

Medication errors and adverse drug events in a UK hospital during the optimisation of electronic prescriptions: a prospective observational study



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Summary

Background WHO's Third Global Patient Safety Challenge, Medication Without Harm, focused on reducing the substantial burden of iatrogenic harm associated with medications by 50% in the next 5 years. We aimed to assess whether the number and type of medication errors changed as an electronic prescribing system was optimised over time in a UK hospital.

Methods We did a prospective observational study at a tertiary-care teaching hospital. Eight senior clinical pharmacists reviewed patients' records and collected data across four adult wards (renal, cardiology, general medical, and orthopaedic surgical) over a 2-year period (from Sept 29, 2014, to June 9, 2016). All medication errors and potential and actual adverse drug events were documented and the number of medication errors measured over the course of four time periods 7–10 weeks long. Pharmacists also recorded instances where the electronic prescribing system contributed to an error (system-related errors). A negative-binomial model and a Poisson model were used to identify factors related to medication error rates.

Findings 5796 primary errors were recorded over the four time periods (period 1, 47 days [Sep 29–Dec 2, 2014]; period 2, 38 days [April 20–June 12, 2015, for the renal, medical, and surgical wards and April 20–June 15, 2015, for the cardiology ward]; period 3, 35 days [Sep 28–Nov 27, 2015] for the renal ward, 37 days [Sep 28–Nov 23, 2015] for the medical ward, and 40 days [Sep 28–Nov 20, 2015] for the cardiology and surgical wards; and period 4, 37 days [Feb 22–April 15, 2015] for the renal and medical wards and 39 days for the cardiology [April 13–June 7, 2015] and surgery [April 18–June 9, 2015] wards; unanticipated organisational factors prevented data collection on some days during each time period). There was no change in the rate of primary medication errors per admission over the observation periods: 1.53 medication errors in period 1, 1.44 medication errors in period 2, 1.70 medication errors in period 3, and 1.43 medication errors in period 4, per admission. By contrast, the overall rate of different types of medication errors decreased over the four periods. The most common types of error were medicine-reconciliation, dose, and avoidable delay-of-treatment errors. Some types of errors appeared to reduce over time (eg, dose errors [from 52 errors in period 1 to 19 errors in period 4, per 100 admissions]), whereas others increased (eg, inadequate follow-up of therapy [from 12 errors in period 1 to 24 errors in period 4, per 100 admissions]). We also found a reduction in the rates of potential adverse drug events between the first three periods and period 4. 436 system-related errors were recorded over the study period.

Interpretation Although the overall rates of primary medication errors per admission did not change, we found a reduction in some error types and a significant decrease in the rates of potential adverse drug events over a 2-year period, during which system optimisation occurred. Targeting some error types could have the added benefit of reducing others, which suggests that system optimisation could ultimately help improve patient safety and outcomes.

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Introduction

The UK National Health Service (NHS) aims to become one of the safest health-care systems in the world.^{1,2} Globally, the cost associated with medication errors has been estimated to be US\$42 billion per year.³ In 2017, WHO announced its Third Global Patient Safety Challenge, Medication Without Harm, which was aimed at reducing the substantial burden of iatrogenic harm

associated with medications by 50% in the following 5 years.³

The previous UK Secretary of State for Health and Social Care, Jeremy Hunt, announced how a new government initiative to reduce medication and prescribing errors in England would concentrate on the use of electronic prescribing systems in hospitals.⁴ However, implementation of electronic prescribing has been slow and, indeed,

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Research in context

Evidence before this study

In 2014, Nuckols and colleagues did a systematic review and meta-analysis to assess the effectiveness of Computerized Provider Order Entry (CPOE) at reducing preventable adverse drug events in hospital-related settings and examine the reasons for heterogeneous effects on medication errors. They identified studies using MEDLINE, Cochrane Library, Econlit, web-based databases, and bibliographies of previous systematic reviews. Implementing CPOE was associated with a greater than 50% decline in preventable adverse drug events, although the included studies used weak designs and were mostly done in the USA using extensively customised electronic prescribing systems. We further searched Ovid MEDLINE for articles published from Jan 1, 2014, to July 10, 2019, using search terms relating to medical order entry systems or electronic prescribing, or decision-support systems, clinical and medication errors, and hospitals. Specifically, we used the medical subject headings "Medical Order Entry Systems/ OR Electronic Prescribing/, OR Decision Support Systems, Clinical AND Medication Errors/ AND Hospitals/". Our review revealed

only a few additional studies that focused on specific clinical areas such as intensive care units or discharge prescriptions.

Added value of this study

This is the largest UK study to examine whether the overall rate of medication errors per admission and the types of errors changed over time during the optimisation of an electronic prescribing system. We found no significant change in the rates over time; however, the rate of some types of errors (eg, dose) decreased across the study period, whereas the rate of other errors (eg, inadequate follow-up of therapy) increased over time. Our study revealed how some error types, such as dose and medicine-reconciliation errors, were more likely to occur together.

Implications of all the available evidence

To reduce the substantial burden of iatrogenic harm associated with medications and maximise the effect of future clinical decision support systems on reducing errors in the hospital setting, electronic prescribing systems will need to monitor for those types of error that are likely to occur together.

further funding has been allocated to speed up implementation of these systems in 13 English hospital trusts by 2021.

Electronic prescribing, which usually refers to the ordering or prescribing of medication electronically, has been shown to reduce the risk of medication errors and adverse drug events.⁵ A systematic review and meta-analysis reported a 50% reduction in preventable adverse drug events with the implementation of electronic prescribing systems in the hospital setting.⁶ However, most of the studies included in the systematic reviews^{5,6} were done in the USA using extensively customised electronic prescribing systems. One UK study, done more than 10 years ago on a general surgery ward, suggested that a closed-loop system including electronic prescribing, automated dispensing, barcode patient identification, and electronic medication-administration records could stop two prescribing errors per 100 prescriptions written.⁷ However, electronic prescribing systems are likely to have changed quite substantially over the past 10 years, with more robust clinical decision support.⁸ Furthermore, studies^{9–11} have also shown how these systems can contribute to new types of errors, specifically those associated with use of the system (eg, drop-down menu selection errors). Up-to-date evidence from the UK about the incidence and types of errors occurring in hospitals is needed to guide the decisions of policy makers and managers.

We did the largest UK study to date to examine whether the rate of medication error per admission and types of errors changed as changes were made to an electronic prescribing system over time. We also explored whether some types of medication errors tended to occur together

(or clustered) because this could help identify how to target error prevention strategies to reduce multiple error types and assessed the incidence and preventability of actual or potential adverse drug events. Finally, we also assessed whether the system functionality or design of the electronic prescribing system could have contributed to the errors, which we described as system-related errors.

Methods

Study design and participants

This was a prospective observational study done at a tertiary-care teaching hospital with approximately 1800 beds, belonging to one of the largest NHS trusts in the UK. The study was done across a range of clinical settings including renal, cardiology, general medical, and orthopaedic surgical services, with approximately 20–30 beds per each of the four adult wards. All newly admitted patients to the study wards were included. Data were collected by clinical pharmacists at four separate time periods which were 7–10 weeks long, in line with a previous study.¹² A decision was made to avoid data collection during the month of August to limit bias from errors made by newly qualified prescribers during the junior-doctor handover period. Eight senior clinical pharmacists who were employed as permanent members of the hospital pharmacy team collected 3864 h of data in total.

The hospital trust originally implemented a commercial electronic prescribing system in adult inpatient wards between Oct 6, 2008, and March 25, 2011. Approximately 5720 medication orders were written daily across the trust; this included 70–180 orders daily on each of our four study wards. Chemotherapy orders were entered into a separate electronic prescribing system and patient-controlled

analgesia and epidurals, intravenous fluids, and high-frequency eye medication were ordered on paper charts. Pharmacists were able to clinically screen and validate medication orders electronically and nurses documented administrations in the system.

Ethics approval was obtained from the Health Research Authority National Research Ethics Service Committee North East-Sunderland 14/NE/0072 (IRAS project ID 141106) and Trust R&D Permission (project 6785). The Health Research Agency—Confidentiality Advisory Group confirmed that informed consent from patients was not necessary for this study.

Procedures

Serial changes were made to the system over the four data collection periods. During period 1, the system consisted of the most basic features with little clinical decision support. Orders were typically selected from a locally configured medications catalogue with structured order sentences via a drop-down menu, which included the medication name and a range of routes, doses, and frequencies (eg, omeprazole 20 mg orally once per day). Drug allergy checks were active and prescribers and pharmacists were notified about a small number of drug–drug interactions and drug laboratory checks using a pop-up alert after these orders had been made. Order sets (a group of clinically related orders grouped together for prescriber convenience and efficiency) were also used. Immediately before period 1, pharmacy staff were granted access to the NHS Summary Care Record (an electronic record of important patient information, created from general-practice medical records in England). This access was extended to medical staff in acute settings in the following months. In period 2 dosage alerts for certain medications were introduced and pharmacy staff were informed when a range of high-risk medications were prescribed (eg, anticonvulsants and clozapine). In period 3, a new version of the electronic prescribing system was installed, which resulted in changes to the visual display and users being provided with a link to access the patient's previous electronic outpatient letters and details of their clinic appointments. Furthermore, from this point, prescribers were able to prescribe insulin on the electronic prescribing system, which offered options for the user to prescribe short-acting, intermediate-acting, or long-acting insulin. In period 4, a number of high-risk drug–drug interaction alerts were introduced to prescribers and pharmacists. Order sets for omeprazole infusions and peritoneal dialysis were also used. In addition, email notifications were sent to a named clinician if certain medications were ordered (eg, an email was sent to a designated clinician if a novel oral anticoagulant was initiated for a patient admitted to care in the ward for older patients). Further detail about changes that were made to the system over time are outlined in the appendix (pp 1, 2).

All patients admitted to one of the four study wards during the data collection periods were reviewed daily by

a pharmacist to reveal any medication-related problems. Each ward was assigned a specific clinical pharmacist to collect data during the study period. Each day, the pharmacist would meet any new patients and do an advanced medication review, assessing each patient's in-patient electronic and paper drug chart(s) alongside any blood test results, observations, and medical notes.¹³ Pharmacists considered the patient's usual medication-taking behaviour. However, any drug-related problems associated with medication adherence or administration while at home were addressed but not included in this study as a medication error. Pharmacists would also perform a daily review of each inpatient's electronic and paper drug chart(s) to identify new orders and any unresolved errors. The potential consequences of errors were assessed using the pharmacist's clinical knowledge and judgement about the patient at the time the drug was prescribed. Furthermore, a more detailed investigation of the patient's medical notes was done if the reviewer identified an adverse drug event (eg, major bleeding, new confusion, nausea, constipation, cardiac arrest, or changes to blood test results). This detailed investigation involved reviewing the patient's full medical notes, including their electronic medication chart and any blood results taken, and making an assessment about whether the drug error could have possibly caused the adverse outcomes identified. All medication errors and actual and potential adverse drug events were documented on a data collection form. Incidents were excluded if a patient injury was not clearly drug related.

All incidents were evaluated as to whether they represented medication errors as per the definitions in a Harvard University study (Cambridge, MA, USA).¹²

Medication errors were classified by type using a modified classification structure (appendix pp 3–5). Medicine-reconciliation error was added to capture errors that occurred at the medicine-reconciliation stage. Pharmacists could select one primary error type and multiple secondary error types for one medication order (figure 1). Error options were dose error (eg, inappropriate dose), route error (eg, route not specified or inappropriate route), frequency error (eg, frequency omitted), strength error (eg, strength inappropriate), formulation error (eg, formulation omitted), administration error, substitution (eg, wrong drug given), unnecessary drug, inappropriate drug, generic-name or brand-name error, known allergy to drug, duplication, drug–drug interaction, contraindication, inadequate follow-up of therapy, avoidable delay of treatment, premedication not ordered, preparation error, medicine-reconciliation error, course length or duration, policy not followed, monitoring not requested, monitoring requested but not done, monitoring results not available, monitoring results available but not acted upon and other. Different types of errors could occur at different stages of the medication use process (medicine-reconciliation, prescribing, verification or dispensing, administration, and monitoring stage; figure 1). Primary errors were

See Online for appendix

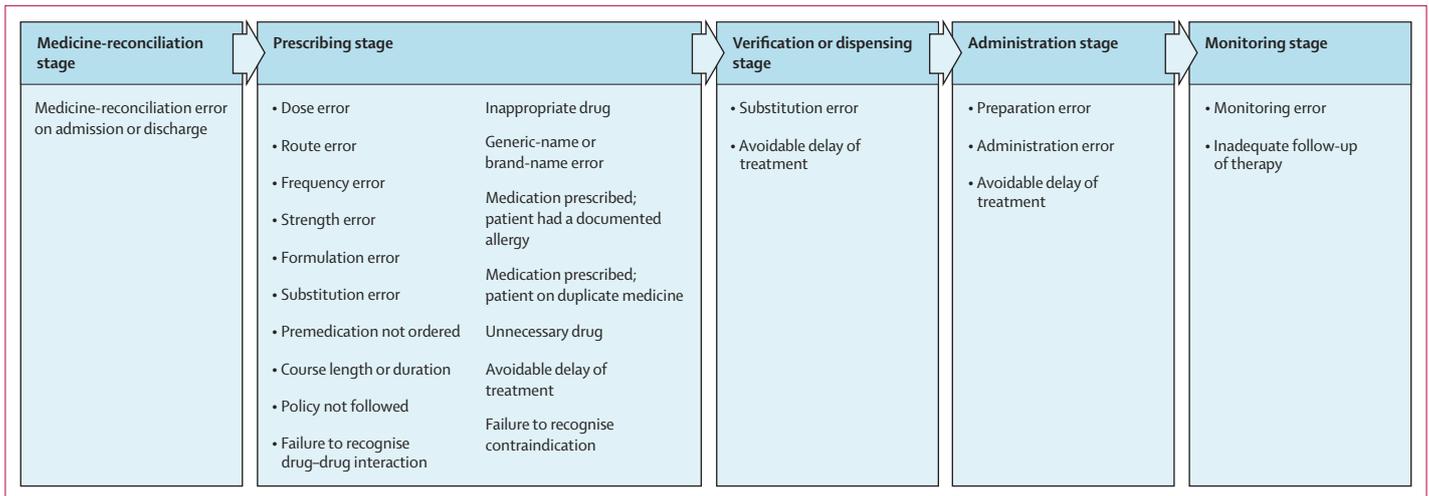


Figure 1: Flow chart showing medication error types according to stage in the medication use process

defined as the main error that occurred with a specific order and secondary errors were errors related to that. For example, the pharmacist would select medicine-reconciliation error as the primary error if a medication was prescribed incorrectly on admission. They could also select dose error as a secondary error if the error was related to the dose. Regular meetings were held between the study team and senior clinical pharmacists to ensure consistency in error classification. Pharmacists were also asked to record if the electronic prescribing system could have contributed to the occurrence of the medication error in this UK study (which could have occurred, for example, if the wrong drug was selected from a drop-down menu list as it was located next to a similarly named drug). Pharmacists could select one or more options from a set of predetermined system-related errors (appendix p 6).

Incidents suspected of being actual or potential adverse drug events were evaluated by the data-collection ward pharmacist reviewer and classified into one of four categories as adverse drug event, potential adverse drug event, medication error with little potential for harm, or no error or adverse drug event. Potential adverse drug events were categorised as intercepted or not intercepted. All adverse drug events and potential adverse drug events were classified according to severity: fatal, life-threatening, serious (eg, decrease in blood pressure), or significant (eg, nausea), similar to a previous study.¹² Preventability was classified as definitely preventable, probably preventable, probably not preventable, and definitely not preventable. A non-preventable adverse drug event was defined as “an injury due to a medication where there is no error in the medication process”¹⁴ (eg, an allergic reaction in a patient not known to be allergic to a medication). This four-point scale was collapsed into preventable and not preventable during the analysis stage. All classifications were double-checked by a second reviewer (CLT), who was not masked, and any discrepancies or queries were discussed with reclassification of the adverse drug event, if

necessary. Reviewers considered an adverse drug event preventable if it was due to an error or was preventable by any means currently available. The pharmacist who did the chart review also recorded the evidence that supported their decision to classify the error. They could select that there was little or no evidence, slight to modest evidence, moderate evidence, strong evidence, or virtually certain evidence. A working copy of medication error scenarios and the appropriate classification was maintained by the pharmacist reviewers during meetings and referred to periodically to aid classification.

Outcomes

The main outcomes of the study were the rate of medication error per admission and the type of medication errors selected by the data collection pharmacist. We defined medication errors as “errors in the process of ordering, dispensing, or administering a medication, regardless of whether an injury occurred or whether the potential for injury was present”.¹² As secondary outcomes, we also collected data on adverse drug events (both preventable and non-preventable), and potential adverse drug events defined as “errors with the potential for harm that did not result in an injury”.¹² Potential adverse drug events included both errors that were intercepted before the medication reached the patient and non-intercepted errors that did reach the patient but did not cause injury. This study captured all medication errors that occurred at specified time periods, which might or might not have resulted in patient harm. We also assessed the co-occurrence (clustering) of error types and factors related to medication error rates, including age, number of medications, sex, ward, and period.

Statistical analysis

Medication error rates were calculated as the number of primary medication errors per admission or per collection day in each of the study periods. Patients could have

had more than one error recorded per day over their admission; these errors were summed over their stay and recorded as one entry per patient. Each error recorded on a given day was counted again on the following days if it was not resolved, with the expectation that pharmacists would take steps to resolve all errors on the same day they were identified, such that each error would only be counted once. Models for count data (ie, the negative-binomial and Poisson models) were used to identify factors related to medication error rates in the four wards during the study periods. The total number of days each patient stayed in the hospital was used as an offset in these models. The number of medication error types was calculated from the incidence of primary and secondary errors. The study periods were considered as categorical variables in the models to test whether the incidence rate ratio (IRR) of medication errors differed between the study periods and wards.¹⁵

The Poisson and negative-binomial models were also used to test for equality of error-type rates per admission during the study periods. *p* values were obtained from a likelihood ratio χ^2 test by comparing an empty model with a model comprising of only a categorical period variable. The patients admitted to all study wards in each period were used as an offset in the model.

Further analysis of cases in which medicine-reconciliation errors were selected as the primary error type was also done with an agglomerative hierarchical clustering approach to identify groups of medication error types exhibiting both intracluster similarity and intercluster dissimilarity, according to whether a particular medication error type occurred or not. The co-occurrence of an error type (ie, similarity) was based upon the Tanimoto coefficient, which is an appropriate distance measure for binary data.¹⁶ Frequencies were used to summarise the frequencies of system-related errors for each study period. The significance threshold was set at *p*=0.05. We focused on medicine-reconciliation errors as they were the most commonly occurring error type for this exploratory analysis.

Role of the funding source

There was no specific funding for this study. The staff who contributed their time to data collection, analysis, and interpretation were employed by Newcastle University and Newcastle Upon Tyne Hospitals NHS Foundation Trust. No funding has been received to write this Article from a pharmaceutical company or other agency. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Study periods varied in duration between study wards, mainly because of unanticipated organisational factors that prevented data collection on a few days during each period. Period 1 lasted 47 days (Sep 29–Dec 2, 2014);

period 2 lasted 38 days (April 20–June 12, 2015, for the renal, medical, and surgical wards and April 20–June 15, 2015, for the cardiology ward); period 3 lasted 35 days (Sep 28–Nov 27, 2015) for the renal ward, 37 days (Sep 28–Nov 23, 2015) for the medical ward, and 40 days (Sep 28–Nov 20, 2015) for the cardiology and surgical wards; and period 4 lasted 37 days (Feb 22–April 15, 2015) for the renal and medical wards and 39 days for the cardiology (April 13–June 7, 2015) and surgery (April 18–June 9, 2015) wards. There were 1150 patients admitted to study wards in period 1, 930 in period 2, 824 in period 3, and 920 in period 4. There were 15.8 medications ordered per admission in period 1, 13.7 in period 2, 15.9 in period 3, and 13.1 in period 4. There were about nine to 11 regular medications ordered per patient admission and less than one medication ordered but held or suspended (usually for a clinical reason) per admission across the four study periods (table 1). A trend test for medication error rates per admission showed no significant results (*p*=0.88). There were significant differences between error rates per admission during the four periods (likelihood ratio χ^2 test *p*<0.0001). Further analyses showed that there were significant differences between periods 2 and 3 (*p*=0.0005, adjusted for multiple tests) and between periods 3 and 4 (*p*=0.0004, adjusted for multiple tests).

The rate of primary medication errors per admission did not change significantly during the four periods (1.53 medication errors in period 1, 1.44 medication

	Period 1	Period 2	Period 3	Period 4
Duration, days	47	38	38	38
Patients admitted to all study wards	1150	930	824	920
Patient-days	5023	4129	3780	3682
Medications ordered	18 170	12 742	13 100	12 023
Medications ordered per patient-day	3.62	3.09	3.47	3.27
Medications ordered per admission	15.80	13.70	15.90	13.07
Regular medications	12 318	8 465	8 925	8 488
Suspended medications	705	534	525	535
Regular medications ordered per admission	10.71	9.10	10.83	9.23
Suspended medications per admission	0.61	0.57	0.64	0.58
Total number of primary medication errors	1762	1337	1377	1320
Primary medication errors per admission*	1.53	1.44	1.70	1.43

*We used the likelihood ratio χ^2 test to compare the equality of the medication error rates across the four study periods and obtained *p*<0.0001 ($\chi^2=20.76$; 3 degrees of freedom).

Table 1: Overview of medications ordered across each of the study periods

	Period 1, n=1150		Period 2, n=930		Period 3, n=824		Period 4, n=920		p value
	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	
Dose	598	52	379	41	224	27	172	19	<0.0001
Frequency	134	12	121	13	150	18	114	12	0.0010
Formulation	83	7	48	5	64	8	44	5	0.21
Unnecessary drug	154	13	93	10	94	11	92	10	0.069
Inappropriate drug	144	13	136	15	106	13	47	5	<0.0001
Medication prescribed; patient on duplicate medicine	119	10	60	6	74	9	57	6	0.0017
Inadequate follow-up of therapy	141	12	166	18	164	20	225	24	<0.0001
Avoidable delay of treatment	341	30	228	25	194	24	19	2	<0.0001
Medicine reconciliation	975	85	781	84	697	85	662	72	0.0031
Course length or course duration	78	7	68	7	72	9	28	3	<0.0001
Policy not followed	190	17	167	18	187	23	162	18	0.016
Other*	80	7	321	35	171	21	130	14	<0.0001
Total	3037	264	2568	276	2197	267	1752	190	<0.0001

In all tests, the Poisson model performed better than the negative binomial model. p values compare the equality of rates in the four study periods. Error types with a rate of fewer than five errors per 100 admissions have been removed (these included route error, strength error, administration error, substitution error, generic-name or brand-name error, medication prescribed that patient had a documented allergy to, failure to recognise drug-drug interaction, failure to recognise contraindication, monitoring not requested, monitoring results available but not acted upon). *Included error types (such as spelling errors and allergy status not documented) that were not included in the data collection form but were recorded as part of the study.

Table 2: The rates of different types of medication errors per 100 admissions across four study periods (calculated from the total number of primary and secondary medication errors)

errors in period 2, 1.70 medication errors in period 3, and 1.43 medication errors in period 4; table 1). By contrast, the overall rate of different types of medication errors decreased over the four periods (table 2). The most common error type (calculated from the total of primary and secondary errors) was the medicine-reconciliation error, with 85 errors in period 1, 84 errors in period 2, 85 errors in period 3, and 72 errors in period 4 per 100 admissions (table 2). When the medicine-reconciliation error was selected as the primary error, 351 (47%) of 753 patients in period 1, 215 (33%) of 654 patients in period 2, 121 (24%) of 514 patients in period 3, and 115 (39%) of 293 patients in period 4 also had a secondary dose error recorded (appendix p 7). The next most common error types (both primary and secondary errors) were dose error (with 52 errors in period 1, 41 errors in period 2, 27 errors in period 3, and 19 errors in period 4 per 100 patient admissions) and avoidable delay-of-treatment error (with 30 errors in period 1, 25 errors in period 2, 24 errors in period 3, and two errors in period 4 per 100 admissions). Although the rate of dose errors (52 errors in period 1 vs 19 errors in period 4 per 100 admissions), course-length or course-duration errors (seven errors vs three errors per 100 admissions), and inappropriate-drug errors (13 errors vs five errors per 100 admissions) decreased, the rate of the error classified as inadequate follow-up of therapy (12 errors vs 24 errors per 100 admissions) increased over time (table 2). Except for when medicine-reconciliation error was the primary error, we did not

distinguish between primary and secondary errors in our analyses.

The rates of actual adverse drug events decreased from period 1 to period 3; however, the rate went up again in period 4. There was a significant decrease in potential adverse drug events across the four study periods from ten per 100 admissions, in period 1, to six per 100 admissions, in period 4 ($p=0.0376$; table 3).

436 system-related errors were recorded over the four study periods. Of these errors, 81 (19%) were inflexibility errors (37 recorded in period 1, 20 in period 2, 21 in period 3, and three in period 4), which included inflexibility in order screens (eg, when attempting to modify a medication order), and 286 (66%) were system-related errors classified as other (ie, not selection, placement, hazardous, keypad, or inflexibility errors; 70 in period 1, 68 in period 2, 69 in period 3, and 79 in period 4; table 4). The least common system-related error was placement error (eg, listing penicillamine in the middle of various penicillin products, resulting in wrong drug selection) with none recorded in periods 1, 3, and 4, but with three errors (rate <1 per 100 admissions) recorded in period 2. There was no significant change in the reporting of system-related errors over the study periods ($p=0.42$).

The clustering of medication error types for period 1, when medicine reconciliation was considered as the primary error, shows how dose, avoidable delay-of-treatment, and frequency errors were likely to occur together (figure 2). These three error types also tended to occur

	Period 1, n=1150		Period 2, n=930		Period 3, n=824		Period 4, n=920		p value
	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	Number of errors	Error rate per 100 admissions	
ADE									
ADE	34	3	20	2	15	2	29	3	..
Potential ADE	113	10	110	12	90	11	59	6	..
Total actual and potential ADEs	147	13	130	14	105	13	88	10	0.0376
Severity of ADEs									
Fatal	0	0	0	0	0	0	0	0	..
Life-threatening	1	<1	0	0	0	0	3	10	..
Serious	7	1	3	0	4	0	6	1	..
Significant	26	2	17	2	11	1	20	2	..
Total severity of ADEs	34	3	20	2	15	2	29	3	0.22
Severity of potential ADEs									
Life-threatening ADE	12	1	11	1	8	1	4	<1	..
Potential for serious	87	8	58	6	73	9	28	3	..
Potential for significant	14	1	41	4	9	1	27	3	..
Total severity of potential ADEs	113	10	110	12	90	11	59	6	0.0007

p values compare the equality of rates in the four study periods. ADE=adverse drug events.

Table 3: Incidence and preventability of ADEs and potential ADEs

	Period 1, n=1150		Period 2, n=930		Period 3, n=824		Period 4, n=920	
	Number of system-related errors	Rate per 100 admissions	Number of system-related errors	Rate per 100 admissions	Number of system-related errors	Rate per 100 admissions	Number of system-related errors	Rate per 100 admissions
Selection error	9 (7%)	1	5 (5%)	1	8 (7%)	1	16 (16%)	2
Placement error	0	0	3 (3%)	<1	0	0	0	0
Hazardous error	7 (6%)	1	5 (5%)	1	1 (1%)	<1	0	0
Keypad error	0	0	5 (5%)	1	9 (8%)	1	1 (1%)	<1
Inflexibility error	37 (30%)	3	20 (19%)	2	21 (19%)	3	3 (3%)	<1
Other	70 (57%)	6	68 (64%)	7	69 (64%)	8	79 (80%)	9
Total	123	11	106	11	108	13	99	11

Data are n (%) or rates per 100 admissions. The p value testing global trend across the four study periods was 0.42.

Table 4: System-related errors and event rate by period

together in periods 2 and 3 (appendix pp 8–11). Strength and generic-name or brand-name errors were more likely to occur together in periods 1 and 2, as were errors classified as inadequate follow-up of therapy, and policy-not-followed errors in periods 2 and 4 (appendix pp 8–11).

We found that the negative-binomial model fitted our data better than the Poisson model (the Akaike information criteria was 12489.15 for the negative-binomial model and 15506.82 for the Poisson) and hence present the results that we obtained from this model here. Older patients were found to be more at risk of medication errors than younger patients, with an IRR of medication error of 1.004 (95% CI 1.001–1.007) per year of increase in age ($p=0.0230$; table 5). Total number of medications was also an important risk factor for medication error, with an IRR of medication error of 1.022 (1.017–1.026; $p<0.0001$) per medication added. The error rate for

female patients was 1.2 times higher than for male patients (with an average of 0.31 errors per day [95% CI 0.29–0.34] for female patients and 0.27 errors per day [0.25–0.29] for male patients; data not shown). The estimated IRRs were dependent on the ward and the period in which patients were reviewed.

Discussion

We recorded more than 5000 primary errors in this study, the most common types being medicine-reconciliation, dose, and avoidable delay-of-treatment errors. Although we found no significant change in the overall rate of medication errors per admission, the rates of dose and inappropriate-drug errors were found to have reduced over time. There was also a significant decrease in potential adverse drug events across the four study periods. It is possible that the cumulative effect of system

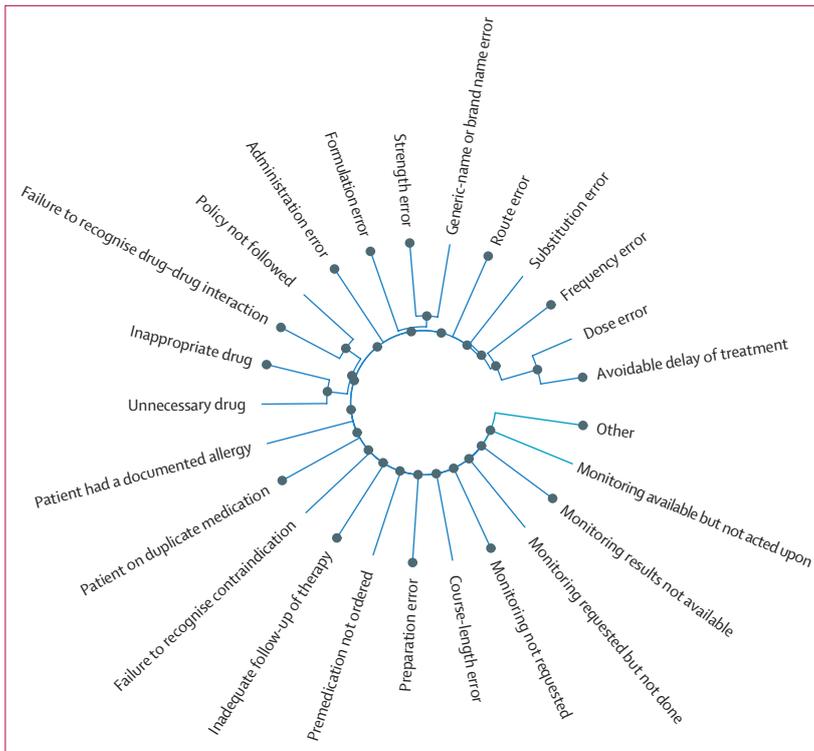


Figure 2: Clustering of medication error types for period 1, when medicine reconciliation was considered as the primary error

optimisation, including clinical decision support and system design changes, contributed to this finding, although further research is needed to confirm this. The clustering of different types of errors appeared to change across the four time periods. This finding is important because future clinical decision support systems will need to monitor and prevent specific types of error that are more likely to occur together.

The medication error rates are similar to those reported by Westbrook and colleagues at two Australian hospitals using commercial electronic prescribing systems.¹⁷ Shulman and colleagues noted a significant reduction in medication errors made after the implementation of an electronic prescribing system in the University College London Intensive Care Unit (London, UK) in 2002, which the authors suggested could have been due to improvements made to the system in light of experience.¹⁸ Similar to our study, Van Doormaal and colleagues also observed a reduction in dosing errors across four wards in two hospitals in the Netherlands more than 10 years ago, but they did not detect a significant change in therapeutic errors (eg, drug interactions, contraindications, and duplicate therapy) or in preventable adverse drug events, possibly because of the insufficiently advanced clinical decision support used.¹⁹ We also found that the incidence of some error types, such as errors due to inadequate follow-up of therapy, increased over time and plan to explore whether advanced clinical decision support could

	Incidence rate ratio (95% CI)	p value
Model intercept	0.166 (0.120–0.228)	<0.0001
Age, per 1-year increase	1.004 (1.001–1.007)	0.0230
Total medication, per added medication	1.022 (1.017–1.026)	<0.0001
Sex*	1.172 (1.060–1.296)	0.0019
Ward†		
Medical ward	0.398 (0.279–0.567)	<0.0001
Surgical ward	1.237 (0.916–1.669)	0.17
Cardiology ward	1.279 (0.955–1.714)	0.10
Period‡		
Period 1	1.354 (0.978–1.876)	0.0679
Period 2	1.193 (0.860–1.657)	0.29
Period 3	0.679 (0.465–0.99)	0.0444
Period 1 medical ward§	1.713 (1.084–2.708)	0.0212
Period 1 surgical ward§	0.492 (0.328–0.738)	0.0006
Period 1 cardiology ward§	0.474 (0.318–0.706)	0.0002
Period 2 medical ward§	1.249 (0.733–2.129)	0.41
Period 2 surgical ward§	0.724 (0.480–1.093)	0.12
Period 2 cardiology ward§	0.74 (0.493–1.11)	0.15
Period 3 medical ward§	2.126 (1.258–3.591)	0.0048
Period 3 surgical ward§	1.747 (1.113–2.741)	0.0153
Period 3 cardiology ward§	1.104 (0.705–1.728)	0.67

*Male was used as reference. †Renal ward was used as reference. ‡Period 4 was used as reference. §Interaction exists between any two of these variables.

Table 5: Factors associated with medication error rates during the study period

reduce this increase by, for example, using targeted reminders for clinicians. We found that the rate of some types of medication error (eg, dose, strength, and inappropriate-drug errors) declined over time. A few checks were introduced into the system that could have contributed to this reduced rate, including dosing alerts and order sets (which presents prescribers with a list of medications and approved doses for a specific condition, such as a peritoneal dialysis order set). Further controlled studies would be helpful in determining the effect and any unintended consequences (such as alert fatigue) of specific forms of clinical decision support and system design changes.

Our clustering analysis revealed how some secondary errors (eg, dose error, avoidable delay-of-treatment, and frequency errors) were more likely to occur together. This clustering is possibly due to the locally configured order sentences—ie, as each medication name was linked to a route, dose, and frequency, selection of the wrong dose would also be linked to an incorrect frequency.

Similarly, these results also showed that errors due to policy not followed and inadequate follow-up of therapy were more likely to occur together, which suggests how further improvements could be made to the electronic system to both improve adherence and patient follow-up. Little has been published about how errors are clustered,

which could be an important area for future work and the customisation of electronic prescribing systems, as targeting one type of error for prevention might have the added benefit of reducing other error types. More advanced and patient-specific clinical decision support, which integrates information from the patient's medical record, could possibly inform clinicians if they were to prescribe an inappropriate dose and associated frequency. Medicine-reconciliation errors also occurred alongside dose errors, highlighting the admission stage as a time of potential risk. Hellström and colleagues found that 313 (47%) of 670 patients had a medication-history error on admission, one of the most common error types being wrong dose error.²⁰ Although advanced clinical decision support could potentially help reduce the rate of such errors, increased involvement of pharmacy services at the point of admission²¹ and improved access to medication information collected in primary care are also crucial.²²

Our study had a few limitations. First, different clinical pharmacists collected data for three of the study wards over the study periods and, although regular meetings were held between the study team and senior clinical pharmacists, it is still possible that there might have been subtle differences between how these pharmacists classified errors. We, therefore, acknowledge that the lack of inter-rater reliability data is a limitation of our work. Second, it is also possible that pharmacists' discussion of errors with physicians resulted in a learning effect, which contributed to the reduced number of certain types of error over time. Third, since this study began, a new standardised medication error classification system has been developed, which includes a tool specifically designed to classify medicine-reconciliation errors.^{23,24} Fourth, data were collected from four wards at one UK hospital trust, which might limit the generalisability of our findings. Fifth, we acknowledge that interrogating the system with a retract and reorder tool might have yielded additional information about potential errors, although this investigation was beyond the scope of our study.²⁵ Future studies should consider the use of such tools. Finally, although the pharmacists recorded whether the electronic prescribing system could have contributed to the occurrence of a medication error (system-related error), we did not investigate the actual cause of these errors.

We found that the number of primary medication errors per admission did not change significantly over the four study periods. However, there was a reduction in some types of error and a significant decrease in the rates of potential adverse drug event between the first three periods and period 4. The identified clustering of different types of errors changed across the different time periods and this observation could be an area for future research, particularly as targeting one type of error for prevention might have the added benefit of reducing other types of error. Optimisation of electronic prescribing systems could contribute to improvements

in patient safety and help harness the full potential of these systems.

Contributors

SPS and DWB conceived this study. SPS, CLT, DWB, AH, and NWW contributed to the study design. RF, KB, and SN contributed to the collection of data. TB did the data analyses, with assistance from AK and EJO. All authors contributed to interpretation of the data. SPS and CLT wrote the first draft of the manuscript. All authors provided critical revisions to the manuscript before seeing and approving the final version. SPS acts as guarantor.

Declaration of interests

DWB consults for EarlySense; receives cash compensation from CDI Negev; receives equity from ValeraHealth, Clew, and MDCOne; and will receive research funding from IBM Watson Health. DWB's financial interests have been reviewed by Brigham and Women's Hospital and Partners HealthCare in accordance with their institutional policies. NWW reports grants from the National Health Service England, National Institute for Health Research, and EU Horizon 2020 outside of the submitted work. All other authors declare no competing interests.

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