The Vulnerabilities of Computerized Physician Order Entry Systems:

A Qualitative Study

Sarah P. Slight MPharm PhD PGDip\textsuperscript{1,2}, Tewodros Eguale MD PhD\textsuperscript{2,3}, Mary G. Amato PharmD MPH\textsuperscript{2,3}, Andrew C. Seger PharmD\textsuperscript{3}, Diana L. Whitney BS\textsuperscript{4}, David W. Bates MD MSc\textsuperscript{2,5,6}, Gordon D. Schiff MD\textsuperscript{2,5}.

Author affiliations:

\textsuperscript{1} Division of Pharmacy, School of Medicine, Pharmacy and Health, Durham University, Durham, UK;

\textsuperscript{2} The Center for Patient Safety Research and Practice, Division of General Internal Medicine, Brigham and Women’s Hospital, Boston, MA, USA;

\textsuperscript{3} MCPHS University, Boston, MA, USA;

\textsuperscript{4} Baylor College of Medicine, Houston, TX, USA;

\textsuperscript{5} Harvard Medical School, 250 Longwood Ave, Boston, MA, USA;

\textsuperscript{6} Harvard School of Public Health, 677 Huntington Avenue, Boston, MA, USA.

Correspondence to:

Dr. Gordon Schiff

The Center for Patient Safety Research and Practice,

Division of General Internal Medicine,
Brigham and Women’s Hospital,

Boston, MA, USA

Tel: +1 617 732 4814

Fax: +1 617 732 7072

E-mail: gschiff@partners.org

**Word Count:** 4,537 words

**Keywords:** clinical decision support, patient safety, electronic prescribing, workarounds, alerts, medication errors.
Objective: To test the vulnerabilities of a wide range of CPOE systems to different types of medication errors, and develop a more comprehensive qualitative understanding of how their design could be improved.

Materials and Methods: We reviewed a random sample of 63,040 medication error reports from the U.S. Pharmacopeia MEDMARX reporting system where CPOE systems were considered a “contributing factor” to errors and flagged test scenarios that could be tested in current CPOE systems. Testers entered these orders in 13 commercial and homegrown CPOE systems across 16 different sites in the U.S. and Canada, using both usual practice and where-needed workarounds. Overarching themes relevant to interface design and usability/workflow issues were identified.

Results: CPOE systems often failed to detect and prevent important medication errors. Generation of electronic alert warnings varied widely between systems, and depended on a number of factors, including how the order information was entered. Alerts were often confusing, with unrelated warnings appearing on the same screen as those more relevant to the current erroneous entry. Dangerous drug-drug interaction warnings were displayed only after the order was placed rather than at the time of ordering. Testers illustrated various workarounds that allowed them to enter these erroneous orders.

Discussion and Conclusion: We found high variability in ordering approaches between different CPOE systems, with major deficiencies identified in some systems. It is important that developers reflect on these findings and build in safeguards to ensure safer prescribing for patients.
BACKGROUND AND SIGNIFICANCE

Medication errors are extremely common. According to the Institute of Medicine (IOM), a hospitalized patient experiences on average at least one medication error per day in the United States.\(^1\) It is widely acknowledged that computerized physician order entry (CPOE) systems can help prevent medication errors in both inpatient and outpatient settings.\(^2, 3\) CPOE systems with clinical decision support (CDS) can provide dosing suggestions, eliminate illegible orders, assist with calculations, check for allergies and monitor for drug-drug interactions.\(^4-7\) Recognizing these well-established benefits, the federal government attempted to accelerate their adoption by offering financial incentives to those U.S. hospitals demonstrating meaningful use of electronic health records, including CPOE systems.\(^8\) Many studies have concentrated on the effectiveness of internally developed systems from academic centers of excellence,\(^9\) but far fewer have evaluated commercially-purchased systems in community hospitals even though these vendor-developed applications represent the vast majority of systems today.\(^10\)

Concerns about harm from the use of CPOE systems have also emerged. One study conducted in a U.S. teaching hospital showed how the use of a system could promote medication error risks in addition to reducing them.\(^11\) Examples included fragmented computer screen displays that prevented a coherent view of patients’ medications, failure to differentiate between look-alike drug names, and inflexible ordering formats generating wrong medication orders. Horsky et al.\(^12\) revealed how a serious dosing error of potassium chloride resulted from failures in human-computer interaction, such as confusion about on-screen laboratory results review, uncertainty on the part of physicians about how to manage unusual ordering scenarios, and the absence of automated safeguards that help prevent
errors. A multi-national study by Ash and colleagues also found instances where technology seemed to foster rather than reduce the likelihood of errors.(6) Another study showed CPOE systems delivered an overdose of alerts or warning messages to physicians, many of which were felt to be irrelevant or inappropriate.(13) Physicians often disregarded these messages, and run the risk of overlooking clinically important alerts as well as those that were considered unimportant.

CPOE systems are constantly evolving, but their safety is dependent not only on how they are designed, but also on how they are implemented and used in clinical practice, and individual institutions have considerable latitude. One study found that about half of event fatal medication errors did not result in a warning, and there was almost no correlation with vendor.(14) The IOM Committee report Health IT and Patient Safety: Building Safer Systems for Better Care discussed various safety issues associated with health IT and recommended that specific examples of potentially unsafe processes and risk-enhancing interfaces be shared amongst the health IT community.(15) This committee also called for a more streamlined approach to the reporting of health IT-related adverse events, and for both vendors and users to rectify systemic issues.

We performed detailed testing of the vulnerabilities of a wide range of leading vendor and homegrown, inpatient and outpatient CPOE systems to different types of medication errors.(16) Here, we present the qualitative findings from this large, mixed methods study conducted over two years in a broad range of healthcare settings to provide a more comprehensive understanding of human factors design issues and how these could be improved.

MATERIAL AND METHODS
As part of a National Patient Safety Foundation-funded project, we approached a range of diverse organizations (e.g., academic medical centers, private medical practices) using different commercial and homegrown CPOE systems across the United States and Canada. Test participants (mostly medical residents or primary care attending physicians, henceforth referred to as “testers”) were identified at each of the 16 sites and asked if they would be willing to participate. Each tester was offered a small remuneration ($100 gift card) for their time.

Test case scenarios

The design of test case scenarios has been discussed at length in our previous publication(16) but, in short, we downloaded all 63,040 medication error reports where CPOE systems were considered a “contributing factor” to errors from the United States Pharmacopeia (USP) MEDMARX reporting system between January 2003 to April 2010. A team of pharmacists (MGA, JJB, ACS, MS) and a general internist (GDS) manually reviewed a sample of these reports (16.0%, n= 10,060), which included all 191 reports, categorized as E-I (an error that resulted in patient harm) according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification. A random sample of the remaining A–E category reports (no patient harm caused) were also included. Of note, 98.18% of the errors occurred in Categories A to D. Category B (an error occurred but did not reach the patient) contained the largest number of errors (64.1%), followed by Category A (an event occurred that had the capacity to cause error) 18.9% and Category C (an error occurred that reached the patient but did not cause harm) with 13.9% of errors.
We identified a total of 338 error reports as potential candidates for test scenarios and narrowed these down by combining similar scenario types (i.e., orders for drug to which patient was allergic) and prioritised based on preselected criteria of (a) frequency, (b) seriousness and (c) testability. We then attempted to determine the extent to which current CPOE systems were vulnerable to similar errors. These test scenarios described 13 categories of erroneous or problematic orders arising from realistic clinical encounters including: wrong drug, amount, dose, route, units or frequency errors; omission errors; duplicate drug or therapy; adjacency errors; drug allergies; drug-drug interactions; and drug-disease contraindications (see Appendix 1).

**Conducting the tests**

After obtaining the necessary ethical and institutional approvals, testers were instructed to enter these problematic orders on test patients; these were based on CPOE-related errors reported to a leading medication error reporting system. For example, testers were instructed to enter Synthroid® (levothyroxine) 100 mg PO daily (instead of 100 mcg PO daily), which represented a 1000-fold overdose (Test Case 9). They were encouraged to enter these orders in the usual and customary way, and where necessary perform workarounds that they might typically use to enter such orders. A research assistant (DLW) accompanied by either a research pharmacist (MGA, ACS) or general internist (GDS) independently observed the testers while they attempted to enter these erroneous orders at U.S. sites. Similarly, at the Canadian sites an academic physician (TE) observed the testers enter these orders. For each test scenario, the observer rated the ease or difficulty using a specially designed data collection sheet and operational definitions (see Appendix 2 and 3,
respectively). Testers were also asked to reflect on the overall process, sharing their knowledge and experience of using their CPOE system. All test sessions were conducted between August 2011 and March 2012.

Data Analysis

An excel file was created and detailed descriptions of testers’ observations and verbalizations were recorded. These were then transferred to a Research Electronic Data Capture (REDCap) tool. Three independent researchers (SPS, TE, MGA) read through these descriptions and annotated them for possible categories. Comparisons were then made between testers using the same or different CPOE systems in similar or diverse settings (e.g., inpatient or outpatient) at the same or different sites. These annotated transcripts were then reviewed as a group and any discrepancies in the coding categories resolved by discussion. Overarching themes relevant to interface design, usability and workflow issues were identified.

RESULTS

We examined 13 unique CPOE systems across 16 different sites in the U.S. (n=11; Sites 1 to 11) and Canada (n=5; Sites 12 to 16). Two different testers entered the orders at each site, apart from Sites 8, 9 and 11 (see Table 1), and we tested two versions of the same system (inpatient and outpatient) at two specific sites (i.e., Site 6 and 7). Table 1 also includes observers’ rating scores relating to the ease or difficulty in placing the order; no particular
setting (in patient vs. outpatient) or type of system (commercial vs. in-house) appeared substantially better than any other.

**Generation of alert warnings**

We found instances where the same vendor CPOE system responded differently at two different sites for Test Case 1 (allergy-drug checking), with one displaying no warning messages (e.g., Site 8) and the other providing warning messages that required the tester to give a coded reason to override the alert (e.g., Site 2). These different responses may relate to how the information was entered in the system. For example, when the tester entered ‘allergy to lisinopril’ in an unstructured format (free-text), no allergy warning appeared after selecting ‘captopril 12.5mg tabs’ from the medication list. However, when the tester added the allergy in a structured format (by selecting lisinopril from a medication list), a red warning appeared stating: “captopril 12.5 mg tabs note prior adverse reaction with lisinopril”.

A similar situation arose for Test Case 12 (wrong dose frequency), with no warning messages displayed when the tester entered the dose frequency “QID” (four times each day) in free text for Cardizem® CD (diltiazem extended release) 120mg at one site (e.g., Site 2). However, when the order was placed by changing the dose frequency from “daily” to “QID” (structured format) in the same system at another site (e.g., Site 8), a warning message was displayed stating: “This product is usually given ONCE DAILY” although it could easily be overridden with a single keystroke.

In Test Case 4 (duplicate drug checking), a duplicate drug warning was generated in one system (e.g., Site 1) when the tester entered an order for Lovenox® (enoxaparin sodium injection) 40mg subcutaneous daily followed by a second order for Lovenox® 100mg subcutaneous twice a day. However, no duplicate alert warnings were displayed if the tester
drafted both medication orders in succession in electronic scratchpad before signing. (18) Scratch pad (buffer) can hold orders and not deliver them to ancillary departments (e.g., pharmacy) for actioning unless required. (18) Testers appeared to be unaware that the duplicate drug checking had been switched off in scratchpad, a decision which the IS Director explained helped to reduce the ‘noise’ in the system. For Test Case 3 (drug-disease checking), the tester understood that the “system has the capability but [it has] not [been] programmed locally to date” (e.g., Site 1). No alert warnings were displayed at most of the other sites after entering “congestive heart failure” (CHF) on the patient problem list and ordering pioglitazone (a situation where it is contraindicated). Several testers commented on how they had “never actually seen any alerts for drug-disease interactions previously in their system” (e.g., Site 6 and Site 10). For Test Case 2, the tester reported how no drug-drug interaction checking was in operation at Site 10 for “non-formulary” drugs.

No look-alike sound-alike (LASA) warnings were displayed at any of the sites when “penicillamine” was ordered instead of “penicillin” in Test Case 10 (adjacency error). Yet at one site (e.g., Site 5), LASA warnings were being generated for other drugs including glyburide: “GlyBURIDE LASA Intervention- GlyBURIDE is an oral blood-glucose-lowering drug which belongs to sulfonyl-urea class. It should not be confused with GlipiZIDE, a different oral blood-glucose-lowering drug which belongs to the sulfonyl-urea class.” Also, no duplicate therapy alerts were displayed when metformin and Glucovance® (glyburide and metformin combination) were ordered in sequence in Test Case 6 (duplicate therapy checking) at Site 6 or 11. According to the respective testers at these sites, “all duplicate order checking is in name only, i.e. there is no ingredient checking” for combination drugs (e.g., Site 11) and “order set capability is geared toward ordering multiple tabs in combination to obtain desired dose” (e.g., Site 6). There may be situations when two drugs from the same class should be prescribed, and thus providing a system warning for
individual drug duplicates as opposed to class duplicates would be more appropriate. Finally, we were sobered to find that in one system all alerts were inadvertently turned off—an unintended consequence of an upgrade to a new release six months earlier, only discovered when we undertook our scenario testing of that system.

**The wording of alert warnings**

Testers often found the wording of alert warnings and ways the information was displayed confusing. In Test Case 4 (duplicate drug checking), the duplicate drug warning never explicitly said “duplicate” but specified how the drug “already exists ... under the selected assessment” (e.g., Site 9). The tester felt this wording was unclear and disliked the way warnings for all active orders appeared on the same screen, including those not relevant to the current erroneous order (for which an alert would be most relevant). Another tester also shared a similar view, explaining how alert warnings (including those generated from previous orders) were listed in the same pop up window in the same type of commercial CPOE system at a different site (e.g., Site 11). He found himself sifting through all of these warnings in order to find the relevant one(s). Although they could be ordered in terms of severity, this tester felt that the way these warnings were displayed added to the burden of “alert fatigue” at this site.

In Test Case 3 (drug-disease checking), the tester at one site (Site 2) received a best practice advisory warning (as opposed to a drug-disease alert) noting that pioglitazone was contraindicated in patients with CHF. These types of alerts were felt to be common and for “less severe warnings/interactions”. The tester explained how this particular warning - which was arguably more “critical” than most - could easily “get lost in the long list of other warnings that show
up simultaneously”. The drug-disease warnings that appeared in another system (e.g., Site 9) were considered “prominent but confusing” to the tester. He reflected on how it was hard to know which of the two warnings (that appeared in quick succession) were “actually more severe”, with one bright red warning stating “Not recommended” and another in orange stating “Extreme Caution”.

The timing of alert warnings

The timing of alert warnings differed across CPOE systems. Testers noted how for Test Case 2, drug-drug interaction warnings were displayed after both Imdur® (isosorbide mononitrate) and Revatio® (sildenafil) had been selected and the order was already signed in two different systems (e.g., Sites 2 and 7). It was relatively easy to get to the signing stage but an override box still ‘needed to be checked’ before the order could be sent to pharmacy (e.g., Site 7). Similarly, in Test Case 6 (duplicate therapy checking), the duplicate therapy warning appeared only after both metformin and Glucovance® (glyburide and metformin combination) had been ordered and signed (e.g., Site 1). In contrast, the same duplicate therapy warning appeared before the second order was signed in a different system (e.g., Site 7). Unfortunately, a number of well-timed warnings were ignored by testers who frequently voiced the dangerous assumption that “the pharmacists would catch” any errors that they missed.

The level of severity of alert warnings
Alert warnings varied in their level of severity in different CPOE systems. For example, in Test Case 2 (drug-drug interaction checking) some systems generated an ‘Information only’ alert when Imdur® (isosorbide mononitrate) and Revatio® (sildenafil) were ordered together (e.g., Site 6). This was in contrast to others, which generated a hard stop ‘critical alert’ [highlighted in red] (e.g., Site 4 and 5); the latter required the testers to either cancel the current order or discontinue one of the drugs in order to proceed. Similarly, for Test Case 4 (duplicate drug checking), the tester was presented with a hard stop alert warning after entering an order for Lovenox® (enoxaparin sodium injection) 40mg subcutaneous daily followed by a second order for Lovenox® 100mg subcutaneous twice a day in the inpatient system (e.g., Site 7). When placing the same order using the equivalent outpatient system at the same site, the tester was presented with an interruptive alert warning that could easily be overridden with a single keystroke. Testers at Sites 3, 5 and 11 commented on how they might often need to prescribe the same drug twice in certain cases e.g., a different dose of a diabetic drug in both the morning and evening, and thus developed workarounds such as entering the brand name of the drug e.g., Glucotrol® (glipizide) for the morning and the generic name of the drug (glipizide) for the evening dose to avoid getting duplicate drug alert warnings.

CPOE workarounds

Testers overcame certain challenges when entering Test Case 9, 11 and 13, as the drug name was presented alongside the dose, route or indication in some CPOE systems respectively; they developed various workarounds which they had previously learned in using the system, such as (i) using the “other” option, (ii) making free text entries in the special
instructions or comments field, (iii) changing the default settings, and (iv) selecting ‘off
formulary’ drugs. For example, in Test Case 9 (wrong units), testers were presented with the
dose alongside the drug name or dosed product (e.g., Synthroid® 100 mcg), which made it
difficult to enter the wrong units or dose (mg vs. mcg). One tester successfully placed the order
for a 1000-fold overdose of Synthroid® (levothyroxine) by selecting the “other” option from
the pull down menu, entering “100” in the free text box, and selecting the units “mg” from
the dose list (e.g., Site 7). Testers successfully changed the default strength from “100mcg” to
“100mg” in the same system without any difficulties at two other sites (e.g., Site 9 and 11).
Finally, another tester selected Synthroid® (levothyroxine) from the ‘off formulary’ list as
this had no dose attached to it (e.g., Site 6) and then successfully entered “100mg by mouth
daily” in free text in the “instruction” field.

Testers were presented with the route alongside the drug name in some CPOE
systems e.g., Tylenol® (acetaminophen) PO (by mouth) tabs (Site 4), a protection which
made it difficult to select the wrong route in Test Case 11 (wrong drug route/directions).
However, testers were able to circumvent this critical safety feature and successfully place
the erroneous order by making a free text entry in the special instructions or comments field.
One tester was able to type over the default value of “take 2 tabs” in their CPOE system (e.g.,
Site 11) and noted how “1 puff” and “1 spray” were also presented as selectable options for
Tylenol® tablets. No relevant warnings were generated in any of the CPOE systems (where
the successful orders were placed). Another tester at a different site (Site 3) found it hard to
find the right drug form, and so (based on previous experience of using such a workaround)
intentionally selected the wrong form from the product list and provide instructions to
pharmacy to give a different form.
Finally, in some systems, testers were presented with the indication alongside the drug name which could help prevent selection of the wrong dose for the intended indication in Test Case 13 (wrong dose for indication; a dangerous not infrequently reported error).(19) A maximum weekly dose of methotrexate was associated with each of the drug-indication options in one system (Site 4), including 12.5mg for “Methotrexate (RHEUM) PO” and 15mg for “Methotrexate (Non Oncology Use)”. Testers performed workarounds by either typing “15mg” in free text in the dose field and “QD” (every day) in the frequency field for “Methotrexate (RHEUM) PO”, or selecting “QD” from a structured list for “Methotrexate (Non Oncology Use)”. No alert warnings were displayed in either case. This erroneous order was able to be readily placed in all CPOE systems except one (Site 5) where the testers were unable to change or select “other” to enter a free text frequency; special authorization was required in this system to prescribe higher doses/greater than weekly frequencies for “chemo” orders.

DISCUSSION AND CONCLUSION

We found an array of CPOE systems often failed to detect and prevent previously documented and potentially dangerous medication errors. The generation of electronic alert warnings varied widely between systems, and depended on how the order information was entered into the system (i.e., in a structured or unstructured way); whether a specific alert functionality (e.g., duplicate-drug checking) was operational in the system; and which drugs or drug combinations were included in the CDS algorithms). The wording of alert warnings was often found to be confusing, with unrelated warnings appearing on the same screen as those more relevant to the current erroneous entry that was made. The timing of alert warnings differed across CPOE systems, with many dangerous drug-drug interaction
warnings displayed only after the order was placed. Alert warnings also varied in their level of severity in different systems and even within the same institution (outpatient vs. inpatient system). Testers demonstrated a variety of workarounds which they had discovered (and used in their practice) to enter such erroneous orders such as (i) using the “other” option, (ii) making free text entries in the special instructions or comments field, (iii) changing the default settings, and (iv) selecting ‘off formulary’ drugs. Thus, “free text” represented both a blessing (ability to overcome frustrations in entering desired orders, and communicating intent directly with pharmacy) and curse (circumvented CDS safety checks).

Testing revealed a range of CDS protections that were either switched off or non-existent in the different CPOE systems. For example, none of the systems generated LASA alerts when “penicillamine” was ordered instead of “penicillin”. In contrast, LASA warnings were generated for other drugs at one site. Errors relating to the incorrect selection of adjacent drugs from drop-down menus are increasingly being reported in the literature.(20) The United States Pharmacopeia identified approximately 1,470 unique drugs implicated in medication errors due to brand and/or generic names that looked or sounded alike.(21) It is therefore important that relevant LASA warning capability is operational in CPOE systems and targets at least the most frequent drug pairs previously implicated in medication errors. Also, incorporating the “indication for use” as part of the medication orders could potentially prevent drug name error (e.g., “penicillamine” being ordered for the treatment of rheumatoid arthritis or Wilson’s disease rather than penicillin for bacterial infection).

The wording of alert warnings was found to be unclear in some CPOE systems. Human factors principles always need to be considered when developing and implementing medication-related alerts and the content of these alerts validated for clarity and understandability with the intended users.(22) Display of various warnings completely
unrelated to erroneous order (e.g., obscure DDI warnings) was frequently noted in some CPOE systems and warrants further attention as excessive irrelevant warnings are likely to contribute to alert fatigue with providers overlooking more relevant serious warnings. The need to strike the right balance between useful alerting and over-alerting in CPOE systems has previously been emphasised, with valuable guidance published on which drug-drug interaction alerts should be set as interruptive and non-interruptive.\textsuperscript{(23, 24)} One academic institution reported the potential of reducing their alert volume by about a third by safely making 33 specific DDI alerts non-interruptive.\textsuperscript{(24)}

Dangerous drug-drug interaction warnings were displayed only after the order was placed in this study. It is less useful for a clinician to spend time finishing the construction of a medication order only to be informed after-the-fact that there is a hazardous interaction between two of the selected drugs. To enhance alerting efficiency, drug-drug and drug-allergy warnings ideally should be presented at the time the physician selects the new medication.\textsuperscript{(18)} The timing of the alert’s appearance in the clinical workflow is also critical for end-user acceptance of the CPOE system and an important predictor of whether it will improve clinical practice.\textsuperscript{(25)}

This study also sheds light on the different attempts testers made to individually problem solve and overcome limitations of CPOE systems. For example, presenting the drug name alongside the dose was designed to prevent the ordering of excessive medication doses. However, testers appeared to be very good at circumventing this intended forcing function when conducting Test Case 9 \textit{(1000-fold overdose)} by (i) using the “other” option, (ii) making free text entries in the special instructions or comments field, (iii) changing the default settings, and (iv) selecting ‘off formulary’ drugs. One tester purposefully selected the wrong drug form from the product list (when he found it hard to find the right form) and
provided instructions to pharmacy to give a different form. However, the fact that testers had to resort to workarounds for these prescriptions can also be possibly viewed as a positive feature of CPOE systems, i.e., the correct dosages and routes of administration were easier to enter than the incorrect ones. It is plausible that real users would not go to the trouble when confronted by accurate dosages and routes that were easier to enter than incorrect ones. That said, it is less reassuring that many of the erroneous orders (in the words of the testers and observers) “sailed right though” with no warnings what so ever. This raises important patient safety concerns, as space is sometimes restricted in the ‘other’ frequency field of CPOE systems. We recognize that some testers may have been more adept at finding workarounds than others, and this variation is a limitation of our study. However, careful study of the workarounds by organizations may identify potential threats to patient safety and help provide solutions as technology is introduced and updated.

This study has several implications. Despite two decades of development of CPOE systems and CDS, organizations are probably not getting all the safety benefits that they could, given the level of variability we found. We fear this slow progress means both that patient safety is not being protected, and learning and improvement needs to be accelerated. Second, it would not have been possible to anticipate all the sorts of issues that have arisen. Thus, there is a clear role for post-implementation testing using a variety of clinical scenarios that could enable organizations to improve their systems.(14) The net result is that both vendors and hospitals can draw valuable lessons from this kind of evaluation.

This study has several limitations. It was performed at only a small number of institutions, which may not be representative of institutions at large. We also tested a limited number of errant orders, but these were actual issues that had been reported as problematic in the MEDMARX database. By “instructing” testers to enter these erroneous prescriptions,
we introduced an element of artificiality; this was unavoidable in a study of this sort. We also do not know how many of these “erroneous orders” would be detected vs. overlooked by pharmacists receiving and reviewing these orders. Finally and most importantly, this study did not aim to assess the right balance between under-alerting and over-alerting. We focused on examples of failure to alert, while also documenting evidence of over-alerting from the tester comments we collected. Certainly duplicate warnings for the same drug, e.g., Glucovance® and metformin, are appropriate; alerting on all class duplications e.g., NSAIDS and aspirin may not be particularly helpful.

In conclusion, we found a high degree of variability in ordering between different CPOE systems. Major deficiencies were identified in some of these systems and it is therefore critical that developers reflect on these findings and build in safeguards to ensure safer prescribing for patients. Human factors principles should always be considered when introducing medication-related alerts, and the concerns of clinical users who are likely to be directly affected by the decision support capabilities openly discussed.(26) We believe that these findings can assist hospitals in selecting areas for new implementation of decision support or improvement of their current CPOE system.
Ethical approval: This study was reviewed and approved by the Partners Human Research Committee (PHRC), which is the Institutional Review Board (IRB) of Partners Research Management at Partners HealthCare. (ref #2009-P-002678/1; BWH)

Acknowledgements: We are grateful to all the testers who kindly gave their time and participating hospitals and private practices for supporting this work. We gratefully acknowledge the National Patient Safety Foundation for providing the funding for this study, as well as United States Pharmacopeia Inc and Quantrros for providing the MEDMARX error report data. We also acknowledge the additional assistance received from Thu-Trang Hickman in organising research group meetings, and Marjan Sadegh and Jennifer J. Boehne in helping to review the medication error reports. Study data were collected and managed using the REDCap tool hosted at Brigham and Women’s Hospital, Boston.

Contributorship Statement: GDS, ACS and DWB conceived and designed this study, and secured the funding for this work. MGA, DLW and TE conducted the data collection. SPS, MGA, TE, GDS, DWB contributed to the analysis and interpretation of data. SPS led the writing of this manuscript with all coauthors commenting on drafts of the paper. All authors gave their approval for the final version to be published. SPS and GDS act as guarantors.

Funding Statement: This work was supported by the National Patient Safety Foundation. The views expressed in this publication are those of the authors and not necessarily those of the National Patient Safety Foundation.
Competing Interests Statement: The authors have no competing interests to declare.
REFERENCES


doi:10.1371/journal.pone.0085071


drug interactions that should be non-interruptive in order to reduce alert fatigue in electronic health records. *J Am Med Inform Assoc.* 2013;20(3):489-93.


Appendix 1 – Instructions for testers

**Test Case 1: Allergy checking**

1. Enter patient allergy for lisinopril in test patient’s chart.
2. Enter order for captopril 12.5 mg PO (by mouth) TID (three times a day)

*Special instructions:* If lisinopril is not available on formulary, use enalapril 5 mg PO daily.

**Test Case 2: Drug-drug interaction (DDI) checking**

1. Enter order for Imdur® (isosorbide Mononitrate) 30 mg PO daily.
2. Enter order for Revatio® (sildenafil) 20 mg PO TID.

*Special instructions:* Enter both orders in sequence without discontinuing the first order.

**Test Case 3: Drug-disease checking**

1. Enter “congestive heart failure” or equivalent to patient’s problem list.
2. Enter order for pioglitazone 45 mg PO daily.

*Special instructions:* Note nature of contraindication warning, if any.

**Test Case 4: Duplicate drug (same exact drug)**

1. Enter order for Lovenox® 40 mg SQ (subcutaneous) daily.
2. Enter order for Lovenox® 100 mg SQ BID (twice daily).

*Special instructions:* Enter both orders in sequence without discontinuing first order. Note: intention is for first order to be prophylactic dose, second order to be later initiation of therapy without discontinuing prophylactic dose. If Lovenox® is not on formulary, use:
(a) dalteparin 5,000 units SC daily AND dalteparin 15,000 units SC daily (for 75 kg person @ 200 units/kg), OR (b) Arixtra® (fondaparinux sodium) 2.5 mg SC every 24 hrs AND 2. Arixtra® (fondaparinux sodium) 7.5 mg every 24 hrs (for 50-100 kg person)

**Test Case 5:** *Wrong units*

1. Enter order for Insulin Aspart, 60 ml (rather than 60 units) SQ BID.

*Special instructions:* None.

**Test Case 6:** *Duplicate therapy (different drugs, same active ingredient),*

1. Enter order for metformin 1,000 mg PO BID
2. Enter order for Glucovance® (glyburide/metformin) 5 mg/500 mg PO BID

*Special instructions:* Enter both orders in sequence without discontinuing first order.

**Test Case 7:** *Wrong dispense amount*

1. Enter order for metronidazole 250 mg with instructions: “Take two tablets by mouth twice a day.” Duration: seven days. Dispense amount: 14 tablets.

*Special instructions:* Enter order using 250 mg tablets only (total dose: 500 mg BID).

**Test Case 8:** *Omission errors (missing dose, missing instructions)*

1. Enter order for sertraline PO daily (without entering a dose).
2. Discontinue first order

[3. Enter order for sertraline 25 mg PO (without instructions).]

*Special instructions:* This is a two-part test.

**Test Case 9:** *Wrong units (mg vs. mcg), 1000-fold overdose*

1. Enter order for Synthroid® (levothyroxine) 100 mg PO daily.

*Special instructions:* None.
**Test Case 10:** Wrong drug (Look-alike-sound-alike); adjacency error

1. Type “penicil” into drug search function.
2. Select penicillamine from menu (even though what was desired was penicillin).

*Special instructions:* Note carefully whether penicillin and penicillamine are adjacent on the pull-down menu.

**Test Case 11:** Wrong drug form/route, Wrong instructions

1. Enter order for Tylenol® Junior Strength Chewable Tabs, 160 mg, 24 tablets with instructions to administer “1 dropperful every 4 hours.”

*Special instructions:* None.

**Test Case 12:** Wrong frequency for drug form

1. Enter order for Cardizem® CD (diltiazem extended-release) 120 mg PO QID

*Special instructions:* Make sure to select CD (extended-release) formulation.

**Test Case 13:** Wrong dose for indication, order set issues, pull-down menu errors

1. Enter order for methotrexate 15 mg PO daily.

*Special instructions:* Erroneous order being placed inadvertently for patient with rheumatoid arthritis who should receive weekly, i.e., this is correct dose but incorrect frequency for indication. Daily frequency is used for treatment of NH-lymphoma.
1. Tester/Test ID
2. Site Name
3. CPOE System/Vendor
4. **Was the order able to be placed?** (Yes; No; Uncertain/Maybe; Untestable) Any additional comments?
5. **How easy was it to place the order?** (Easy; Minor workarounds; Some difficulty; Difficult but possible; Impossible; see Appendix 3)
6. Type of warning?
7. **Were any warnings displayed in the course of entering the order?** Any additional comments?
8. Describe what happened in the course of entering the order?
9. Describe workaround efforts attempted/required by the tester?
10. Does the tester have any additional comments about this particular order?
11. Has the tester seen or experienced a similar situation while trying to prescribe this drug (or others) in this CPOE system? Other CPOE systems? Any additional comments?
12. How frequently?
13. Other comments?
ERRONEOUS Orders

How easy was it to place the order?

1 2 3 4 5
Easy Minor Some Difficult Impossible

Workarounds protections

1. Easy
   - Tester successfully and quickly entered the order
   - No alerts/warnings
   - No workarounds or additional mouse clicks required
   - Order “sailed through”

2. Minor Workarounds
   - Tester is able to enter the order fairly easily
   - No alerts/warnings
   - Requires some kind of additional workarounds (e.g., forced to enter all or part of the order in free text, or use of comments field to complete order)

3. Some protections
   - Tester is able to enter the order
   - “Passive” alerts/warnings appear
a. Warning appears but it can be ignored (no override required)

b. Warning appears but can override with single mouse-click (this includes selecting a reason for override from pull-down menu)

- Typical response from the provider is to say “I usually just blow through these [warnings]” or equivalent

4. Difficult

- Tester is able to enter the order, but doing so requires a conscious, concerted effort
- “Active” alerts/warnings appear that require additional action from provider (e.g. typed reason for override)
- Often, typed workarounds AND extra mouse clicks are required to override
- Order often does not go through on first attempt
- Significant time and thought required to enter successfully
- Palpable tester frustration

5. Impossible

- Order could not be entered, despite attempted workarounds and tester frustration
- No way to enter order in free text comments field
- Hard stop warnings appear or significant changes are required to send to pharmacy (e.g. required to d/c order or remove drug/diagnosis)
- System is completely “bulletproof,” at least in regard to this particular order
Table 1. Characteristics of Data Collection Sites and scores

<table>
<thead>
<tr>
<th>Site</th>
<th>Site Classification</th>
<th>Inpatient/Outpatient Setting</th>
<th>Number of beds</th>
<th>CPOE System*</th>
<th>Sum of scores†</th>
<th>Average scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Academic Medical Center</td>
<td>Combination--</td>
<td></td>
<td></td>
<td>301-500</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inpatient/Outpatient</td>
<td></td>
<td>Commercial</td>
<td>34</td>
<td>2.6</td>
</tr>
<tr>
<td>2</td>
<td>Multispecialty Group Practice</td>
<td>Outpatient</td>
<td>&gt;500,000 outpatient visits/year</td>
<td>Commercial</td>
<td>34</td>
<td>2.6</td>
</tr>
<tr>
<td>3</td>
<td>Community Teaching Hospital</td>
<td>Inpatient</td>
<td>101-300</td>
<td>Commercial</td>
<td>48</td>
<td>3.7</td>
</tr>
<tr>
<td>4</td>
<td>Academic Medical Center</td>
<td>Outpatient</td>
<td>&gt;700,000 outpatient visits/year</td>
<td>In-house</td>
<td>30</td>
<td>2.4</td>
</tr>
<tr>
<td>5</td>
<td>Academic Medical Center</td>
<td>Inpatient</td>
<td>500 or more</td>
<td>In-house</td>
<td>41</td>
<td>3.2</td>
</tr>
<tr>
<td>6A</td>
<td>Community Hospital</td>
<td>Inpatient</td>
<td>101-300</td>
<td>Commercial</td>
<td>29</td>
<td>2.2</td>
</tr>
<tr>
<td>6B</td>
<td>Community Outpatient Clinic</td>
<td>Outpatient</td>
<td>12,000 patients</td>
<td>Commercial</td>
<td>21</td>
<td>1.6</td>
</tr>
<tr>
<td>7A</td>
<td>Academic Medical Center</td>
<td>Outpatient</td>
<td>&gt;500,000 outpatient visits/year</td>
<td>In-house</td>
<td>32</td>
<td>2.5</td>
</tr>
<tr>
<td>7B</td>
<td>Academic Medical Center</td>
<td>Inpatient</td>
<td>500 or more</td>
<td>In-house</td>
<td>38</td>
<td>2.9</td>
</tr>
<tr>
<td>8</td>
<td>Academic Medical Center</td>
<td>Inpatient</td>
<td>500 or more</td>
<td>Commercial</td>
<td>35</td>
<td>2.7</td>
</tr>
<tr>
<td>9</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Commercial</td>
<td>26</td>
<td>2.0</td>
</tr>
<tr>
<td>10</td>
<td>Community Teaching Hospital</td>
<td>Inpatient</td>
<td>101-300</td>
<td>Commercial</td>
<td>42</td>
<td>3.2</td>
</tr>
<tr>
<td>11</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Commercial</td>
<td>34</td>
<td>2.6</td>
</tr>
<tr>
<td>12</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Commercial</td>
<td>43</td>
<td>3.3</td>
</tr>
</tbody>
</table>

* Our agreement with the test sites precludes revealing more specific details about each system.
† The sum and average scores across all 13 tests in answer to the question “How easy was it to place the erroneous order?”
‡ Private practice physician offices did not contain beds hence not applicable (n/a)
<table>
<thead>
<tr>
<th></th>
<th>Private practice physician office</th>
<th>Outpatient</th>
<th>n/a</th>
<th>In-house</th>
<th>28</th>
<th>2.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Commercial</td>
<td>31</td>
<td>2.4</td>
</tr>
<tr>
<td>15</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Commercial</td>
<td>37</td>
<td>2.8</td>
</tr>
<tr>
<td>16</td>
<td>Private practice physician office</td>
<td>Outpatient</td>
<td>n/a</td>
<td>Not-for-profit corporation</td>
<td>27</td>
<td>2.1</td>
</tr>
</tbody>
</table>