A Systematic Approach to Optimize Electronic Health Record Medication Alerts in a Health-System

by

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ABSTRACT

Purpose: Limited literature evaluates a sustainable process for optimization of medication alerts when implementing a new electronic health record (EHR) technology with clinical decision support (CDS) capabilities. This study aimed to provide health-system enterprises with a systematic approach to optimize medication alerts with new EHR technology and evaluate the effect of strategic interventions to improve the effectiveness of medication related CDS.

Methods: An 81 week quasi-experimental study was conducted to evaluate the impact of interventions made to medication related CDS alerts by a multi-disciplinary committee. The primary endpoint was weekly modification and acknowledgement rates of medication alerts after drug-drug interaction reclassification. Secondary endpoints included weekly modification and acknowledgement rates of drug-drug interaction and duplicate therapy alerts, pharmacist and provider modification and acknowledgment rates in response to drug alerts, and monthly number of alerts per 100 medication orders. Data on alert and warning frequency, severity, and response type were analyzed before and after committee interventions to determine the impact of committee led interventions. Interrupted time series regression analysis was utilized to assess primary and secondary endpoints over the study time period.

Results: After reclassification of drug-drug interactions, a significant increase in weekly provider modification and acknowledgement rates occurred ($2.06 \pm 0.18\%$, $p < 0.001$; $1.49 \pm 0.25\%$, $p<0.001$). Total alerts per 100 medication orders significantly decreased after drug-drug interaction classification (Pre-intervention median: 88.4 vs Post-intervention 63.1, $p=0.017$).

Conclusion: Committee led interventions to drug-drug interactions facilitated an overall increase in both medication alert acknowledgement and modification rates, as well as an overall reduction in the total quantity of generated alerts.

PURPOSE/BACKGROUND

CPOE/EHR

The almost universal adoption of electronic health records (EHRs) by hospitals and health-systems in the United States has driven implementation of computerized provider order entry (CPOE) with clinical decision support (CDS).[1] Many CDS systems incorporate mechanisms of delivering information at specific points in patient care, and a common example in EHRs is medication related alerts at the point of prescribing and verifying a medication.[2] Almost exclusively, EHR CDS mechanisms rely on commercial medication knowledge bases for clinical decision support alerts including medication related alerts; however, these alerts are designed and deployed without institution specific customization.[3] Thus, the adoption of stock alerts from commercial databases may result in a large number of inconsequential alerts that may contribute to alert fatigue in the clinical setting.[4]

ALERT FATIGUE

Alert fatigue is defined as a state of irritability or exhaustion triggered by alert over stimulation, or alerts with a perceived history of irrelevance. This fatigue causes the user to ignore some or all of CDS alerts, thereby reducing the safety benefit of the decision support system.[5,6] Consequences of alert fatigue may encompass lost efficiency, overdependence on technology, decreased clinician satisfaction with EHR technology, desensitization to alerts leading to potential patient harm, and suboptimal clinical decisions in the setting of erroneous alerts. In addition, the significance of alert fatigue is accentuated by the extensive number of hospitals and providers adopting new EHRs with CDS to ensure provision of optimal patient care and meet meaningful-use criteria.[1] With CDS systems varying in the degree of sensitivity, specificity, and informational content for alerts,

institutions have the opportunity to optimize these systems to provide the most benefit to one's hospital or health system.[7]

EVIDENCE/GAP

A pivotal study by Paterno and colleagues demonstrated tiered alerting by severity was associated with higher response rates with drug-drug interaction alerts in the inpatient setting, and lack of tiering was associated with greater override rates of severe alerts.[8] Published optimization strategies have shown to be impactful, but the majority of "stock" medication related CDS mechanisms are ignored.[3,9] Additional literature supports evaluation of interaction severity, probability, clinical implications, patient characteristics, and evidence when identifying clinically important drug-drug interactions.[4] Evidence supports the benefits of medication-related CDS systems in improving practitioner performance, reducing morbidity, and reducing ADE rates.[10,11] However, these benefits cannot be realized without a sustainable process for evaluation of alerts when implementing a new EHR technology with CPOE and basic and advanced CDS capabilities. In addition, strategies to monitor and refine medication alerts is crucial to the success of a newly implemented medication-related CDS system.[7] Recent evidence has described interventions such as prioritizing alerts based on severity, customizing commercially available systems, and learning from previously overridden alerts to prevent future alerting in an effort to reduce alert fatigue.[12] Combinations of these strategies and their impact may be of value to health-systems aiming to implement or refine their CDS systems. The sustainability of a combination of multiple strategies to improve the acknowledgment of electronic alerts in a newly adopted EHR system has not been fully explored.[8,13,14]

PURPOSE STATEMENT

The purpose of this study was to develop a systematic optimization strategy for medication related CDS and measure the impact of targeted interventions to improve patient safety and outcomes.

METHODS

DESIGN AND SETTING

This quasi-experimental study evaluated the impact of a risk-based systematic intervention designed to streamline medication related alerts and warnings. This study was reviewed by both University of Houston and Houston Methodist Hospital institutional review boards and was designated as non-human subjects research. The study was performed at an academic, quaternary care institution located in the Texas Medical Center between June 2016 and January 2018. The institution adopted an electronic medical record system (Epic Systems, Verona, WI) in May 2016 that involved CPOE integrated with medication related CDS and commercial knowledgebase information (Fist Databank, South San Francisco, California) to support the alerting structure. A health-system committee composed of physicians, pharmacists, and bioinformatics specialists was formed in October 2016 to review alert data and categorize alerts based on acuity and ability to guide decision making while minimizing the potential for unanticipated negative outcomes. A risk-based systematic approach consisting of modification to existing knowledge database alerts, intra-order set medication alert suppression, and drug-drug interaction tiering and reclassification was employed to improve appropriate acknowledgement rates while minimizing alert fatigue (Figure 1).

COMMITTEE ESTABLISHMENT

The System Medication-Related Clinical Decision Support Subcommittee (MRCDS) composition included physicians, pharmacists, medication safety officers, bioinformaticists, and other healthcare professionals across the health-system involved in the medication use.

Representatives from each of the 8 entity hospitals within the system were included in the committee membership to facilitate system-level decision making, a majority of which were pharmacists. Other pertinent parties supporting the committee included the Chief Quality Officer, Chief Medical Informatics Officer, EHR Analysts, and the System Medication Safety Officer. The MRCDS committee was responsible for proposing, updating, maintaining, and assessing electronic medication alerts that align with the Houston Methodist System Medication Safety Committee's (SMSC) responsibilities.

Through clinical decision support mechanisms, the committee supports the functions and activities of SMSC in assessing the medication use process, identifying best practices from literature and vulnerabilities identified through adverse drug event review, and developing and implementing decision support solutions to improve the safety and effectiveness of the medication use process. Using decision making algorithms approved by MRCDS, each hospital representative collected provider and pharmacist feedback in order to improve medication related clinical decision support, the committee reviewed alerts appropriate action was taken by a system hospital vote.

These recommendations were presented to the System Medication Safety and Pharmacy and Therapeutics (P&T) committees on an informational basis on a quarterly schedule, however decision making power was within the committee itself and recommendations and decisions were not presented with the intent of gaining approval. The committee decisions involving physician functionality changes were reviewed post-committee decision by a system clinical practice collaborative composed primarily of physician leaders, some of whom served on the MRCDS committee. Upon review and approval, changes would be implemented. The MRCDS committee

met once per month during this study timeframe. A graphical depiction of committee structure is provided in Figure 2. In January 2017 the committee made their first major interventions to suppress drug-drug interactions and duplicate therapy alerts within order sets built in the EHR. Based on this key decision, the post-intervention timeframe was post January 2017. The study timeframe included 29 weeks pre intervention and 52 weeks post interventions.

EHR/CDS SYSTEM

The institution utilized a new EHR system with CPOE and CDS features that was implemented in May 2016 with commercial knowledge base support. During the order entry process and verification process, providers and pharmacists receive unfiltered drug-drug interaction, drug-allergy, dose, drug-inactive ingredient allergy, duplicate therapy, duplicate medication order, pregnancy, lactation, drug-disease interaction, i.v. incompatibility, and total parenteral nutrition (TPN) alerts. Severity levels for drug-drug interactions in the system were categorized as moderate, severe, and contraindicated through the commercial knowledge base system. Initial system settings allowed for both severe and contraindicated level alerts to be seen by providers, and all three categories visible to pharmacists. Drug-disease alerts were only enabled for infectious disease providers based on initial implementation plans. Other system settings for all other alert types were not modified from vendor settings upon initial implementation of the EHR.

DATA COLLECTION AND STATISTICAL ANALYSIS

Data on alert and warning frequency, severity, and response type was analyzed before and after committee interventions to determine the impact of the systematic approach. The primary endpoint was weekly modification and acknowledgement rates of medication alerts after drug-drug interaction reclassification. Secondary endpoints included weekly modification and acknowledgement rates of drug-drug interaction and duplicate therapy alerts, pharmacist and

provider modification and acknowledgment rates in response to drug alerts, and monthly number of alerts per 100 medication orders. Alert acknowledgements were defined as actions that included a discontinuation of a medication order or viewed alerts that did not result in an override at the time of alerting, including alerts that resulted in holding of a medication order by nursing staff. Alert modifications were defined as alert actions that directly led to the discontinuation of an offending medication order from within the medication alert.

Descriptive statistics were used to describe all study measures. After testing for normality using Shapiro-Wilk test, bivariate analysis was performed using the non-parametric Wilcoxon rank-sum test to compare study measures before and after drug-drug interaction reclassification. In addition, interrupted time series regression analysis was employed to assess both primary secondary endpoints over the study time period.[15,16] Autocorrelation was assessed using the Durbin-Watson statistic, positive autocorrelation was evaluated through autoregressive modelling. All statistical analysis were performed using the statistical software package STATA®15, (StataCorp, College Station, TX). A p-value less than 0.05 was considered statistically significant for all endpoints evaluated.

RESULTS

KEY COMMITTEE LED INTERVENTIONS

Key committee led decisions involved the reclassification of 73 (8.3%) of the 875 moderate drug-drug interactions to the severe category and turning off the other 802 alerts. Consequently, providers at the point of entry saw an increase in the number of alerts, but pharmacists saw a decrease at the point of verification. A total of 1,265 drug-drug interaction alerts were active as a result of this change, 446 (35%) and 819 (65%) of which were in the contraindicated and severe categories, respectively. Examples of alerts that were upgraded and suppressed are shown in

Appendix A. Additional committee led interventions included the filtering of specific categories of pregnancy alerts, drug-drug interaction suppression for medications ordered from electronic order sets and order panels, suppression of duplicate therapy alerts that were triggered by medications ordered across different phases of care (e.g. intra-op, post-op, post-anesthesia care) given these medications are only available to be administered in the context ordered and other profiled medications are not available until reconciliation and patient transfer is performed. A timeline of key interventions completed during the study timeframe are provided in Figure 3. The reclassification of drug-drug interactions based on the algorithmic approach served as the point of statistical comparison for the endpoints measured in this study. During the study timeframe, introduction of narrative based pregnancy categories from the former risk categories (A, B, C, D, and X) led to an increase in the quantity of alerts generated given both categories were active and not aligned with previous system settings established upon EHR implementation, the committee's third intervention corrected this setting. Drug allergy checking settings were also reverted to previous system settings and were alerting for inactive excipient ingredients, a correction of this setting was also performed and was not included as a key committee led decision, and statistical splining was used to adjust results for the increase in alert volume.

ALERT RESULTS

After drug-drug interaction reclassification, weekly modification and acknowledgement rates significantly increased ($2.10 \pm 0.18\%$, $p<0.001$; $1.51 \pm 0.24\%$, $p<0.001$, respectively). After adjustment for first degree autocorrelation (Durbin-Watson= 1.39, 1.60), modification and acknowledgement rates increased ($2.06 \pm 0.18\%$, $p<0.001$; $1.49 \pm 0.25\%$, $p<0.001$, respectively) from the pre-intervention baseline. For modification rates, statistical analysis showed a non-

significant changes in during the pre and post-implementation time periods, 0.8 and -0.6%, respectively ($p>0.05$). Additional statistical analyses and trends in variables pre and post-implementation are illustrated in Table 2 and Figure 4. Monthly pharmacist modification and acknowledgement rates increased post-intervention ($1.4 \pm 0.06\%$, $p<0.001$; 1.6 ± 0.76, $p= 0.056$) whereas provider modification and acknowledgement rates remained relatively unchanged (0.03 ± 0.46, $p= 0.944$; 0.56 ± 0.69, $p= 0.433$). Total monthly alerts per 100 medication orders significantly decreased after the reclassification (pre-intervention median: 88.4 vs post-intervention 63.1, $p=0.017$), of this reduction drug-drug interactions decreased by 18.1 ± 2.2 alerts per 100 medication orders.

DISCUSSION

This quasi-experimental study at a single institution revealed that a committee led series of interventions increased alert modification and acknowledgement rates in the inpatient setting. Statistical analysis demonstrated a 2.06% increase in weekly modification rates for all inpatient alerts which translated to approximately 1000 weekly alerts that led to a direct modification of an offending medication order. The decision to reclassify and suppress drug-drug interactions served to be the most impactful intervention in the study timeframe given the reduction of alert burden from this change. Differences in provider and pharmacist acknowledgement and modification rates suggest that pharmacists were the primary driver of intervention as a result of optimized medication alerts.

UNINTENDED CONSEQUENCES AND CHALLENGES

During the study timeframe, there were decisions that were delayed in implementation given the lack of ability to make and/or track changes made to EHR settings. Using a third party commercial knowledge base without the ability to modify setting prior to importation into the EHR served as a limitation in allowing the committee to be more proactive than reactive to changes that were unable to be anticipated. As a result of this, the committee reacted to unanticipated changes resultant to knowledge base updates. Two examples of this included the activation of both old and new FDA pregnancy category alerts in the EHR, and the triggering of inactive excipient ingredient checking in the drug-allergy module. Both examples resulted in committee time and decisions that quite possibly may have been averted if changes were reviewed or anticipated. Challenges in translating committee decisions to EHR interaction setting changes entailed waiting on information technology support to prioritize requests was often a cause for delay in being able to assess effectiveness of changes.

COMPARING AND CONTRASTING WITH EXISTING LITERATURE

The findings of this study are consistent with evidence examining the impact of similar and unique approaches to reducing alert volume to increased responses to important alerts. Minimal impact was seen in overall monthly alert override rates, which is consistent with results published in other studies.[3,9,13] The nature and stagnancy of alert override rates was indicate that this is no longer the best marker of the effectiveness of a medication related decision support system, observing actions that are taken post-override or in lieu of overriding are often equally if not more significant and meaningful.[12,14] Results of this study support the effectiveness of certain interventions that have been reported, notably, customization of commercial decision support systems, prioritizing alerts based on severity, and the routine evaluation and reevaluation of medication alerts.[7,12,17] Our study examined alert actions longitudinally as opposed to smaller timeframes reported by others.[9,13] Unique strengths of this study included the committee led approach to optimizing medication alerts, decision making structure, longitudinal data review, large sample size, and statistical analysis techniques. The length of our study compared to other, for the sustainability of interventions to be assessed as well as seasonal variation in clinical practice (i.e. new medical residents starting July, increased order volume in winter months, etc.). Frequent and regular committee meeting allowed the committee to respond swiftly to unexpected developments in terms of updates to the commercial knowledge database. To the best of the authors' knowledge, this is the first study examining a committee led optimization of medication alerts upon implementation of a new EHR. The decision making structure and committee organization structure was a unique attribute of this study, the ability to streamline decision making was pivotal to implementing key interventions. The endpoints examined in this study also served as a more effective way to monitor responses to alerts post serial interventions to

better understand actions taken in place of overrides alone. This study was undertaken at a large academic medical center, which may limit generalizability to outpatient practice settings and other health systems. A multidisciplinary committee was integral to decision making for optimization strategies, other health systems may have limited resources or lower prioritization of resources to enhance medication related clinical decision support.

Future research endeavors include evaluating alert actions to patient outcomes, systematic optimization of drug-disease interactions, and refining dosage and duplicate therapy medication alerts.

CONCLUSION

Routine committee led evaluation of medication alert data may facilitate opportunities for optimizing alerts.

KEY POINTS *(AJHP)*

- Medication related clinical decision support alerts should be continuously evaluated and optimized
- Overrides are not the only method to review effectiveness of medication alerts
- A committee led approach to optimizing of decision support can lead to a sustainable impact on alert acknowledgment and modification rates

TABLES

Table 1. Descriptive Analysis of Medication Alerts Pre and Post Drug-Drug Reclassification

Variable	**Pre-Intervention (median, Q1, Q3)**	**Post-Intervention (median, Q1, Q3)**	***p*-value**
Weekly All alerts			
Alert Acknowledgement Rate (%)	11.8 (11.4, 12.1)	13.7 (13.3, 14.0)	<0.001
Alert Modification Rate (%)	5.0 (4.9, 5.3)	7.3 (7.0, 7.6)	<0.001
Total Inpatient Alerts (in thousands)	68.9 (66.3, 70.9)	50.3 (48.6, 53.6)	<0.001
Weekly Drug-drug interactions alerts			
DDI Acknowledgement Rate (%)	9.1 (8.6, 9.6)	8.2 (7.8, 8.5)	<0.001
DDI Modification Rate (%)	1.5 (1.5, 1.7)	3.0 (2.7, 3.3)	<0.001
DDI Alerts (in thousands)	30.6 (29.1, 32.0)	13.2 (12.6, 13.9)	<0.001
Weekly Duplicate therapy alerts			
DT Alert Acknowledgement Rate (%)	13.6 (13.0, 13.9)	15.1 (14.7, 15.4)	<0.001
DT Alert Modification Rate (%)	7.4 (7.1, 7.8)	7.6 (7.3, 7.8)	0.246
DT Alerts (in thousands)	13.4 (12.7, 14.1)	14.1 (13.5, 14.5)	0.014
Monthly Actions by Providers and Pharmacists			
Pharmacist Modification Rate	2.1 (2.0, 2.2)	4.3 (3.9, 4.6)	<0.001
Pharmacist Acknowledgement Rate	13.2 (11.6, 14.4)	17.6 (16.7, 18.7)	<0.001
Provider Modification Rate	11.4 (10.9, 12.2)	10.7 (10.4, 11.0)	0.049
Provider Acknowledgement Rate	12.9 (12.2, 13.4)	12.0 (11.7, 12.4)	0.075

Table 2. Interrupted Time Series Regression Analysis for Primary Endpoints

Endpoint	Difference (%) ± S.E.	Slope Pre-implementation, %, (95% CI)	Slope Post-implementation, %, (95% CI)
Weekly Modification Rate	2.06 ± 0.18[c]	0.0080 (-0.0074, 0.0234)	-0.0066 (-0.0239, 0.0106)
Adjusted Weekly Modification Rate[a]	1.98 ± 0.17[c]	0.0087 (-0.0045, 0.0221)	-0.0059 (-0.0207, 0.0087)
Weekly Acknowledgement rate	1.49 ± 0.25[c]	0.0232[b] (0.0023, 0.0441)	-0.0193 (-0.0420, 0.0033)
Adjusted Weekly Acknowledgement Rate[a]	1.45 ± 0.23[c]	0.0236[b] (0.0058, 0.0415)	-0.0179 (-0.0376, 0.0017)

[a]Adjusted for drug-allergy alert activation and pregnancy category reclassification

[b]Difference in slope statistically significant at $p < 0.05$

[c]Difference statistically significant at $p < 0.01$

FIGURES

FIGURE 1. Medication Alert Algorithm

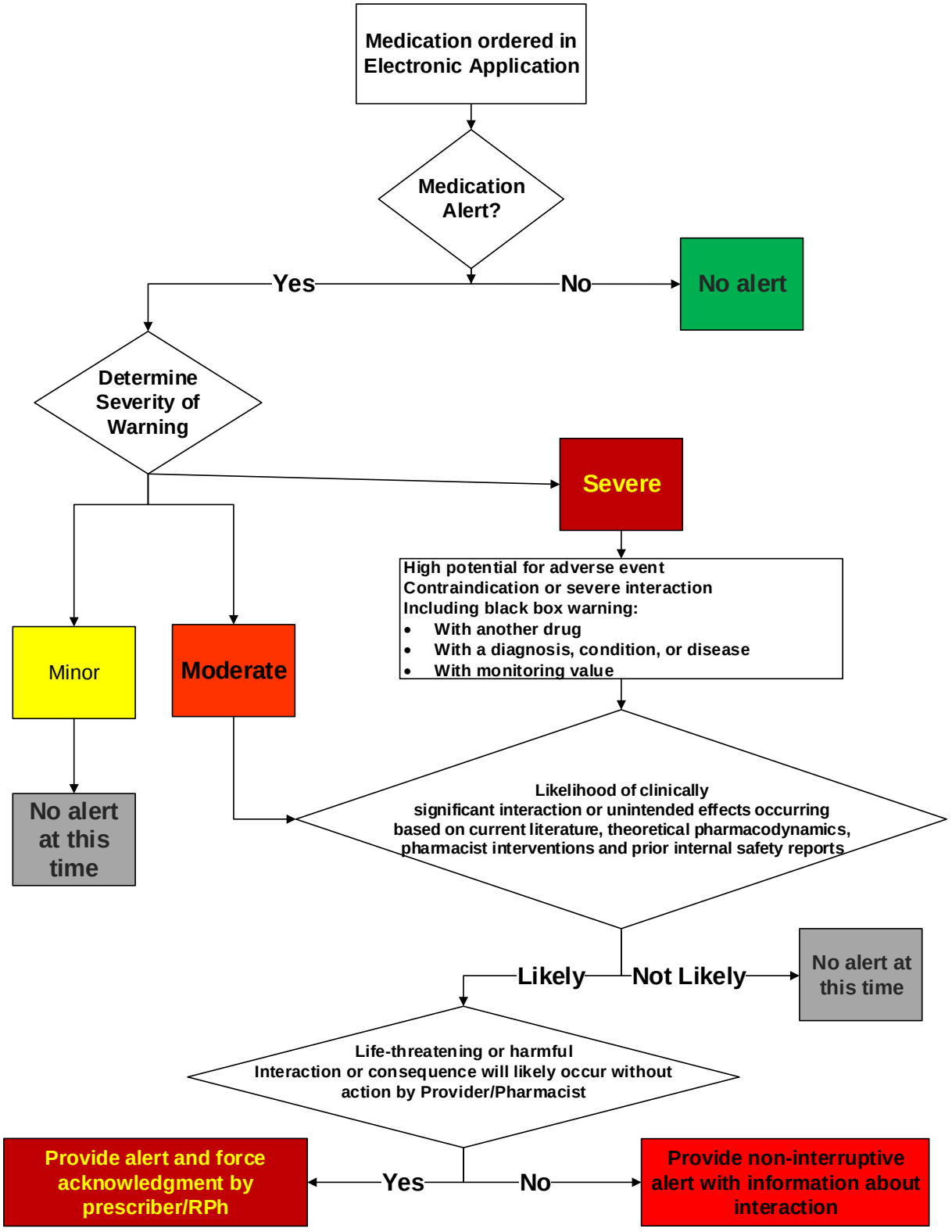


FIGURE 2. Committee Structure

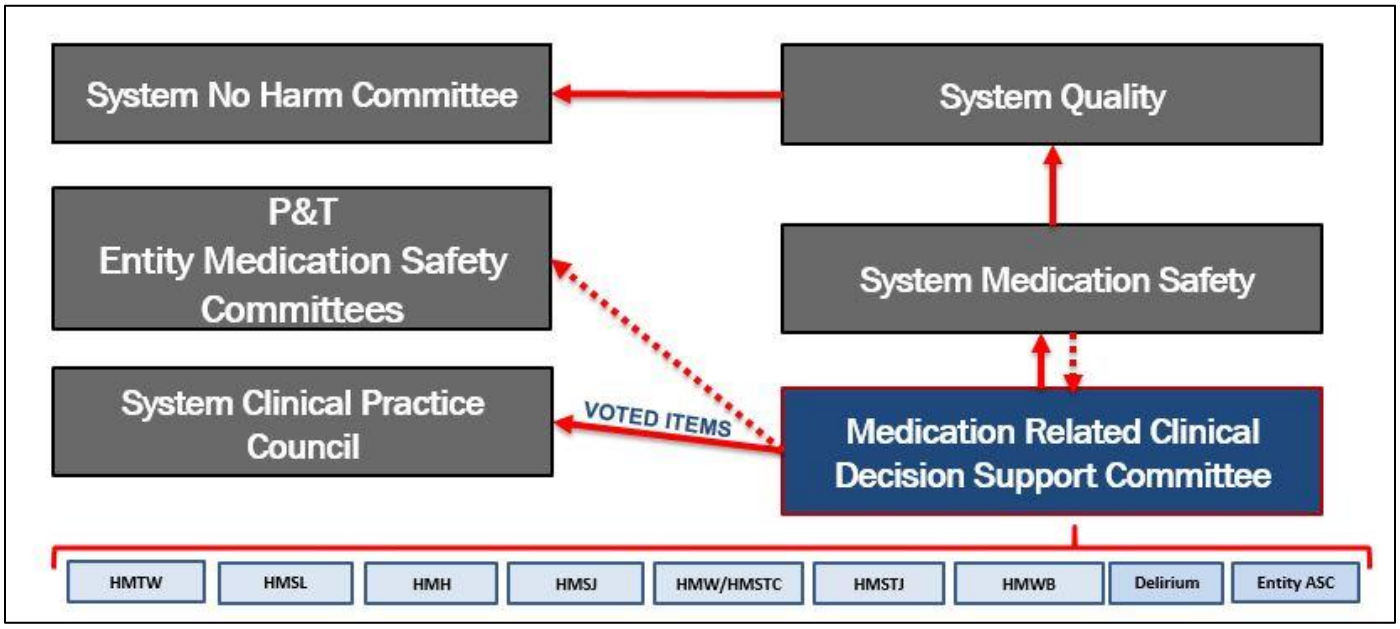


FIGURE 4. Weekly acknowledgement and modification rates

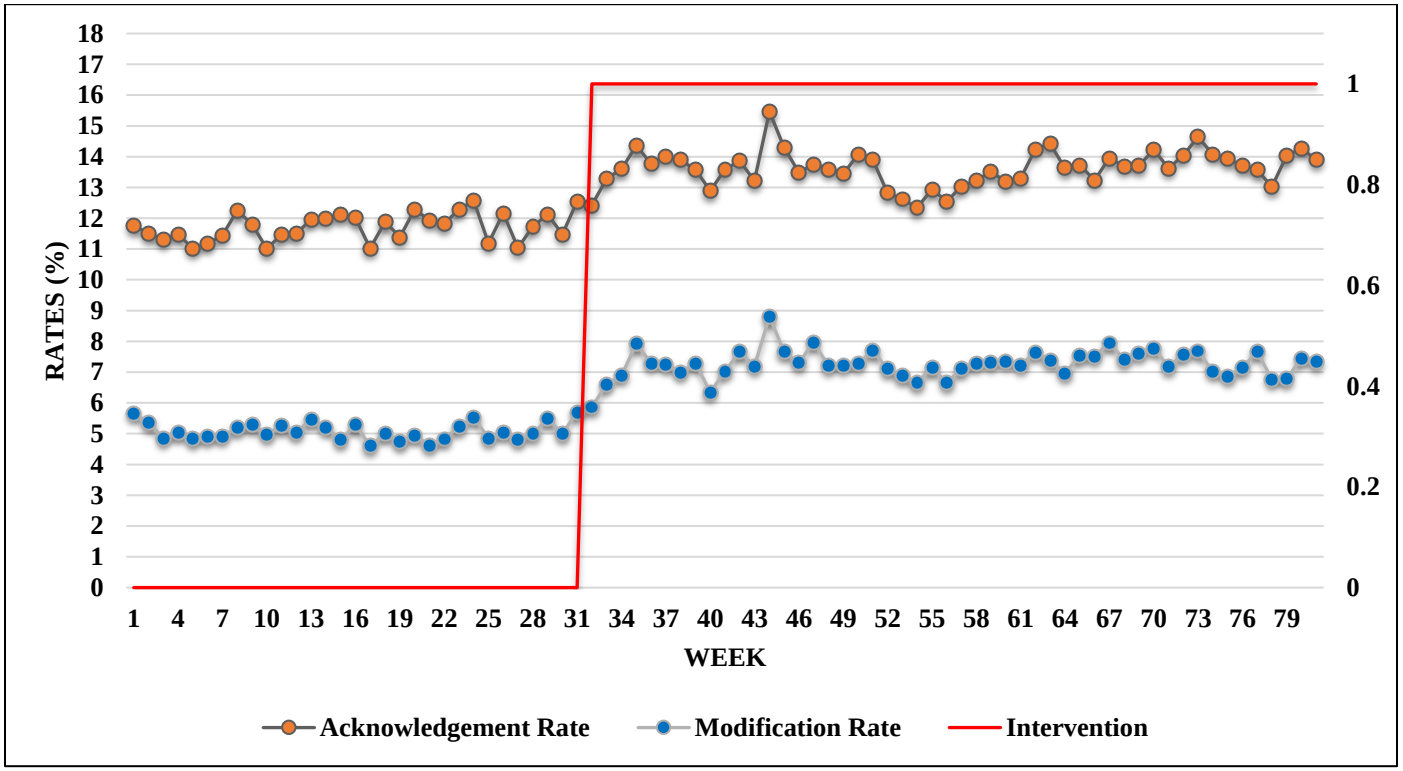


Figure 4. Monthly Actions by Providers and Pharmacists

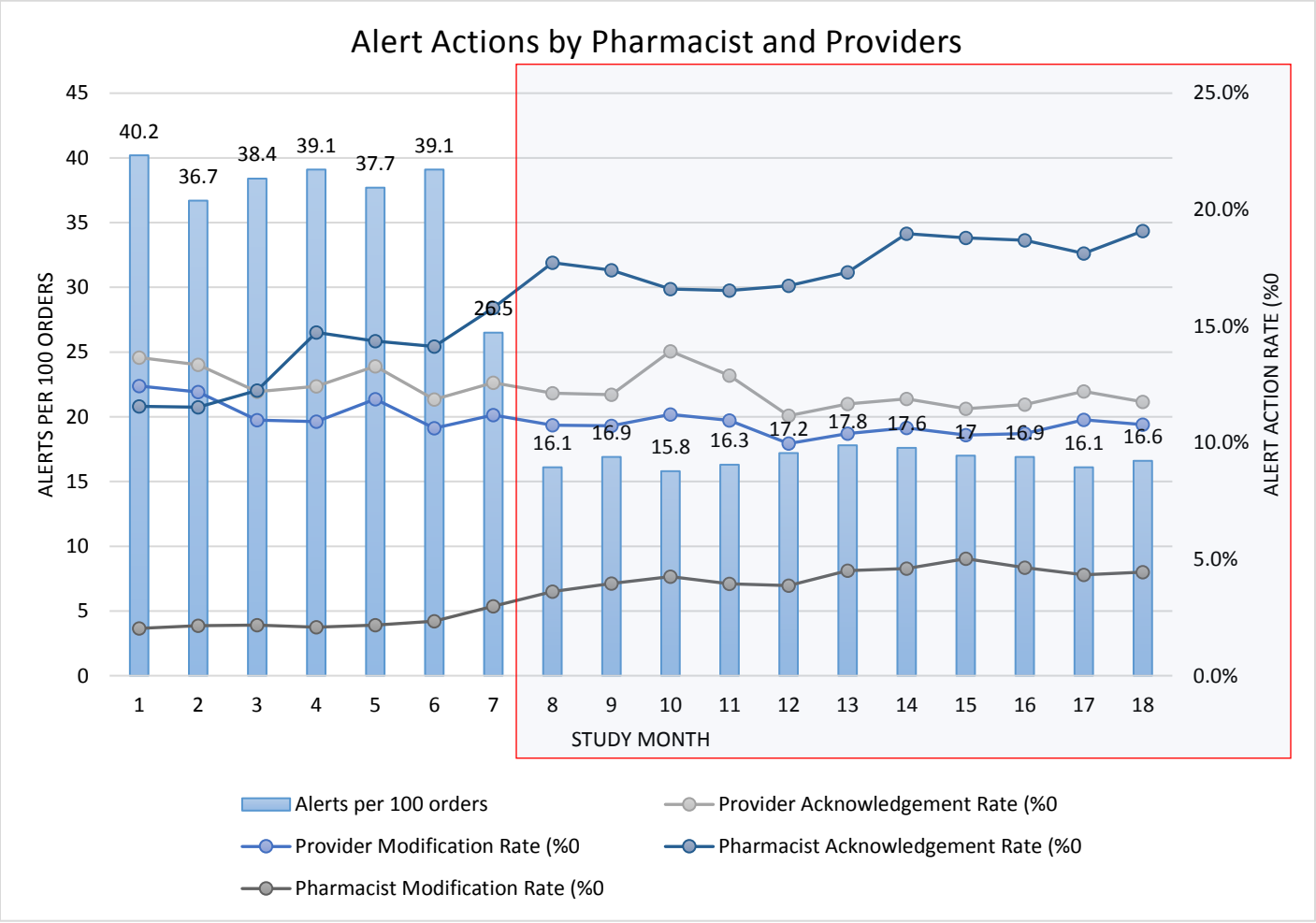
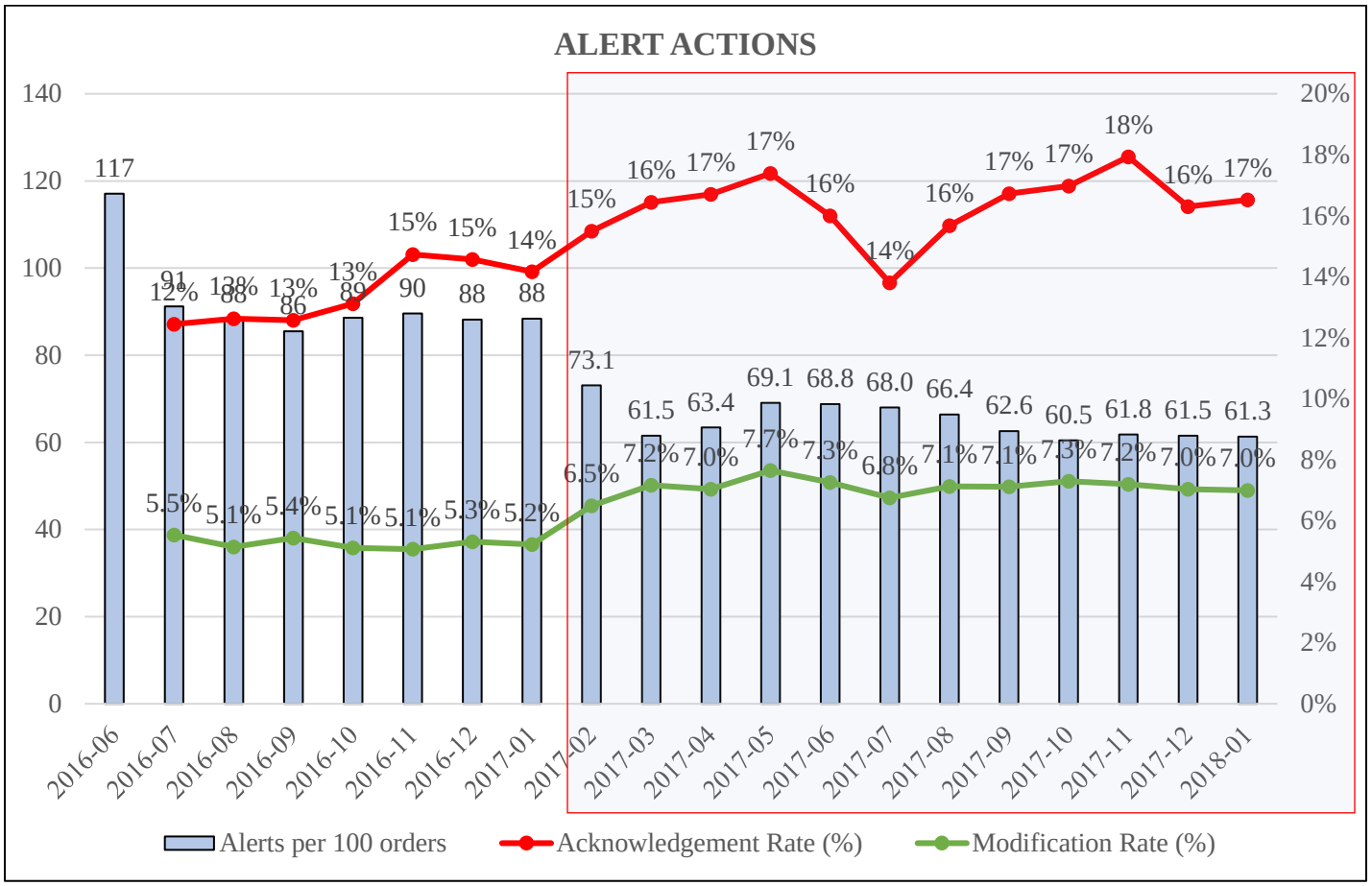


FIGURE 4. Monthly alert actions view



Appendix A

Table 1. Examples of drug-drug interactions reclassified to high severity

Drug-Drug Interaction
HEPARINS / SELECTED ANTICOAGULANTS
TRAZODONE / POSSIBLE QT PROLONGING AGENTS
LEVOFLOXACIN / QT PROLONGING AGENTS
QUETIAPINE / POSSIBLE QT PROLONGING AGENTS
FLUCONAZOLE / POSSIBLE QT PROLONGING AGENTS
OPIOIDS / NALBUPHINE
ATORVA; LOVA (<=40MG); SIMVASTATIN (<=20MG) / AMIODARONE
AZITHROMYCIN / POSSIBLE QT PROLONGING AGENTS
ESCITALOPRAM / QT PROLONGING AGENTS
CIPROFLOXACIN / QT PROLONGING AGENTS

Table 2. Examples of drug-drug interactions suppressed post-reclassification

ANTIDIABETICS / NON-CARDIOSELECTIVE BETA-BLOCKERS
CALCIUM CHANNEL BLOCKERS / CALCIUM SUPPLEMENTS
ACE INHIBITORS; ARBS / LOOP DIURETICS
BETA-BLOCKERS / HYDRALAZINE
NARCOTICS / PHENOTHIAZINES
ANTIDIABETICS / EPINEPHRINE
ANTIDIABETICS / EPINEPHRINE

Table 3. Literature Table

Study	Decision making body	Setting	Outcomes	Results
M.A. Del Beccaro et al.	• Informatics and Patient Safety, and Physician Leader	Tertiary referral center for pediatric care	Alerts can be systematically reduced over time without increasing the reported rate of errors associated with the CPOE process.	• Alerts decreased in all clinical areas without an increase in reported medication errors. • 13.5% to 4.8% order triggering drug-interaction alert • RR 1.63 95% CI (1.60-1.66) p<0.0001 for getting DDI
Parke et al.	• Expert panel was composed of three clinical pharmacists, two informatics pharmacists, and two physicians.	Acute care hospital	Reduce the number of nonactionable drug–drug interaction alerts by recategorization of severity levels.	• No significant difference was detected in the numbers of reported medication errors related to clinically significant drug–drug interaction alerts before and after alert recategorization. • Comparison of drug–drug interaction alerts before (n = 8023) and after (n = 7270) alert recategorization indicated significant differences in pharmacists' documentation of override responses in four evaluated categories ($p < 0.001$ for all comparisons); notably, alerts overrides in the "not clinically significant" category declined 22%.
Paterno et al.	• Group of physicians and pharmacists that represents the two institutions, which meets to consider and review the intervention knowledge base on an on-going basis.	Two teaching hospitals	Rate of compliance to alerts at a tiered site compared to a non-tiered site.	• Compliance with DDI alerts was significantly higher at the site with tiered DDI alerts compared to the non-tiered site (29% vs. 10%, $p <0.001$). At the tiered site, 100% of the most severe alerts were accepted, vs. only 34% at the non-tiered site; moderately severe alerts were also more likely to be accepted at the tiered site (29% vs. 10%).
Bryant et al.	• A panel of physicians, pharmacists, and information technology staff	Two teaching hospitals	Current rates in our hospitals would be significantly lower than historical rates from other studies due to our	• The drug-drug alert override rate was 95.1%, statistically higher than the rate for drug-allergy alerts (90.9%) ($p < 0.001$). There was no

			ongoing quality improvement processes. Further, we hypothesized that physicians who saw higher quantities of alerts would have higher override rates, as predicted by the theory of alert fatigue.	significant difference in override rates between attendings and residents, or between hospitals. (3) ● Physicians saw a mean of 1.3 alerts per day, and the number of alerts per physician was not significantly correlated with override rate ($R2 = 0.03$, $p = 0.41$).

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