMOR makes a decision about the medication order and routes it to the appropriate next step. If the medication order passes the conditional logic of EPMOR, it would proceed to dispense. If the medication order fails conditional logic, it would proceed to pharmacist verification.

medication order review methodologies (Figure 1A). Pharmacists were unable to view EPMOR outcomes in the verification queue, preventing bias in pharmacist PMOR outcomes. In addition to storing outcome data, these CDS alerts served as a timestamp to calculate the time difference between the time a pharmacist opened the verification queue and when the pharmacist PMOR completed.

While it is possible to build CDS alerts to store the reason an order fails EPMOR conditional logic, doing so increases the complexity of the build and limits the ability to mimic real-world EPMOR build. Therefore, a report was developed using structured query language to independently evaluate if a medication order should pass or fail the EPMOR conditional logic, describe why an order failed conditional logic, and estimate the amount of time required for pharmacist PMOR. During validation, inconsistencies between the report and the production rules were identified and remedied as appropriate.

Data collection

Medication orders of interest were identified retrospectively from inpatient medication orders intended for non-procedural areas. Medication orders that were placed but discontinued before a pharmacist viewed them were excluded as our primary outcome would not be able to be assessed. The real-world outcome of pharmacist review, the gold standard, was compared to the electronic pass or fail stored for the order by the EPMOR system. Pharmacist rejection of a medication order was considered in 3 ways: (1) order rejection verification outcome, (2) modification of the order in the verification queue by the pharmacist, or (3) discontinuation of the order after pharmacist viewing in the verification queue took place but before verification.

The outcome assessment created 4 groups of medication orders (Figure 2). The first group represented the "true positives (TP)" and included medication orders verified by the pharmacist that passed EPMOR conditional logic. This group can be used to hypothesize the amount of pharmacist time that may be reallocated for other clinical activities. The second group represented the "false negatives (FN)" and consisted of medication orders verified by the pharmacist that failed EPMOR conditional logic. This indicated potential missed opportunities for EPMOR or medication orders outside the EPMOR production rules. The third group consisted of "false positives (FP)" and included medication orders not verified by the pharmacist that passed EPMOR conditional logic, indicating potential PMOR errors requiring additional investigation. The fourth group was considered our "false negative (FN)" group and consisted of medication orders not verified by the pharmacist that failed EPMOR conditional logic, indicating concordance in error identification.

For the FNs and FPs, sub-analyses were performed to gather additional details on the discrepancies identified. Among the FN medication orders, conditional logic failed was reported. For the FP medication orders, the patient's chart was manually reviewed to assess clinician documentation and order audit trails to determine the most likely reason for pharmacist rejection.

To evaluate pharmacist time spent performing PMOR, the difference between the verification instant of the medication order of interest and either the time of last medication verification or the verification queue open instant, whichever occurred later, was used. This approximated the time the pharmacist spent looking at the order of interest.

Data analysis

Using the pharmacist as the gold standard, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the EPMOR system were calculated, along with the corresponding 95% confidence intervals. Of

		Simulation EPMOR Outcome	
		Pass	Fail
Pharmacist Outcome	Pass	True Positive	False Negative
	Fail	False Positive	False Negative

EPMOR: electronic prospective medication order review

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most interest was the proportion of medication orders that would have been verified via EPMOR that were verified by a pharmacist (PPV). A single proportion test was run to compare this rate to 100%. To have 80% power to detect the difference between 99% and 100% at a level of significance of 0.05, we estimated that we needed to include 420 medication orders in the analysis. After collecting the time pharmacists spent on medication orders that could be verified via EPMOR, we weighted the results so that the distribution of medication orders reviewed was similar to the weekly medication orders reviewed. Using this, we calculated the average time per day that could be repurposed by implementing the EPMOR system, along with the 95% confidence interval.

Results

From April 5, 2022 to April 10, 2022, there were a total of 32 697 medication orders that were of interest to this study. A total of 19 293 medication orders were excluded from the study sample due to patient age being less than 18 years ($N = 1354$), out of scope based on medication or department ($N = 17\ 371$), and due to a system limitation, where there was an inability to validate the chronological order and timing of 568 medication orders. This left 13 404 medication orders that were evaluated by the simulation EPMOR system (Figure 3). Of the 13 133 medication orders verified by pharmacists, 7388 passed and 5745 failed EPMOR conditional logic (Table 1).

The sensitivity of the EPMOR system was 56.3% and the specificity was 61.3% (Table 1). The PPV suggests that 98.6% of medication orders reviewed by EPMOR would appropriately pass EPMOR. The NPV indicates that a medication order will appropriately fail EPMOR approximately 2.8% of the time. There was an expected amount of variability in the sensitivity, specificity, PPV, and NPV of the individual medications because the EPMOR system was designed with patient safety in mind, intentionally passing fewer medications than what would be expected of pharmacist PMOR.

The most common reasons medication orders did not pass simulation EPMOR conditional logic were dose, route, and frequency issues (Table S2). Of the 271 medication orders failed by a pharmacist due to order rejection, discontinuation, or modification, 105 passed and 166 failed EPMOR. Of the 105 medication orders that were failed by the pharmacist but passed by simulation EPMOR, scheduling changes alone

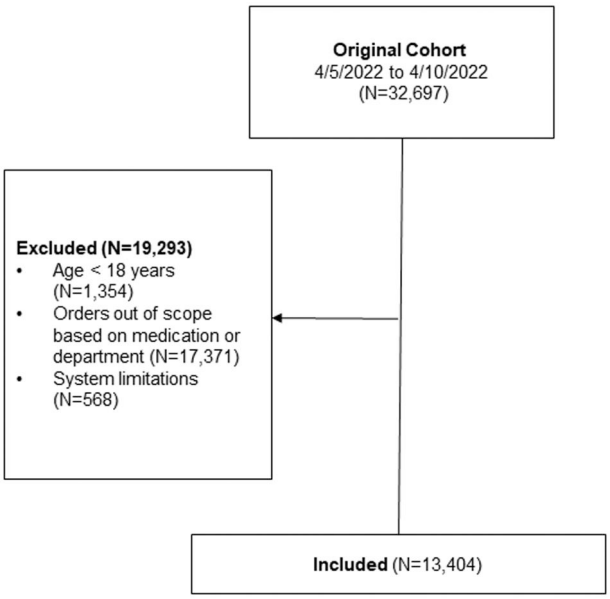

Figure 3. The original cohort consisted of 32 697 medication orders. Medication orders were excluded based on patient age less than 18 years ($N = 1354$), medication orders that were out of scope based on medication or department ($N = 17\ 371$), and due to system limitations prohibiting precise temporal comparisons ($N = 568$). This limited the study population to 13 404 medication orders.

represented 43% of the modifications made to the medication orders (Table 2).

The next most common change was discontinuation of the order of interest because of a duplicate medication order being present in the verification queue. This was expected because our system was designed to identify and pass only one medication order if duplicate medication orders were present but could not predict which medication order a pharmacist may ultimately decide to pass or fail. The third most common change was provider discontinuation of a medication order prior to pharmacist verification. The study team did not identify any modifications that suggested that the simulation EPMOR system deviated from its intended configuration or posed any significant safety concerns when configured according to specifications.

The median medication order verification time was 10 s (IQR 4, 34). There was variation based on medication, with naloxone having the lowest median time of 5 s (IQR 2, 25) and bisacodyl having the highest median time of 15 s (IQR 1,

Table 1. Comparison of pharmacist verification outcomes to simulation EPMOR outcomes.

Pharmacist outcome Simulation EPMOR outcome	TP Pass Pass	FN Pass Fail	FP Fail Pass	TN Fail Fail	Sensitivity [TP/(TP + FN)] Percent of medication orders that were passed by pharmacist and simulation EPMOR (95% CI)	Specificity [TN/(TN + FP)] Percent of medication orders that were failed by pharmacist and simulation EPMOR (95% CI)	PPV [TP/(TP + FP)] Percent of medication orders that were passed by simulation EPMOR and pharmacist (95% CI)	NPV [TN/(FN + TN)] Percent of medication orders that were failed by simulation EPMOR and pharmacist (95% CI)
Overall	7388	5745	105	166	56.3% (55.4%-57.1%)	61.3% (55.2%-67.1%)	98.6% (98.3%-98.9%)	2.8% (2.4%-3.3%)
Acetaminophen	1328	1314	50	52	50.3% (48.3%-52.2%)	51.0% (40.9%-61.0%)	96.4% (95.2%-97.3%)	3.8% (2.9%-5.0%)
Bisacodyl	643	266	0	1	70.7% (67.7%-73.7%)	100% (2.5%-100%)	100% (99.4%-100%)	0.4% (0%-2.1%)
Diphenhydramine	71	269	1	9	20.9% (16.7%-25.6%)	90.0% (55.5%-99.7%)	98.6% (92.5%-100%)	3.2% (1.5%-6.1%)
Haloperidol	92	374	2	16	19.7% (16.2%-23.7%)	88.9% (65.3%-98.6%)	97.9% (92.5%-99.7%)	4.1% (2.4%-6.6%)
Naloxone	1066	216	1	5	83.2% (81.0%-85.2%)	83.3% (35.9%-99.6%)	99.9% (99.5%-100%)	2.3% (0.7%-5.2%)
Ondansetron	968	899	8	21	51.8% (49.6%-54.1%)	72.4% (52.8%-87.3%)	99.2% (98.4%-99.6%)	2.3% (1.4%-3.5%)
Pantoprazole	585	445	26	27	56.8% (53.7%-59.8%)	50.9% (36.8%-64.9%)	95.7% (93.8%-97.2%)	5.7% (3.8%-8.2%)
Polyethylene Glycol	1061	433	11	4	71.0% (68.6%-73.3%)	26.7% (7.8%-55.1%)	99.0% (98.2%-99.5%)	0.9% (2.3%-0.2%)
Potassium chloride	545	1315	1	30	29.3% (27.2%-31.4%)	96.8% (83.3%-99.9%)	99.8% (99.0%-100%)	2.2% (1.5%-3.2%)
Senna-docusate	1029	214	5	1	82.8% (80.6%-84.8%)	16.7% (0.4%-64.1%)	99.5% (98.9%-99.8%)	0.5% (0%-2.6%)

Abbreviations: CI, confidence interval; EPMOR, electronic prospective medication order review; FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

Table 2. Rates of medication order modification or discontinuation by type.

Modifications after medication order signed	Modification count[a]
Scheduling change[b]	51
Duplicate order[c]	19
Order discontinued by provider before pharmacist verification	14
Dispense location change[d]	9
Product selection change[e]	7
Dose reduction to an alternative dose that would have also passed EPMOR conditional logic[f]	6
Lab value[g]	5
Discontinued by pharmacist without documentation or a clinical contraindication	5
Discontinued after med history performed and patient not taking	1
Dose increase[h]	1

Abbreviation: EPMOR, electronic prospective medication order review.
[a] A total of 105 medication orders passed EPMOR conditional logic but were not verified by a pharmacist as signed. About 13 medication orders underwent 2 modifications before pharmacist verification.
[b] Changes could be grouped into (1) changing pantoprazole dosing to be before meals, (2) changing medication frequency from an hourly frequency to a scheduled times a day frequency to maximize daytime doses (eg, every 6 h to 4 times a day), and (3) moving scheduled doses to "include now" so they would be administered sooner.
[c] In all scenarios, the EPMOR conditional logic identified the duplicate medication orders, but performed the opposite action of the pharmacist (eg, EPMOR system passed for the order that the pharmacist failed and failed for the order that the pharmacist passed.).
[d] Selected alternative nearby automated dispensing cabinet.
[e] Changes included changing capsule to tablet, suspension to solution, oral to intravenous, powder to powder packet.
[f] In all scenarios, acetaminophen orders were reduced from 1000 to 650 mg per dose.
[g] In most scenarios, the pharmacist appeared to have been referencing to a QTc result that was more than 7 days old or not yet finalized. There were 2 cases where the system did not identify QTc results that were in an unconfirmed status.
[h] Pantoprazole dose increased from 20 to 40 mg.

Table 3. Time taken to verify medication orders.

Drug	Time (s), median (IQR)	Hours calculated over 1 week[a]
Overall	10 (4, 34)	28.7
Acetaminophen	12 (4, 35)	6.2
Bisacodyl	15 (1, 78)	3.8
Diphenhydramine	7 (3, 24)	0.2
Haloperidol	13 (4, 61)	0.5
Naloxone	5 (2, 25)	2.1
Ondansetron	11 (4, 44)	4.1
Pantoprazole	8 (4, 21)	1.8
Polyethylene glycol	7 (3, 31)	2.9
Potassium chloride	11 (5, 27)	2.3
Senna-docusate	7 (3, 37)	2.8

Abbreviation: IQR, Interquartile range.
The median time taken to verify the medication orders, overall and stratified by medication in the time period studied. Additionally, an estimation of hours over the course of 1 week that could be repurposed for pharmacist patient care activities at the study institution based on the time in seconds and historical order volumes when considering the medication orders that passed EPMOR conditional logic and were verified by a pharmacist.
[a] Calculated using rate of 7388 medication orders total generated over 5 days and broken down by specific medications ordered in the row.

78). A breakdown of each medication verification time is listed in Table 3.

Implementation feasibility was evaluated. Some production rules took about 3 hours to build because several rows of conditional logic had to be custom developed. Other production rules had fewer conditional logic components that did not require custom development and took closer to an hour to build and configure.

Discussion

Our results demonstrate the feasibility of using an EHR to deploy a collection of medication-related production rules, thereby developing and validating an embedded proof-of-concept EPMOR system. Secondarily, we established a framework to evaluate this type of automation to ensure that such systems can be iteratively refined and adhere to configured specifications and expected outcomes when applied in a real-world setting. We developed EPMOR conditional logic using recommendations of clinical stakeholders and effectively translated those specifications into a simulation EPMOR system that stored production rule pass or fail outcomes for each order reviewed by a pharmacist. The performance of the system was independently validated by a report to confirm production rule performance and, when relevant, identify the specific patient or order criteria that did not pass. The report allowed for an independent double check of the production rule build to assure data could be extracted in a meaningful method. The simulation EPMOR system had good discrimination and, with evidence-based refinements facilitated by our evaluation framework, has the capability to effectively triage medication orders.

The intent of this study was to identify orders that would benefit from pharmacist PMOR, recognizing that pharmacists are good at identifying global concerns not discretely captured in the EHR. The conditional logic in our production rules reflected scenarios where the clinical SMEs felt confident that the medication order would be appropriate for the

patient and not require additional pharmacist review. It was purposeful to have some medication orders fail EPMOR so that in future states (Figure 1B), these orders would be reviewed by a pharmacist. Therefore, a lower sensitivity was acceptable. There were also many scenarios where the EPMOR system passed the opposite duplicate medication order than the pharmacist. In such scenarios, the EPMOR system performed appropriately but specificity was reduced. The amount of time spent developing the production rules is highly dependent on the complexity of the conditional logic that is built into the rules. Overall, this build is generally quite scalable because the conditional logic can be reused with minor edits across the production rules. It is relevant to note that the biggest challenge to the development and upkeep of these systems is the maintenance of clinical build guidance documents. When clinical practice changes, there needs to be a mechanism to clinically evaluate new guidelines and request updates to production rules.

Since Flynn's article in 2009, there have been significant developments in automation and EHR capabilities, but the development of systems for EPMOR has lagged behind due to the regulatory environment that does not allow for electronic triage of medication orders using automated systems in the inpatient setting.[8] Discussions surrounding the use of EPMOR began as early as 2013, with the publication of the first ASHP Pharmacy Forecast.[11] In the most recent 2023 ASHP Pharmacy Forecast, a strategic recommendation for practice leaders was to identify opportunities where artificial intelligence (AI) could be used for mundane and low-risk tasks, and implement solutions that allow pharmacists to focus on complex situations.[12] Our study demonstrates the successful development and implementation of a novel real-time background EPMOR tool in the EHR that can be used to iteratively refine these systems while adhering to current regulatory requirements. This novel system represents a significant opportunity to develop evidence-based guidelines for EPMOR, paving the way for eventual support by regulatory and accreditation bodies to fulfill the AI goals of the future. EPMOR is an emerging technology, and many aspects of the EPMOR framework that support it require additional investigation. Based on the observance of variation in pharmacist verification outcomes compared to the criteria developed by the SMEs, we identified that an opportunity exists to establish minimum standards for production rules informing EPMOR systems. For example, in our own study, our SMEs selected a 7-day lookback to identify a QTc interval greater than 475 in the conditional logic for ondansetron. In our analysis of pharmacist verification outcomes, we identified that some pharmacists were evaluating QTc interval results from prior months to inform their verification outcomes. Minimum standards for production rules would reduce variability among institutions for such decisions because consensus-based recommendations could be adhered to when no clear evidence-based recommendation exists.

We observed substantial variation exists in the time taken to review the medication orders. The EPMOR conditional logic established for our system encompassed many clinical parameters, so we anticipated that it would take a significant amount of time for a pharmacist to perform a comprehensive review of these medication orders (Table 3). Interestingly, 25% of the medication orders in our study were passed after a review of 4 s or less, while another 25% of medication orders were passed after 34 s or more. In future studies, it would be worthwhile to investigate how EPMOR systems contribute to pharmacist time spent reviewing medication orders.

Our study is not without limitations. This study was performed within the hospitals of a single health system. It is possible that the population of medication orders in this study was not representative of the frequency and volume of medication orders at all institutions. However, given that our health system spans multiple regions of the United States, we suspect that regional practice variations in medication use are well-represented in our data. Furthermore, our study evaluated EPMOR production rule outcomes for 10 medications. It is possible that production rule outcomes for other medications will differ from the findings represented here. However, we believe that our medication list included sufficient variability in medication classes and monitoring parameters that it is a representative sample of how EPMOR systems could be applied. Additionally, in our initial study plan, we had intended for pharmacists to be directly observed for the verification timing aspect of the study, but there was limited voluntary engagement from staff and the population would not have been representative of all hospitals in our multi-state health system, nor would it have provided the volume of data that was available through our pursued methods. Furthermore, 568 medication orders were excluded due to a system limitation, prohibiting a precise temporal assessment of relevant medication- and patient-specific criteria retrospectively. This limitation likely did not impact our results, as our real-time CDS alerts' pass/fail results for that subset of medication orders were representative of the population studied and due to the small size of the exclusion sample, it would not be enough to impact the validity of the results. Our assessment of time that could be repurposed to other clinical activities did not account for the maintenance of the EPMOR system. In our analysis of medication orders that passed EPMOR conditional logic, but were not verified by the pharmacist, it was not always possible to determine the reason that the pharmacist rejected the order. Although our retrospective design limited this analysis, members of the study team clinically reviewed the medication orders and patient charts to assess any risks or contraindications that could be identified for the relevant patients and medication orders. Lastly, there was limited transparency related to the EPMOR outcomes to clinical end-users. This was by design for our study, but future studies should incorporate greater transparency of such systems.

Conclusion

Our data demonstrate the successful development and implementation of a system designed by clinical and informatics practice using EPMOR conditional logic to simulate outcomes in real time. The methodology of this investigation establishes a framework for which EPMOR systems can be iteratively refined and evaluated for safety and effectiveness while remaining within the boundaries of current regulations. EPMOR is a developing technology and further research and demonstration projects are necessary to address the safety and feasibility of such automation systems across health systems, as well as to provide additional supportive evidence for eventual regulatory agency evaluation or approval.

Author contributions

The authors confirm their contribution to the paper as follows: study conception and design: D.S., B.A., S.F., M.S., B.

K., P.O.; data collection: E.D., B.A., D.S., P.O.; data analysis: E.D., B.A., D.S., P.O.; manuscript preparation: P.O., B.A., E. D., S.F., M.S., K.M., B.K., and D.S. All authors reviewed the results and approved the final version of the manuscript.

Supplementary material

Supplementary material is available at *JAMIA Open* online.

Funding

This work was supported by the Mayo Midwest Pharmacy Research Committee (grant number DF2023P-019).

Conflict of interest

None declared.

Data availability

The institutional deidentified data underlying this article are available from the corresponding author on reasonable request and institutional approval. Interested parties will be required to complete an institutional Data Use Agreement, and data will be made available via Secure Data transfer after institutional approval is secured.

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