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Decision support at the point of prescribing to increase formulary adherence

PIETER J. HELMONS, CARRIE R. COATES, JOS G. W. KOSTERINK, AND CHARLES E. DANIELS

Purpose. Study results demonstrating the effectiveness of order-entry clinical decision support (CDS) alerts as a tool for enforcing therapeutic interchange are presented.

Methods. A retrospective observational study was conducted at an academic medical center to evaluate formulary nonadherence before and after implementation of a fully electronic medical record with computerized prescriber order-entry (CPOE) technology configured to display therapeutic interchange alerts immediately on entry of orders for nonformulary agents. Formulary nonadherence (defined as the proportion of pharmacist-verified nonformulary orders to total verified orders) within eight medication classes was assessed during a six-month baseline period and two consecutive six-month periods after implementation.

Results. In the 12 months after implementation of the therapeutic interchange alerts, the overall rate of formulary nonadherence decreased by 65%, from 3.5% at baseline to 1.2% during the second 6-month postintervention period ($p < 0.001$). The total number of verified nonformulary orders decreased from 300 at baseline to 102 during the second postintervention period. The largest decreases in formulary nonadherence were observed in the intranasal steroid drug class (the rate of nonadherent orders declined by a total of 12 percentage points) and the nonbarbiturate sedatives and hypnotics class (a 5-point decline), with significant 6- and 12-month declines also documented in four of the remaining six drug classes.

Conclusion. The incorporation of hard-stop CDS alerts into the CPOE system improved the overall rate of prescriber adherence to institutional therapeutic interchange protocols.

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Drug formularies are maintained by many hospitals worldwide and are viewed as an important tool to guide prescribers in choosing the safest, most cost-effective agents for treating medical problems.[1] It is generally accepted that having fewer drugs on formulary leads to increased efficiency and improved medication safety.[2] In addition, each therapy initiation with a nonformulary drug is a deviation from normal workflow, with potential medication safety and efficiency implications.[3,4] Consequently, the University of California San Diego Health System (UCSDHS) has implemented a comprehensive formulary management system consisting of monitoring of nonformulary medication use and review of formulary medication use annually. Using dashboards, systematic trends in nonformulary prescribing are detected early and reported to the pharmacy and therapeutics (P&T) committee semiannually. Additional details of this system were described elsewhere.[3]

Therapeutic interchange is widely used to limit the number of drugs on formulary and is defined as the dispensing of a drug that is therapeutically equivalent but chemically different from the drug originally prescribed.[5] In many hospitals, including UCSDHS, therapeutic interchange protocols allow a pharmacist to automatically substitute the pre-

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ferred agent without having to contact the prescriber; this is the least labor-intensive method for pharmacists to manage nonformulary drug requests.[3,6] Therefore, the prescribing of nonformulary medications for which P&T committee–approved therapeutic interchange protocols exist should be particularly discouraged.

The application of clinical decision support (CDS) within computerized prescriber order-entry (CPOE) systems can improve formulary adherence.[7,8]

A CDS system is defined as "any electronic system designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient specific assessments or recommendations that are then presented to clinicians for consideration."[9] CDS can guide physicians to the appropriate alternative when a therapeutically interchangeable medication is prescribed. Successful guidance is dependent on two factors: providing clearly written "to-the-point" guidelines, with links to additional information; and offering a noncontroversial prescribing alternative within the alert window.[10-15] A recent review investigating the features of effective CDS systems concluded that systems requiring the practitioner to give a reason for an alert override were more likely to succeed than those lacking that feature.[16] Factors associated with poor adherence to CDS guidance include the lack of an offered prescribing alternative and strong provider beliefs about a medication, even if those beliefs are not necessarily supported by the available evidence.[8]

In February 2011, UCSDHS implemented an enterprisewide electronic medical record (EMR) that includes a CPOE system with CDS functionality (Epic, version 2010, IU4; Epic Systems Corporation, Verona, WI). One of the features is a pop-up window listing the recommended alternative agent and equivalent dosing information when a therapeutically interchanged drug is ordered. The study described here evaluated formulary adherence for eight therapeutic classes before and after the implementation of decision support at the point of prescribing to facilitate therapeutic interchange.

Methods

Setting. The research involved a retrospective before–after observational study conducted at UCSDHS, a 511-bed academic medical center consisting of two locations. UCSDHS has achieved the highest stage of EMR adoption, which includes an enterprisewide EMR, CPOE, and barcode-assisted medication administration.[17] The medical center includes a level 1 trauma center, a level 3 neonatal intensive care unit, and most medical specialties other than pediatrics. All inpatient areas of the medical center were included in this study except for the emergency department, as the EMR had not been implemented in that department at the time of the study.

Intervention. Nonformulary medications in the following therapeutically interchanged drug classes accounted for 30% of nonformulary medication initiations during the preintervention period and were included in the study: intranasal steroids, nonbarbiturate sedatives and hypnotics, proton pump inhibitors (PPIs), histamine H_2-receptor antagonists, respiratory inhalant combinations, sympathomimetic bronchodilators, systemic fluoroquinolones, and peripherally acting antiadrenergic agents. Information on nonformulary agents in these drug classes, as well as formulary alternatives and baseline formulary adherence, is presented in Table 1. For all nonformulary medications in each class, a therapeutic interchange alert directing the prescriber to the appropriate formulary item and corresponding dose was built (Figure 1). The alert was obtrusive (a pop-up window at the time of ordering) and configured as a hard stop; if a prescriber specifically wished to proceed with the original order, a phone call to the pharmacist to provide justification was required. If such a request was approved, the pharmacist entered the nonformulary order and documented the reason for approval.

Data analysis. Prescribing data from July–December 2010 constituted the preintervention data. The EMR was implemented in February 2011. To assess the initial and long-term effects of the therapeutic interchange alerts, postintervention data were collected during two six-month periods: March–August 2011 (immediately after the intervention was implemented) and September 2011–February 2012. Nonadherence was expressed in relation to the prescribing of other agents in the same drug class. For example, nonadherence to PPI therapeutic interchange protocols was calculated by dividing the number of pharmacist-verified nonformulary PPI orders by the total number of pharmacist-verified PPI orders.

Formulary nonadherence during each six-month period was compared with nonadherence during the preintervention period. Data were entered into spreadsheets (Excel 2010, Microsoft Corporation, Redmond, WA) for initial analysis and summary statistics. NCSS 2007, version 07.1.20 (NCSS Statistical Software, Kaysville, UT) was used for statistical tests. Chi-square analysis was used to compare formulary nonadherence before and after the intervention. The a priori level of significance was 0.05.

Results

Data on the therapeutically interchanged drugs are listed in Table 1 in order of highest to lowest baseline nonadherence, which varied from 13.3% for the intranasal steroid class to only 0.6% for the H_2-antagonist class. Formulary nonadherence and

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number of nonformulary initiations before and after implementation of therapeutic interchange alerts are shown in Figure 2. For seven of the eight evaluated drug classes, formulary nonadherence decreased during the first postintervention period, and the effect persisted during the second postintervention period; for the remaining class (the peripherally acting antiadrenergics), nonadherence increased during the first postintervention period (24 of 408 orders [5.9%] were nonadherent) and decreased sharply during the second postintervention period (7 of 476 orders [1.5%] were nonadherent). Upon investigation of this outlier trend, we found that no therapeutic interchange alert for peripherally acting antiadrenergics had been in force during the first postintervention period. During the second postintervention period, the alert was in place, and a decrease in formulary nonadherence of 3% was observed in this drug class ($p = 0.018$).

The largest decrease from baseline in formulary nonadherence was in the intranasal steroid drug class (declines of 11 and 12 percentage points in the first and second postintervention periods, respectively), with the next largest decrease observed in the nonbarbiturate sedatives and hypnotics class (a decline of 5 percentage points that persisted during both periods). PPIs remained the most frequently ordered therapeutically interchanged nonformulary medications during both time periods (26 and 41 orders during the first and second postintervention periods, respectively). Overall, formulary nonadherence in the eight therapeutically interchanged drug classes decreased by 65%, from a mean of 3.5% at baseline to means of 1.3% and 1.2% during the first and second postintervention periods, respectively ($p < 0.001$). Total nonformulary orders decreased from 300 at baseline to 96 in the first postintervention period and 102 in the second postintervention period.

Table 1.
Medications Targeted for Therapeutic Interchange Enforcement at UCSDHS[a]

Drug Class (Route)	Interchanged Nonformulary Medications	Formulary Alternative	Baseline Formulary Nonadherence[b]
Intranasal steroids (nasal inhalation)	Beclomethasone Budesonide Flunisolide Furoate Mometasone Triamcinolone	Fluticasone	41/308 (13.3)
Nonbarbiturate sedatives and hypnotics (oral)	Eszopiclone Zolpidem CR	Zolpidem	81/1225 (6.6)
Antiadrenergic agents, peripherally acting (oral)	Alfuzosin	Tamsulosin	17/423 (4.0)
Proton pump inhibitors (oral)	Dexlansoprazole Esomeprazole Omeprazole Pantoprazole Rabeprazole	Lansoprazole	92/2499 (3.7)
Fluoroquinolones, systemic (oral)	Levofloxacin	Moxifloxacin	16/441 (3.6)
Sympathomimetic bronchodilators (inhalation)	Levalbuterol	Albuterol	27/988 (2.7)
Respiratory inhalant combinations (inhalation)	Budesonide–formoterol	Fluticasone–salmeterol	12/458 (2.6)
Histamine H_2-receptor antagonists (oral)	Cimetidine Nizatidine Ranitidine	Famotidine	14/2472 (0.6)

[a]UCSDHS = University of California San Diego Health System.
[b]Fraction (%) of total verified orders in class that were nonadherent during preintervention period.

Discussion

Formulary nonadherence decreased in most drug classes after implementation of formulary decision support at the point of prescribing. The only exceptions were the histamine H_2-receptor antagonist and fluoroquinolone drug classes, where we found no significant change in formulary nonadherence. The effect was most pronounced for the intranasal steroid and nonbarbiturate sedative drug classes, where baseline nonadherence rates were relatively high (13.3% and 6.6%, respectively); this was likely because those classes represented the areas of greatest opportunity for improvement. Overall, baseline nonadherence to therapeutic interchange alerts was very low at UCSDHS. It is likely that the continuous focus on nonformulary prescribing at the institution increased pharmacist awareness of therapeutic interchange protocols. However, a reactive approach through which a pharmacist corrects an order for a therapeutically interchanged medication is less efficient than the prescriber entering a cor-

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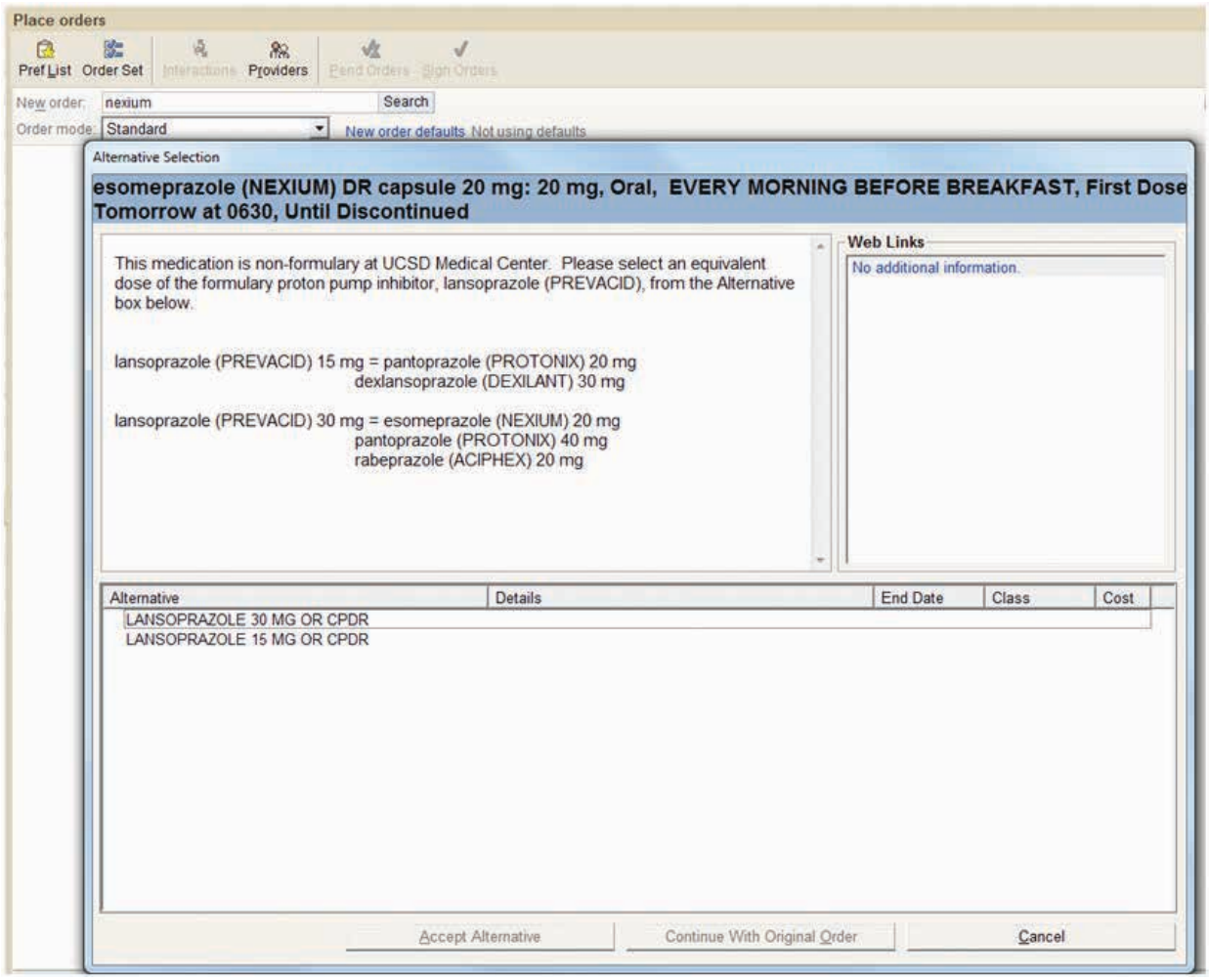
rect order initially. In addition, if a pharmacist fails to correct an order for a therapeutically interchanged medication, the reactive approach could have medication safety implications: therapeutically interchanged medications are typically not available on the patient floor, which could result in a delay of therapy. These risks are prevented by facilitating the selection of the appropriate alternative by the physician at the time of prescribing.

The study had several limitations. First, it was an observational study in which the effect on prescribing practices of implementing an enterprise-wide EMR that included formulary decision support was followed over time. The observed effect could be the result of factors not directly related to the therapeutic interchange alert intervention. One such factor could be the increased focus on prescribing workflow as a result of EMR training sessions for pharmacists and prescribers; however, this is unlikely, as we unintentionally included a negative control in our study (the therapeutic interchange alert for the antiadrenergic class was not implemented until the second intervention period). This drug class was the only drug class where initially an increase in formulary nonadherence was observed and nonadherence subsequently decreased after the alert was implemented. Changes in prescribing behavior as a result of new guidelines or safety warnings could also be a factor. This could explain the modest

Figure 1. Screenshot of a therapeutic interchange alert triggered by an order for the proton pump inhibitor esomeprazole. The alert pop-up window displays equivalent dosing for each member of the drug class. After selecting the appropriate alternative, the prescriber can proceed with the alternative order with one click. When therapeutic interchange protocols exist, the button "Continue With Original Order" is not available for selection by prescribers but can be selected by pharmacists.



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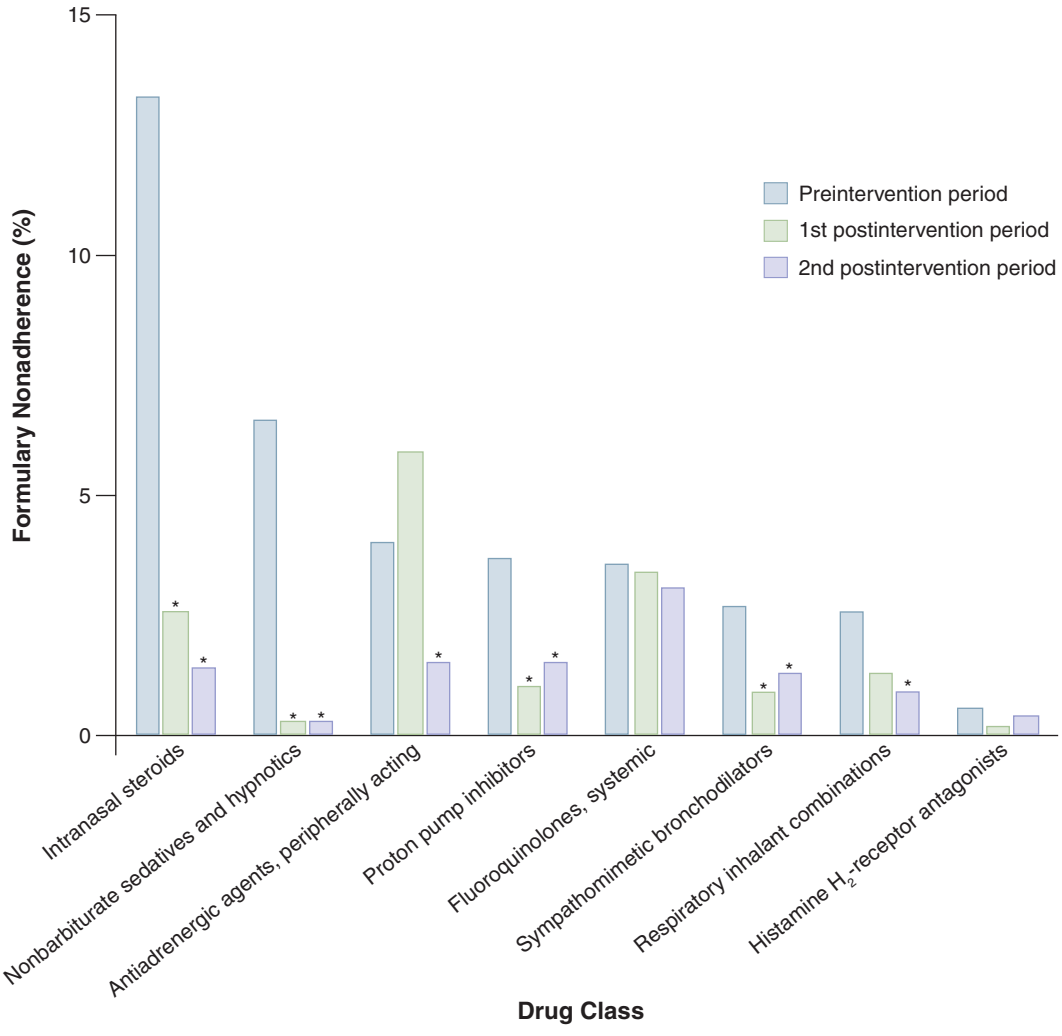
increase in nonadherence observed in the PPI drug class (from 1% to 1.5%) during the second postintervention period, as reports of a possible drug–drug interaction involving the formulary agent lansoprazole and clopidogrel were published around that time; however, this is unlikely, as pharmacists entered "drug interaction with formulary alternative" only once as the reason for allowing nonformulary PPI use.

Second, we did not measure clinical outcomes such as adverse events or medication errors as a result of therapeutic interchange, which could be viewed as a limitation. These consequences should be the subject of further research. However, we focused in this study on improving adherence to therapeutic interchange protocols, as this is common practice in hospitals nationally and internationally.[5]

Our results are in line with those of other studies of inpatient formulary decision support implementations. Teich et al.[8] demonstrated an impressive increase from 12% to 95% in the prescribing of the preferred H_2-receptor antagonist over an eight-week period, an effect that persisted at one- and two-year follow-up assessments. However, most studies reporting the effect of CDS on outcomes are done with locally developed ("homegrown") systems implemented and expanded over many years.[7,8] This is considered a major barrier to CDS system implementation.[18,19] To our knowledge, this is the first study reporting the

Figure 2. Formulary nonadherence before and after implementation of therapeutic interchange decision support. An asterisk indicates a significant change ($p < 0.05$) from the preintervention period.



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effect of formulary decision support included in a commercially available EMR that has been widely adopted by many hospitals in the United States and abroad. Our approach can be used by other institutions using EMRs with the same or similar decision support functionality to improve and monitor formulary nonadherence without the need to develop or purchase additional decision support tools.

Conclusion

The incorporation of hard-stop CDS alerts into the CPOE system improved the overall rate of prescriber adherence to institutional therapeutic interchange protocols.

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