TITLE

The association of a critical care electronic prescribing system with the quality of patient care provided by clinical pharmacists - A prospective, observational cohort study

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ABSTRACT

Background

Despite the strong face validity of electronic prescribing (EP), the empiric data in support of improved patient safety is sparse. The objective of this study was to compare the clinical significance of pharmacist contributions between an established EP and paper-based prescribing (PBP) system in the intensive care unit (ICU) to understand the EP impact on the quality of patient care.

Materials and Methods

We conducted a prospective longitudinal study in two 18-bed ICUs; one with EP and the other, PBP. Pharmacist contributions were analysed over three months. Demographic, clinical and adjunctive intervention data were also collected. A multilevel ordinal logistic regression model was used and patients were followed up for 28 days. The primary outcome was the distribution of clinical significance levels of pharmacist contributions.

Results

There were 303 patients admitted to the ICU between April 1st and June 30th 2018. EP was used in 171 patients and PBP in 132 patients. 1658 contributions were analysed. There were 14.9% highly clinically significant contributions with EP compared to 44.6% with PBP. The EP group had lower odds (OR 0.05, 95% CI 0.02-0.12) for a higher clinical significance contribution compared to the PBP group, but this changed over the admission and differed between groups, with decreasing odds of a higher-level clinical contribution for each additional admission day with PBP (OR 0.57, 95%CI 0.42-0.78).

Conclusion

This study showed a significant difference in the distribution of pharmacist contributions made over time, with clinical significance levels remaining stable in the EP group at low severity, as opposed to PBP which were initially high and then gradually decreased in severity over time. This contemporaneous controlled study found EP improved patient safety. The EP system was associated with pharmacists' contributions of lower clinical significance and is an important advance for patient safety.

Keywords

Clinical Pharmacy; Intensive Care; Electronic Prescribing; Medication Safety; Patient Safety,

Abbreviations

EP, Electronic prescribing; PBP, Paper-Based Prescribing; ICUs, Intensive Care Units

1. INTRODUCTION

Electronic prescribing (EP) enables standardised prescribing, legibility and a full audit trail, as well as mandatory data fields to be completed compared to handwritten prescriptions.[1–3] It is widely advocated to reduce medication errors.[4–6] Despite the strong face validity of EP, the empiric data in support of improved patient safety is sparse.[7]

In most intensive care units (ICUs), patient's drug charts are prescribed by doctors and the pharmacists are responsible in reviewing these prescriptions to ensure safe use and optimisation of medicines. The impact of EP systems in improving the overall prescribing quality in the ICU has not been well studied. Much of the preceding literature studying EP compared to paper-based prescribing (PBP) systems has focused solely on the impact on medication errors,[2, 7–11] with a small number of studies in the intensive care setting.[3, 12–14] Within the ICU setting, a systematic review and meta-analysis concluded that EP is likely to reduce rates of medication errors, particularly prescribing errors[15] but did not focus on other quality aspects of medication safety such as drug interactions or optimisations, or on the clinical significance of these. While ICU pharmacists play a key role in identifying and rectifying medication errors, they also add value by delivering proactive clinical contributions to optimise medication therapy, reduce costs and improve patient outcomes.[16–20] Therefore, we conceptualize pharmacy contributions as a composite of both reducing errors and optimising medical therapy in prescriptions written by doctors.

There are other limitations to existing literature. Most studies in this area used pre- and post-implementation designs,[9–13] which are subject to secular trends.[21, 22] Additionally, there is no standardised denominator for the outcome used. Studies have used a range of denominators such as errors per total number of prescriptions, per total number of drugs and per 1000 patient days. These outcomes are sensitive to the number of prescriptions and number of drugs per patient as well as length of stay, limiting the generalisability of the study findings.[23] These outcome measures also do not account for the bias of repeated measurements in the same patient. To date no studies have compared the pharmacist clinical contributions in improving the quality of prescribing between PBP and EP systems in the ICU.

The primary objective of this study was to compare the distribution of the clinical significance of pharmacist contributions between an established EP and PBP system in the ICU to better understand the EP impact on the quality of patient care. Our study adds to the current body of literature in two ways. Firstly, using a longitudinal design enables the observation of changes over time.[22] Secondly, we employ a novel approach by clustering the outcome to the patient instead of patient days. This allows a more generalisable interpretation of the observed outcome to patients treated and accounts for the repeated measures of bias of multiple prescriptions for the same patient.

To our knowledge, this is the first prospective, longitudinal study with a contemporaneous control of its type.

2. MATERIALS AND METHODS

2.1 Study design and setting

1000-bed urban academic hospital in London, UK, with 50 general intensive care beds of similar patient case-mix across three locations in the same hospital. The study took place on two 18-bed units. The clinical pharmacy service provided to the units was similar, comprising a weekday pharmaceutical review of all patients. Pharmaceutical reviews involved a combination of either being conducted on the multidisciplinary ward round, during an independent pharmacist ward visit or by a phone consultation.

All consecutive patients admitted to one of the two 18-bedded ICUs between April 1st and June 30th 2018, were considered eligible for study participation. Patient inclusion criteria: Adults (aged 18 years or above) admitted to one of the two participating ICUs. Patients with missing identifiers, those not reviewed by an ICU pharmacist due to out-of-hours admission and discharge, and any ICU readmissions were excluded. Included patients were followed up until ICU discharge, death, or 28 days from admission, depending on which was first.

2.2 Exposure

One unit used an informatics system - Philips Healthcare IntelliSpace Critical Care & Anaesthesia (ICCA), revision H - including an EP module, implemented 18 months prior to the study. The system did not have any clinical decision support. The other unit had a PBP system, which used different types of paper drug charts for all prescribing. Both units had electronic access to laboratory (blood results), radiology and clinical notes via electronic patient records.

2.3 Outcome Measures

The primary outcome was the distribution of clinical significance levels of pharmacist contributions overall and over time, using the IMPACCTS (InstruMent for rating PhArmacy Clinical Contributions To Care Significance) rating tool. IMPACCTS has been designed and validated to guide the user to make a decision about the most likely outcome for both errors and optimisations.[24] The tool assigns a clinical significance rating to pharmacists' contributions based on the mitigation of the risk or negative outcome for the patient, had the pharmacist not intervened. It comprises a five-level rating scale, with level I assigned to 'good practice' contributions and level V assigned to contributions which potentially prevented severe harm, organ damage or loss of life (Supplementary File, Figure 4). Contributions could be either in response to a medication error, a medication optimisation, or a consult (Supplementary File, Definitions). Consults were not rated for clinical significance as they were reactive contributions. Where a pharmaceutical daily review resulted in no contribution, called 'no change', these were noted separately.

2.4 Study Size

Based on data from a seven-day pilot study, a sample size of 1191 pharmacist contributions clustered within 268 patients was required to show a difference of 10% in the proportion of highly significant contributions between groups (control group proportion 60%; alpha 0.05; power 90%; intraclass correlation 0.01; mean cluster size 4; attrition rate 10%).

2.5 Data collection

Anonymised data on pharmacist contributions were recorded by the attending pharmacist who was trained to use the rating tool. Pharmacists swapped ICUs half-way through the study period to minimise

reporter bias. The intensive care experience of the pharmacist data collectors ranged from 2.5 to 3.5 years. Contribution data recorded included date, reason, type (medication error, optimisation or consult), contribution setting, day of patient stay, British National Formulary drug category and clinical significance rating. Data was only collected Monday to Friday as there was a limited weekend pharmacy service.

Demographic data included age, sex, pre-existing comorbidities, reason for admission, admission laboratory values, APACHE II score, maximum organ support and level of ICU care. To determine individual patients' ICU length of stay and total patients' length of stay in each group, dates of ICU admission and discharge or death were also recorded.

2.6 Data analysis

Descriptive analyses are presented as median (IQR) or number (%). Univariate comparisons were conducted using Wilcoxon rank-sum tests or chi-square tests, as appropriate for the type of data. The exposure of interest was the type of prescribing system (EP versus PBP). The outcome of interest was the clinical significance level of each pharmacist contribution. The primary unit of analysis was pharmacist contributions, which were considered to be time-dependent and clustered within patients, leading to a longitudinal two-level data structure.

In the main analysis, we used a multilevel ordinal logistic regression model, with patient-level random intercepts and clinical significance levels as outcome levels. Covariate selection and model comparisons were guided by Likelihood Ratio Tests (LRTs), or the Akaike Information Criteria (AIC) for non-nested models. All standard errors were estimated using robust cluster variance (sandwich) estimators. Model fit was tested using plots of predicted and observed values.

2.7 Sensitivity analysis

We also conducted two sensitivity analyses to test the robustness of our primary analysis to alternate specifications of the outcome variable. In the first, we dichotomised the outcome into 'high clinical significance' (level III or above) or 'low clinical significance' (level I and II) contributions in a two-level

logistic regression model. In the second, we used a similar multilevel ordinal regression model to the main analysis but included a separate category called ‘no change’. This approach then measures the ordinal effect from ‘no change’ to ‘low clinical significance’ as an additional category. The additional category of ‘no change’ was sensitive to the potential substitution effect between low clinical significance contributions and no contribution.

All statistical tests were two-sided, with an α-level of 0.05 for statistical significance. We did not impute any missing data. Analyses were performed using Stata/MP version 16.1 (StataCorp). Details regarding the statistical approach are provided in the Supplementary File.

Local and regional regulatory and review board approvals were obtained (Ref: KCH 18-169) and (Health Research Authority project ID 248318) which waived the need for informed patient consent and ethics committee review. The report of our findings is based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement[25] and Statement on Reporting of Evaluation Studies in Health Informatics (STARE-HI).[26]

RESULTS

Between April 1st and June 30, 2018, 388 patients were assessed for eligibility and 303 were included in the study, 132 in the PBP group and 171 in the EP group, as seen in Figure 1.

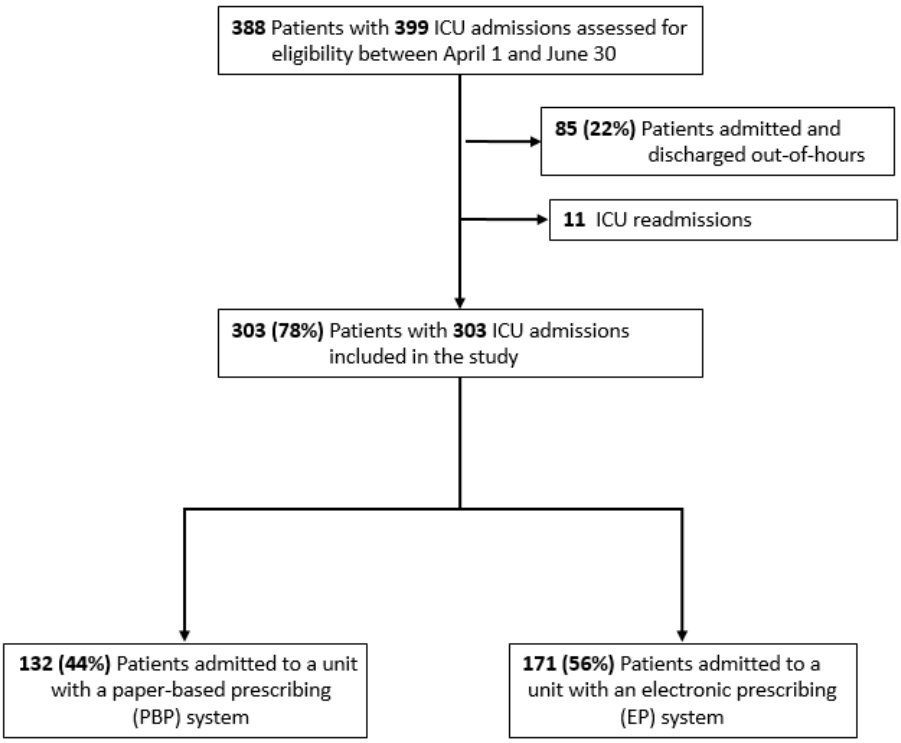

Figure 1. Flowchart of patient inclusion and exclusion from the study

The characteristics of included patients are shown in Table 1.

	Study population (N=303)	Paper Prescribing (N=132)	Electronic prescribing (N=171)	p-value[1]
Age in years [2]	58.5 (44-72.5)	60.5 (48.0-73.0)	57.5 (41.0-72.0)	0.200
18-39 (%)	51 (16.8)	14 (10.6)	37 (21.6)	
40-59 (%)	98 (32.3)	48 (36.4)	50 (29.2)	
60-79 (%)	107 (35.3)	49 (37.1)	58 (33.9)	
≥ 80 (%)	36 (11.9)	15 (11.4)	21 (12.3)	
Female sex [2] (%)	121 (39.3)	54 (40.9)	67 (39.2)	0.668
Comorbidities [3] (%)				
Hypertension	103 (34.0)	36 (27.3)	67 (39.2)	0.034
Diabetes mellitus	58 (19.2)	28 (21.2)	30 (17.5)	0.402
IHD	55 (18.1)	22 (16.7)	33 (19.3)	0.576
ESRD on dialysis	12 (4.0)	5 (3.8)	7 (4.1)	0.903
COPD	31 (10.2)	11 (8.3)	20 (11.7)	0.349
CVA	24 (7.9)	11 (8.3)	13 (7.6)	0.800
Reason for ICU admission [2] (%)				0.174
Surgical	83 (27.4)	41 (31.1)	42 (24.6)	
Medical	209 (69.0)	85 (64.4)	124 (72.5)	

Laboratory values [2]				
Albumin; $g.L^{-1}$	32.0 (27-36)	32.0 (28-36)	32.0 (27-36)	0.829
Bilirubin; $umol.l^{-1}$	11.0 (8-19)	12.0 (8-18)	11.0 (7-20)	0.681
Creatinine; $umol.l^{-1}$	100.0 (72-122)	99.5 (71-120)	100.0 (73-128)	0.423
APACHE II score [4]	11 (7-17)	12 (8-18)	10 (7-15)	0.020
Organ support (%)				
Vasopressors/Inotropes	150 (49.5)	81 (61.4)	69 (40.3)	<0.001
Mechanical ventilation	152 (50.2)	81 (61.4)	71 (41.5)	0.001
RRT	56 (18.5)	20 (15.1)	36 (21.0)	0.189
Level of ICU care [5] (%)				<0.001
Level 1	23 (7.6)	2 (1.5)	21 (12.3)	
Level 2	117 (38.6)	42 (31.8)	75 (43.9)	
Level 3	160 (52.8)	86 (65.1)	74 (43.3)	
Length of ICU stay [2]; days	5.0 (2-9)	5.0 (3-12)	4.0 (2-8)	0.040
Patient-days in ICU [2] (%)				
Total	2422 (100)	1200 (100)	1222 (100)	
Observed	1687 (69.6)	831 (68.4)	856 (70.0)	0.669[6]

Abbreviations: ICU - Intensive Care Unit; ESRD - End-Stage Renal Disease; COPD - Chronic Obstructive Pulmonary Disease; APACHE II - Acute Physiology And Chronic Health Evaluation score version II; RRT - Renal Replacement Therapy; CVA - Cerebrovascular Accident; IHD -Ischaemic Heart Disease

[1] Two-sample Wilcoxon rank-sum (Mann-Whitney) test or chi-squared test, as appropriate

[2] Data were missing for 11 patients (3.6%)

[3] Comorbidity data are missing for 1 patient

[4] APACHE-2 score was missing for 23 patients (7.6%)

[5] ICU level was missing for 3 patients (1%)

[6] z-test for two sample proportions

Table 1 Baseline characteristics of study population. Data are presented as N (%) or Median (IQR), as appropriate

Patients in the two groups were similar in age (median 58.5, overall IQR 44-72.5), sex, reason for ICU admission and admission laboratory values. Nearly three-quarters of the patients in the study were admitted for medical reasons. The mean Acute Physiology and Chronic Health Evaluation (APACHE) II

scores between the two groups of patients were different, with a higher acuity on the unit using a PBP system. The PBP group also had a slightly longer length of stay. There was no statistically significant difference between the comorbidities of both groups, except for hypertension, which was more frequent in the EP group.

The characteristics of pharmaceutical reviews and pharmacist contributions are shown in Table 2.

	Study population	**Paper Prescribing**	**Electronic prescribing**	**p-value**[1]
Pharmaceutical Reviews	**N=1687**	**N=831**	**N=856**	
Reviews per patient	3 (2-6)	4 (2-8)	3 (2-5)	0.028
Review outcome				0.725
no change	825 (48.9)	410 (49.3)	415 (48.5)	
with contribution	862 (51.1)	421 (50.7)	441 (51.5)	
Pharmacist Contributions	**N=1648**	**N=708**	**N=940**	
Contributions per patient	4 (2-8)	4 (2-8.5)	4 (2-7)	0.886
Contribution setting (%)				<0.001
Ward round	1417 (86.0)	648 (91.5)	769 (81.8)	
Ward visit	164 (9.9)	20 (2.8)	144 (15.3)	
Phone consultation	67 (4.1)	40 (5.6)	27 (2.9)	
Day of week [2] (%)				0.025
Monday	330 (20.0)	161 (22.7)	169 (18.0)	
Tuesday	378 (22.9)	162 (22.9)	216 (23.0)	
Wednesday	321 (19.5)	123 (17.4)	198 (21.1)	
Thursday	330 (20.0)	151 (21.3)	179 (19.0)	
Friday	288 (17.5)	110 (15.5)	178 (18.9)	
Pharmacist experience [2] (%)				0.016
<3 years	1490 (90.4)	624 (88.1)	866 (92.1)	
≥3 years	157 (9.5)	83 (11.7)	74 (7.9)	
Contribution type (%) [3]				
Consult	63 (3.8)	38 (5.4)	25 (2.7)	<0.001
Medication error	254 (15.4)	86 (12.1)	168 (17.9)	
Medication optimisation	1329 (80.6)	582 (82.2)	747 (79.5)	
Clinical significance rating (%) [4]				<0.001
Level I	76 (4.6)	21 (3.0)	55 (5.8)	
Level II	1049 (63.6)	331 (46.7)	718 (76.4)	
Level III	419 (25.4)	285 (40.2)	134 (14.3)	
Level IV	37 (2.2)	31 (4.4)	6 (0.6)	
Reason for contribution [4] (%)				<0.001
Medication correction/enhancements	480 (29.1)	212 (29.9)	268 (28.5)	
Untreated indication	279 (16.9)	139 (19.6)	140 (14.9)	

Governance	145 (8.8)	48 (6.8)	97 (10.3)	
Risk reduction	100 (6.1)	61 (8.6)	39 (4.1)	
Adherence to policies/guidelines	80 (4.8)	47 (6.6)	33 (3.5)	
Medication not indicated/ weaning	399 (24.2)	113 (16.0)	286 (30.4)	
Medicines reconciliation on admission	98 (5.9)	48 (6.8)	50 (5.3)	
BNF Drug category [5] (%)				0.037
Nervous system	416 (25.3)	162 (23.0)	254 (27.0)	
Cardiovascular system	328 (19.9)	145 (20.6)	183 (19.5)	
Anti-infective	320 (19.5)	132 (18.7)	188 (20.0)	
Gastrointestinal system	309 (18.8)	145 (20.6)	164 (17.5)	
Endocrine system	96 (5.8)	55 (7.8)	41 (4.4)	
Blood & Nutrition	93 (5.7)	41 (5.8)	52 (5.5)	

Abbreviations: BNF, British National Formulary.

[1] Two-sample Wilcoxon rank-sum (Mann-Whitney) test, chi-squared test, or test of two proportions, as appropriate

[2] Data are missing for 1 contribution (<1%)

[3] Data are missing for 2 contributions (<1%)

[4] Data are missing for 4 contributions (<1%). Also, 63 consults were excluded from this categorisation

[5] BNF category was assigned only to contributions which involved a drug. Data are presented for the 6 most common categories. BNF category was missing in 4 contributions (<1%). Also, 63 consults were excluded from this categorisation

Table 2 Characteristics of pharmaceutical reviews & pharmacist contributions. Data are presented as N (%) or Median (IQR), as appropriate

The PBP group had a significantly higher number of pharmaceutical reviews per patient but the number of pharmacist contributions per patient was not different overall (median 4, overall IQR 2-8). The frequency of pharmaceutical reviews with ‘no changes’ were similar in both groups. 86% of all contributions took place on the ward round, 92% in PBP compared to 82% on EP, with the majority being optimisations in both groups.

68.2% of all contributions were level I or II (low clinical significance) and 27.6% were level III or IV (high clinical significance). There were no level V contributions. The unadjusted distribution of clinical significance rating differed between the two groups. There were significantly fewer level III and IV contributions in the EP group (14.9%) compared to PBP group (44.6%).

After adjustment for confounders, among patients who had a pharmacist contribution, the EP group had a 95% lower odds of having a contribution of higher clinical significance, compared to the PBP group (adjusted OR = 0.05, 95%CI 0.02-0.12, $p<0.001$). The distribution of clinical significance levels changed significantly over the course of admission, with decreasing odds of a higher-level contribution for each additional admission day in the PBP group (OR 0.57, 95%CI 0.42-0.78, $p<0.001$). An area map of the marginal probability over time of a contribution being in one of the four included levels (Levels I-IV) is shown in Figure 2.

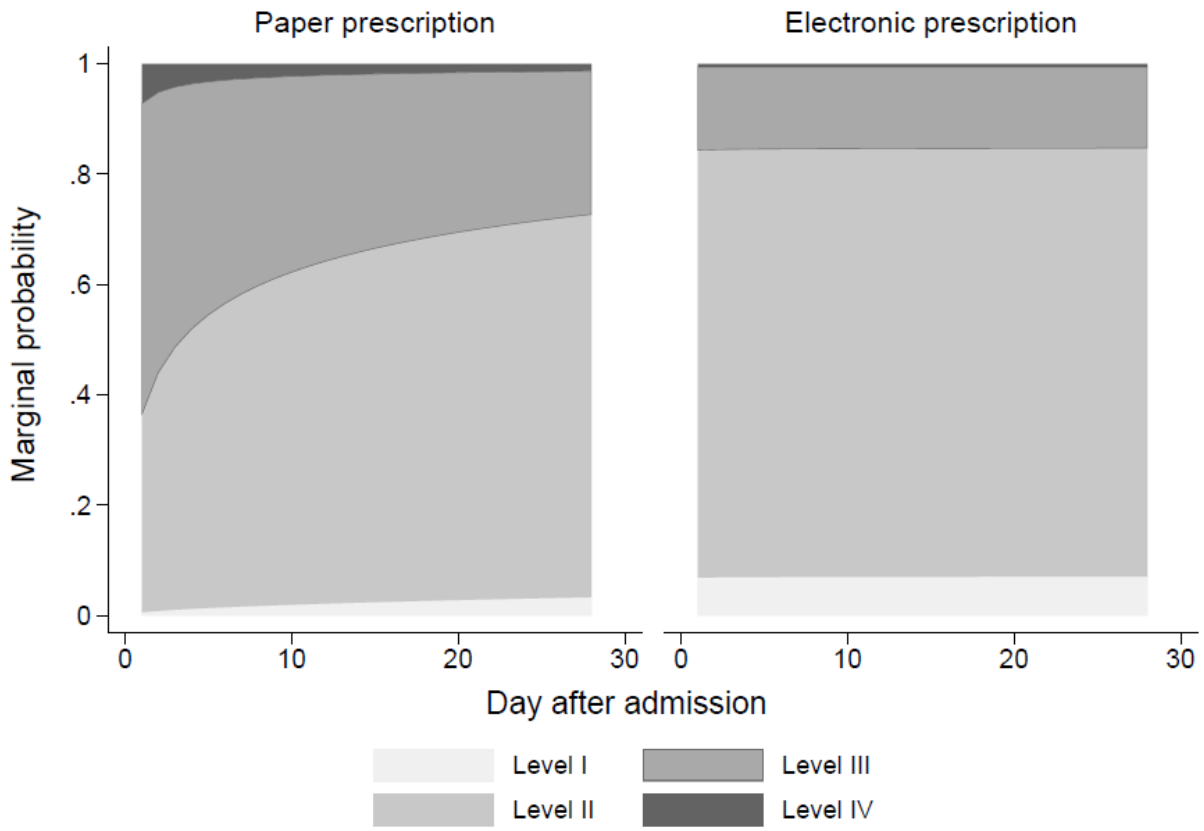

Figure 2. The marginal probability of a contribution being in one of the four levels (Levels I-IV) over the course of the first 28 days of ICU admission

The effects of all other covariates included in the analysis are shown in Figure 3. After adjusting for all covariates, only Renal Replacement Therapy (RRT) (OR 2.23, 95%CI 1.45-3.44, p<0.001) and longer pharmacist experience (OR 8.02, 95%CI 5.01-12.80, p<0.001) remained significantly associated with contributions of a higher clinical significance rating.

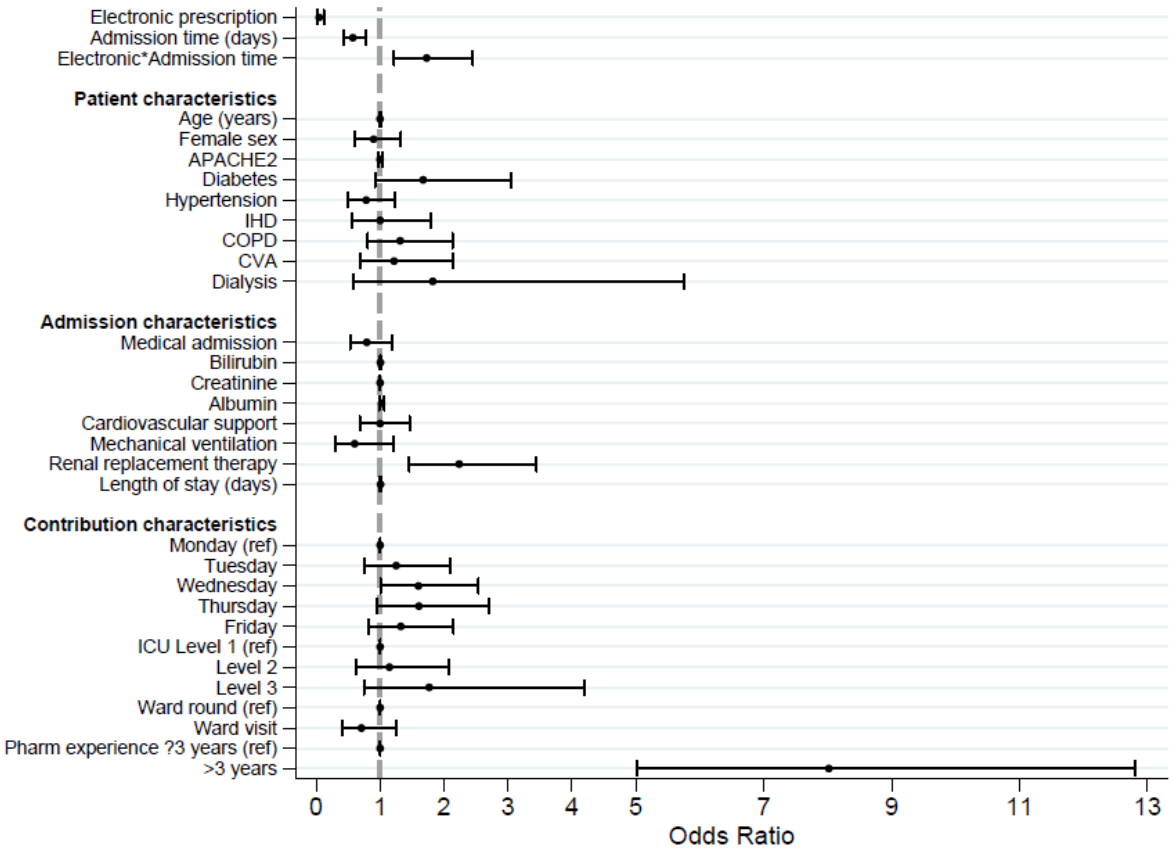

Figure 3. The adjusted effect of all covariates using a multilevel ordinal logistic regression model

All findings described above, including the effect of the prescribing system used, admission time, RRT and pharmacist experience remained unchanged when we took into account the pharmaceutical reviews where no contributions were made, either in a logistic model or as a separate category in an ordinal model as part of our sensitivity analyses (Supplementary File).

A comparison of the characteristics of excluded patients (admitted out-of-hours) and study population can be found in the Supplementary File, Tables 3 and 4. There were no significant differences between the groups except for a shorter length of stay, higher acuity and more deaths in the out of hours admissions.

DISCUSSION

This study showed that the EP system is associated with improved patient safety and quality of prescribing. We also showed that there was a significant difference in the distribution of pharmacist contributions made over time, with clinical significance levels remaining stable in the EP group at low severity, as opposed to PBP which are initially high and then gradually decrease in severity over time.

EP showed a higher proportion of contributions of low clinical significance. Reasons for less severe contributions with EP could be that EP facilitated easier access to data for decision-making. This included access to prescribing support such as clinical guidelines at the point of prescribing, the use of medication order sets with dose limits, easier access to primary care health records, biochemistry and observations. Prescriptions are also more complete and legible. The majority of the level II contributions in EP were failures to discontinue infusion prescriptions which were no longer needed. This phenomenon was seen in previous studies.[2, 14, 27]

Previous studies have suggested the admission stage of an ICU stay is a peak time for potential risk of errors from dosing and medicines reconciliation,[10] associated with increased patient morbidity, mortality and hospital readmission rates.[27] Our study followed the patients over 28 days and this is in keeping with our observations for PBP, where the clinical significance of the contributions at admission were higher but declined over time. This was not observed in the EP group, where on admission the clinical significance of contributions were lower and remained stable over time. This is likely related to the availability of prescribing support provided with EP.[2, 12]

Whilst there are a large number of studies looking at reductions in medication error rates in favour of EP, this study adds to the context of including the full range of clinical pharmacist activities and the impact of these between the two prescribing systems. In other studies, unvalidated scales or those adapted from other scales or tools validated for medication errors only have been used[16, 28–30] to evaluate the potential clinical impact on patient outcomes comparing EP and PBP systems. As a result, the clinical significance of the contributions made in the study cannot be compared to other studies due the high degree of heterogeneity of rating scales used.

Our study has several strengths. First, the EP system had been established for 18 months prior to commencing the study; therefore users were familiar with the system and issues regarding peri-implementation of a new system were not a factor, such as in other studies.[9, 12] Second, the application of a contemporaneous design is an improvement on before-after studies, where the observed effects may be subject to secular trends. Third, no previous studies have followed patients through their stay to examine the longitudinal effects of EP. Finally, we used a novel outcome of both errors and optimisations which more accurately reflects the true value of EP than previous studies.

Our study has some limitations. As different clinical pharmacists collected data, it is possible that there might have been variation between how these pharmacists graded the contributions. We did rotate pharmacists mid-point through the study to reduce bias, but acknowledge that the lack of inter-rater reliability data is a limitation of our work. It is known that all medication errors cannot be detected by one method.[31, 32] As our study did not include live observations of the medication use processes or retrospective chart analysis, it is possible that other differences between EP and PBP have not been identified. However, this was not an objective of the study. The potential patient outcome can only be estimated, as pharmacist contributions are usually preventative in nature. However, IMPACCTS has been designed and validated to guide the user to make a decision about the most likely outcome. Finally, results from this single centre study may not be generalisable to all settings due to differences in software and/or clinical practice.

CONCLUSION

In conclusion, this contemporaneous controlled study found EP improved patient safety and quality of prescribing. The distribution of clinical significance levels differed significantly between the two prescribing systems. The EP system in this study resulted in pharmacists' contributions of lower clinical significance. In addition, with PBP the clinical significance of the contributions changed over time. These findings were robust to several sensitivity analyses. Future studies should consider the cost implications of EP. Cost and resource use are higher in ICU patients than non-ICU patients[33–35] and a cost-benefit

analysis of the contributions made using the respective systems would be beneficial. Reasons for prescribers' behavioural changes with EP also need to be better understood.

This is the first published study of its kind and advances previous knowledge on this topic. The implications of these findings are that EP is an important advance in the patient safety agenda in ICU.

Author contributions

RMeh & RO conceived the study. All authors contributed to the design. Material preparation and data collection were performed by RMeh & RS. SV performed the data analyses. The first draft of the manuscript was written by RMeh and all authors provided comments. All authors read and approved the final manuscript.

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Statement on conflicts of interest

The authors declare that they have no known competing financial or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval

This is an observational study. The Health Research Authority has confirmed that no ethical approval is required.

Summary Table

What is already known on this topic	What this study added to our knowledge
• Electronic prescribing improves some elements of prescription quality, notably standardised prescribing, legibility and a full audit trail	• Electronic prescribing improved the overall quality of prescribing in intensive care as measured by pharmacists' clinical contributions
• Electronic prescribing is advocated to reduce medication errors	• Pharmacy contributions with the electronic prescribing system had lower clinical significance than with paper prescribing
• The admission stage of an ICU stay is a peak time for potential errors from dosing and medicines reconciliation	• Clinical significance of contributions with electronic prescribing remained low throughout a patient's stay, whilst with paper prescribing, contributions were initially of high significance, gradually decreasing in severity over time
• Impact of electronic prescribing on improving overall quality of prescribing and/or optimisation of medicines in intensive care is not well known	• With electronic prescribing, patients had more appropriate and effective medication therapy prescribed

REFERENCES

1. Goundrey-Smith S. EP Systems as a Risk Management Tool. In: Principles of electronic prescribing. 2nd ed, Springer, London 2012:pp 69–95
2. Franklin BD, Puaar S. What is the impact of introducing inpatient electronic prescribing on prescribing errors? A naturalistic stepped wedge study in an English teaching hospital. *J Health Inform* 2020;26:3152–3162. http://doi.org/10.1177/1460458219833112
3. Ali J, Barrow L, Vuylsteke A. The impact of computerised physician order entry on prescribing practices in a cardiothoracic intensive care unit. *Anaesthesia* 2010;65:119–123. http://doi.org/10.1111/j.1365-2044.2009.06134.x
4. NHS Connecting for Health (NHS CFH). Electronic prescribing in hospitals - challenges and lessons learned. 2009. Available at: http://www.connectingforhealth.nhs.uk/eprescribing. Accessed June 15, 2021,
5. Healthcare Safety Investigation Branch. Electronic prescribing and medicines administration systems and safe discharge. 2019. Available at: www.hsib.org.uk/tell-us-what-you-think. Accessed March 03, 2021
6. Department of Health & Social Care. The Report of the Short Life Working Group on reducing medication-related harm. 2018. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/683430/short-life-working-group-report-on-medication-errors.pdf. Accessed June 17, 2021
7. Gates PJ, Hardie R-A, Raban MZ, et al. How effective are electronic medication systems in reducing medication error rates and associated harm among hospital inpatients? A systematic review and meta-analysis. *J Am Med Inform Assoc* 2021;28:167–176. http://doi.org/10.1093/jamia/ocaa230
8. Nuckols TK, Smith-Spangler C, Morton SC, et al. The effectiveness of computerized order entry at reducing preventable adverse drug events and medication errors in hospital settings: a systematic review and meta-analysis. *Syst Rev* 2014;3:56. http://doi.org/10.1186/2046-4053-3-56

9. Donyai P, O'Grady K, Jacklin A, et al. The effects of electronic prescribing on the quality of prescribing. *Br J Clin Pharmacol* 2008;65:230–237. http://doi.org/10.1111/j.1365-2125.2007.02995.x

10. Slight SP, Tolley CL, Bates DW, et al. Medication errors and adverse drug events in a UK hospital during the optimisation of electronic prescriptions: a prospective observational study. *Lancet Digit Health* 2019;1:e403–e412. http://doi.org/10.1016/S2589-7500(19)30158-X

11. Rouayroux N, Calmels V, Bachelet B, et al. Medication prescribing errors: a pre- and post-computerized physician order entry retrospective study. *Int J Clin Pharm* 2019;41:228–236. http://doi.org/10.1007/s11096-018-0747-0

12. Liao TV, Rabinovich M, Abraham P, et al. Evaluation of medication errors with implementation of electronic health record technology in the medical intensive care unit. *J Clin Trials* 2017;9:31–40. http://doi.org/10.2147/OAJCT.S131211

13. Shulman R, Singer M, Goldstone J, et al. Medication errors: a prospective cohort study of hand-written and computerised physician order entry in the intensive care unit. *Crit Care* 2005;9:R516–R521. http://doi.org/10.1186/cc3793

14. Colpaert K, Claus B, Somers A, et al. Impact of computerized physician order entry on medication prescription errors in the intensive care unit: a controlled cross-sectional trial. *Crit Care* 2006;10:R21. http://doi.org/10.1186/cc3983

15. Prgomet M, Li L, Niazkhani Z, et al. Impact of commercial computerized provider order entry (CPOE) and clinical decision support systems (CDSSs) on medication errors, length of stay, and mortality in intensive care units: a systematic review and meta-analysis. *J Am Med Inform Assoc* 2017;24:413–422. http://doi.org/10.1093/jamia/ocw145

16. Bourne RS, Dorward BJ. Clinical pharmacist interventions on a UK neurosurgical critical care unit: a 2-week service evaluation. *Int J Clin Pharm* 2011;33:755–758. http://doi.org/10.1007/s11096-011-9538-6

17. Shulman R, McKenzie CA, Landa J, et al. Pharmacist's review and outcomes: Treatment-enhancing contributions tallied, evaluated, and documented (PROTECTED-UK). *J Crit Care* 2015;30:808–813. http://doi.org/10.1016/j.jcrc.2015.04.008

18. Chant C, Dewhurst NF, Friedrich JO. Do we need a pharmacist in the ICU? *Intensive Care Med* 2015;41:1314–1320. http://doi.org/10.1007/s00134-015-3718-0

19. Borthwick M. The role of the pharmacist in the intensive care unit. *J Intensive Care Soc* 2019;20:161–164. http://doi.org/10.1177/1751143718769043

20. Lee H, Ryu K, Sohn Y, et al. Impact on patient outcomes of pharmacist participation in multidisciplinary critical care teams: A systematic review and meta-analysis. *Crit Care Med* 2019;47:1243–1250. http://doi.org/10.1097/CCM.0000000000003830

21. Aggarwal R, Ranganathan P. Study designs: Part 4-Interventional studies. *Perspect Clin Res* 2019;10:137–139. http://doi.org/10.4103/picr.PICR_91_19

22. Coggon D, Rose G, Barker D. Longitudinal studies. In: Epidemiology for the Uninitiated. 5th ed, BMJ Books, 2009:pp 42–45

23. Reckmann MH, Westbrook JI, Koh Y, et al. Does computerized provider order entry reduce prescribing errors for hospital inpatients? A systematic review. *J Am Med Inform Assoc* 2009;16:613–623. http://doi.org/10.1197/jamia.M3050

24. Mehta R, Onatade R. Content validity of a tool for rating the significance of pharmacists' clinical contributions in hospital settings. In: United Kingdom Clinical Pharmacy Association Symposium. 2016. https://ukclinicalpharmacy.org/wp-content/uploads/2017/05/UKCPA_Conference_Abstracts_November2016.pdf. Accessed Nov 2021

25. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies. *Int J Surg* 2014;12:1495–1499. http://doi.org/10.1016/j.ijsu.2014.07.013

26. Talmon J, Ammenwerth E, Brender J, et al. STARE-HI—Statement on reporting of evaluation studies in Health Informatics. *Int J Med Inform* 2009;78:1–9. http://doi.org/10.1016/j.ijmedinf.2008.09.002

27. Bell CM, Brener SS, Gunraj N, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA* 2011;306:840–847. http://doi.org/10.1001/JAMA.2011.1206

28. Rudall N, McKenzie C, Landa J, et al. PROTECTED-UK – Clinical pharmacist interventions in the UK critical care unit: exploration of relationship between intervention, service characteristics and experience level. *Int J Pharm Pract* 2017;25:311–319. http://doi.org/10.1111/ijpp.12304

29. Bourne RS, Choo CL, Dorward BJ. Proactive clinical pharmacist interventions in critical care: effect of unit speciality and other factors. *Int J Clin Pharm* 2014;22:146–154. http://doi.org/10.1111/ijpp.12046

30. Richter A, Bates I, Thacker M, et al. Impact of the introduction of a specialist critical care pharmacist on the level of pharmaceutical care provided to the critical care unit. *Int J Pharm Pract* 2016;24:253–261. http://doi.org/10.1111/ijpp.12243

31. Montesi G, Lechi A. Prevention of medication errors: detection and audit. *Br J Clin Pharmacol* 2009;67:651–5. http://doi.org/10.1111/j.1365-2125.2009.03422.x

32. Härkänen M, Turunen H, Vehviläinen-Julkunen K. Differences between methods of detecting medication errors: A secondary analysis of medication administration errors using incident reports, the global trigger tool method, and observations. *J Patient Saf* 2020;16:168–176. http://doi.org/10.1097/PTS.0000000000000261

33. Shorr AF. An update on cost-effectiveness analysis in critical care. *Curr Opin Crit Care* 2002;8:337–343. http://doi.org/10.1097/00075198-200208000-00011

34. Dasta JF, McLaughlin TP, Mody SH, et al. Daily cost of an intensive care unit day: The contribution of mechanical ventilation. *Crit Care Med* 2005;33:1266–1271. http://doi.org/10.1097/01.CCM.0000164543.14619.00

35. Kaier K, Heister T, Wolff J, et al. Mechanical ventilation and the daily cost of ICU care. *BMC Health Serv Res* 2020;20:267. http://doi.org/10.1186/s12913-020-05133-5