Medication audit and feedback by a clinical pharmacist decrease medication errors at the PICU: An interrupted time series analysis

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Abstract
Objective: Medication errors (MEs) are one of the most frequently occurring types of adverse events in hospitalized patients and potentially more harmful in children than in adults. To increase medication safety, we studied the effect of structured medication audit and feedback by a clinical pharmacist as part of the multidisciplinary team, on MEs in critically ill children.

Method: We performed an interrupted time series analysis with 6 preintervention and 6 post-intervention data collection points, in a tertiary pediatric intensive care unit. We included intensive care patients admitted during July to December 2013 (preintervention) and July to December 2014 (postintervention). The primary endpoint was the prevalence of MEs per 100 prescriptions. We reviewed the clinical records of the patients and the incident reporting system for MEs. If an ME was suspected, a pediatrician-intensivist and a clinical pharmacist determined causality and preventability. They classified MEs as harmful according to the National Coordinating Council for Medication Error Reporting and Prevention categories.

Results: We included 254 patients in the preintervention period and 230 patients in the postintervention period. We identified 153 MEs in the preintervention period, corresponding with 2.27 per 100 prescriptions, and 90 MEs in the postintervention period, corresponding with 1.71 per 100 prescriptions. Autoregressive integrated moving average analyses revealed a significant change in slopes between the preintervention and postintervention periods ($\beta = -0.21; 95\% \text{ CI}, -0.41$ to $-0.02; P = .04$). We did not observe a significant decrease immediately after the start of the intervention ($\beta = -0.61; 95\% \text{ CI}, -1.31$ to $0.08; P = .07$).

Conclusion: The implementation of a structured medication audit, followed by feedback by a clinical pharmacist as part of the multidisciplinary team, resulted in a significant reduction of MEs in a tertiary pediatric intensive care unit.

KEYWORDS
harm, ITS, medication error, multifaceted intervention, pharmacist, PICU
INTRODUCTION

Medication errors (MEs) are among the most frequently occurring types of adverse events in hospitalized patients, and 3% to 10% of MEs result in patient harm.1-3 Medication errors are also associated with additional costs up to $8,500 per patient, as estimated for hospitals in the United States.4 The reported prevalence of MEs varies from 5 to 24 per 100 prescriptions in pediatric inpatients.5-8 A previous study suggested that MEs are potentially more harmful in children than in adults.6 Children admitted to pediatric intensive care units (PICUs) are especially vulnerable to harmful MEs because of their dependence on multiple and life-supporting medications.9

Because of the growing awareness of the complexity of the medication process and medication safety issues, it has been suggested that active involvement of a clinical pharmacist on pediatric wards might be of additional value. Three systematic reviews report a reduction of MEs after a pharmacist was employed on clinical wards, but the included studies do not provide a clear description of the interventions by the clinical pharmacist.10-12 In addition, quality issues arise as most of the included publications involved observational studies, before-and-after designs were without a control group, or the MEs were self-reported by the intervening pharmacist.10-12 A recent Cochrane systematic review13 included only 1 high-quality, controlled before-after study that showed a significant reduction of serious MEs after the implementation of a multifaceted intervention by a full-time clinical pharmacist on a PICU.14

Since available evidence is scarce, we decided to study the effect of a structured audit of prescribed medication, followed by feedback to the prescribing pediatrician-intensivist and bedside nurse by a clinical pharmacist as part of the multidisciplinary PICU team. We formulated the following research questions:

- Do MEs and medication-related patient harm on a PICU decrease after the implementation of a structured medication audit, followed by feedback from a clinical pharmacist as part of a multidisciplinary team?
- What types of recommendations are made by the clinical pharmacist and to what extent are they accepted by the medical and nursing staff?

METHODS

The Institutional Review Board of the Academic Medical Center in Amsterdam ascertained that medical ethical approval was not required. All patients were informed about the fact that health-related data collected routinely could be used for quality improvement, evaluation of care, and scientific research. Patients were given the opportunity to refuse. All data were analyzed and reported anonymously. This is in line with the research code at the Amsterdam Medical Center, and it complies with Dutch Medical Ethics Law.

2.1 Setting and study population

We performed our study in the tertiary PICU of Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands. This mixed PICU has a capacity of 12 beds and provides care to approximately 600 intensive care patients and 300 high-care patients annually, ranging in age from newborns to 18 years.

At the time of the study, all medications were prescribed or altered during the morning round, using a stand-alone patient data management system (PDMS). This PDMS is a generic ordering system and is not equipped with a medication safety monitoring or decision support system. At the start of every nursing shift, an electronically generated sign-off medication list was printed for every patient separately. Electronic alterations could be made to the medication list by the attending resident, fellow, or staff member. After a mandatory double check, the prescribed medications were administered to the patient, and both nurses signed off the medications on the list. Guidelines of all medications were available on the ward in a hospital formulary.

We included all intensive care patients with at least 1 medication prescription and with an expected length of stay in the PICU of more than 24 hours. We excluded high-care patients from our study.

2.2 Study design and endpoints

We performed an interrupted time series (ITS) with 6 preintervention and 6 postintervention data collection points. We considered 1-month intervals between data collection points as adequate to identify trends in the occurrence rate of MEs. For accurate comparison of the preintervention and postintervention data, the data collection took place during the same calendar months of 2 consecutive years to rule out seasonal effect. The primary endpoint was the prevalence of MEs per 100 prescriptions. Secondary outcomes were medication-related patient harm per 100 prescriptions, the types of the recommendations by the clinical pharmacist, and their acceptance by the clinicians.

We used the definitions and categories for error and harm as described by the National Coordinating Council for Medication Error Reporting and Prevention15 (Appendix S1). High-alert medications were recorded according to the list for pediatric patients.16 A prescription was defined as a recipe written by the pediatrician-intensivist to start or change medication, including change of dose.

2.3 Interventions by the clinical pharmacist

The study intervention was the expansion of the PICU team with a clinical pharmacist. The clinical pharmacists received mandatory training before the implementation period on the PICU started. During their training, they familiarized themselves with prevailing medication protocols and guidelines and with data collection from the electronic hospital systems, including the PDMS.

The clinical pharmacist was present on the PICU for a maximum of 3 hours every morning from Monday through Friday. At the beginning of the workday, patients considered most at risk for MEs were selected for the medication audit by the attending pediatrician-intensivist together with the clinical pharmacist using the following criteria: (a) reduced renal and/or hepatic clearance, (b) oncological diagnoses, (c) high-alert medication prescriptions, (d) receiving more than 5 medications, and (e) medication prescriptions with which the PICU professionals felt unfamiliar. The clinical pharmacist performed a structured audit of the prescribed medication for the selected patients,
followed by feedback and recommendations to the attending pediatric-intensivist and nurse during the ward round later the same morning. Administration of medication was discussed with the bedside nurse, eg, compatibility of medication administration, and infusion pump rates. A structured form was used for the medication audit and bedside evaluation (Appendix S2).

2.4 | Data collection

Data on MEs and patient harm were collected for all included patients, ie, both the patients who were audited by the clinical pharmacist and the nonaudited patients. To establish the prevalence of MEs and patient harm, we used a 3-step approach that was validated in a previous study. During the first step, the clinical records of discharged patients were retrospectively reviewed by one of the investigators (J. M. or M. T.). Potential MEs were identified by reviewing all medication summaries, check-off lists, medical and nursing daily notes, symptom registration, and postoperative notes. We systematically compared the potential MEs with the local protocols and the Dutch pediatric formulary. In addition, the hospital incident reporting system was reviewed for reported MEs during the study period. During the second step, we presented the identified potential MEs to a blinded pediatric-intensivist and a clinical pharmacist, who deemed the identification of potential MEs to be true or false. In the third step, they classified the MEs as harmful according to the National Coordinating Council for Medication Error Reporting and Prevention categories. The process of data collection is visualized in Figure 1.

Every day during the postintervention period, the clinical pharmacists registered information on the recommendations and the acceptance on the structured medication audit form. Acceptance was scored positively when a recommendation was followed up within 24 hours.

The data collection on MEs and potential patient harm was performed by 2 researchers (J. M. and M. T.). Data were collected on paper on self-designed forms and were then transferred electronically (J. M.). During the collection of data on all MEs in the postintervention period, the researchers (J. M. and M. T.) and the experts (V. G. and R. v. H.) were blinded for the patients selected for the medication audits.

**FIGURE 1** Flowchart data collection. ME, medication errors
Two researchers (J. M. and M. T.) collected the data in parallel from the first month of the preintervention period independently, and discrepancies were discussed until consensus was reached. During the other study data collection periods, the investigators performed double checks on the patient files that were considered complex by discretion of the researchers.

2.5 | Power calculation and statistical analyses

We estimated a prevalence of 10 MEs per 100 prescriptions in the preintervention group and 3 MEs per 100 prescriptions in the postintervention group. With a type 1 error of 0.05 and a power of 0.80, we required a sample size of 237 patients per group. Descriptive statistics were used to summarize patient demographics and the recommendations of the clinical pharmacists. If normally distributed, continuous values were expressed as mean with standard deviation; in case of nonnormal distribution, data were expressed as median with interquartile range. Chi-squared analysis, the Mann-Whitney test, or the unpaired Student t test was used to compare the preintervention and postintervention characteristics of patients and medications. Error rates were plotted over time to examine the data visually, and we used autoregressive integrated moving average ITS techniques to study the effect of the intervention. Statistical uncertainty was expressed by 95% confidence interval and a P value of .05 was considered statistically significant. All analyses were performed using the SPSS software (PASW statistics version 22.0, IBM, Armonk, NY).

3 | RESULTS

3.1 | Patients and prescriptions

Patients were included from 1 July 2013 until 31 December 2013 (preintervention) and from 1 July 2014 until 31 December 2014 (postintervention). In total, 254 patients in the preintervention period and 230 patients in the postintervention period met the inclusion criteria of the study and were included in the analyses. Seven patients were excluded owing to missing files. Our total study population represented 1915 admission days, during which 11 959 prescriptions were written and 28 496 doses of medicine were administered. There were significantly more patients with more than 5 prescriptions in the postintervention period compared with the preintervention period (80% and 88%, respectively, P = .02). The patients’ characteristics are summarized in Table 1.

3.2 | Medication errors

We identified 153 MEs in the preintervention period, corresponding to 2.27 per 100 prescriptions, and 90 MEs in the postintervention period,

| TABLE 1 | Patients’ characteristics |
|-----------------|-----------------|-----------------|-----------------|
| Characteristic | Preintervention | Postintervention | P Value |
| Demographics   |                 |                 |       |
| Male, n (%)    | 143 (56)        | 133 (58)        | .74   |
| Age in months, median (IQR) | 32.5 (98) | 35.0 (106) | .37 |
| Severity of illness |             |                 |       |
| PRISM III, median (IQR) | 2.5 (5) | 3.0 (7) | .06 |
| Invasive ventilation, n (%) | 98 (39) | 101 (44) | .23 |
| Invasive ventilation days, median (IQR)* | 3.0 (4) | 2.0 (3) | .60 |
| Surgical patient, n (%) | 118 (46) | 88 (38) | .19 |
| Diagnosis category |             |                 |       |
| Respiratory, n (%) | 88 (35) | 72 (31) | .44 |
| Elective postsurgical, n (%) | 89 (35) | 72 (31) | .38 |
| Cardiac, n (%) | 17 (7) | 30 (13) | .02 |
| Neurological, n (%) | 13 (5) | 16 (7) | .40 |
| Trauma, n (%) | 29 (11) | 12 (5) | .01 |
| Sepsis, n (%) | 2 (1) | 6 (3) | .12 |
| Metabolic, n (%) | 4 (2) | 7 (3) | .28 |
| Other, n (%) | 12 (5) | 15 (7) | .29 |
| Admission |             |                 |       |
| ICU length of stay in days, median (IQR) | 2.0 (3) | 2.0 (2) | .82 |
| 24 h to 7 d, n (%) | 224 (88) | 209 (91) | .34 |
| Medication during ICU admission |             |                 |       |
| Prescriptions, median (IQR) | 12.5 (20) | 15.0 (19) | .46 |
| >5 prescriptions, n (%) | 203 (80) | 202 (88) | .02 |
| Administrations, median (IQR) | 21.0 (40) | 22.0 (38) | .81 |
| Patient with high-risk medication, n (%) | 171 (67) | 161 (70) | .52 |

Abbreviations: ICU, intensive care unit; IQR, interquartile range; PRISM III, Pediatric Risk of Mortality Score III.

*Calculated for patient with invasive ventilation.
corresponding to 1.74 per 100 prescriptions. Autoregressive integrated moving average analyses showed a stable incidence of MEs during the preintervention period ($\beta = .10; 95\% \text{ CI}, -0.03 to 0.23; P = .11$). We observed a significant change in the slopes between the preintervention and postintervention periods ($\beta = -.21; 95\% \text{ CI}, -0.41 to -0.02; P = .04$). Immediately after the start of the intervention, we observed a statistically nonsignificant decrease of 0.61 MEs per 100 prescriptions ($\beta = -.61; 95\% \text{ CI}, -1.31 to 0.08; P = .07$), corresponding to 23% reduction of MEs. These results are corrected for the significant difference between the preintervention group and postintervention group at baseline: patients with more than 5 prescriptions. The results are visually presented in Figure 2. Parameter estimates are summarized in Table 2.

We categorized the identified MEs in different types of error, eg, omission, dosage, or monitoring error. In addition, the stage of medication process in which the MEs occurred was identified. In the preintervention period, 133/153 MEs (87%) were categorized as prescribing errors (87%), as opposed to 82/90 (87%) in the postintervention period. Omissions of prescriptions and errors in dosages were common types of error. An overview of the results is presented in Table 3.

### 3.3 Patient harm

Of the 153 MEs that had occurred in the preintervention period, we identified 23 harmful MEs (15%), corresponding to 0.34 per 100 prescriptions. In the postintervention period, 6 out of 90 MEs (7%) were identified as harmful, corresponding to 0.11 per 100 prescriptions.

**FIGURE 2** Medication errors (MEs) per 100 prescriptions during the study periods

### 4 DISCUSSION

Our study shows that the implementation of structured medication audit, followed by timely feedback by a clinical pharmacist as part of the multidisciplinary team, resulted in a significant reduction of MEs in a tertiary PICU. We observed a nonsignificant decrease in medication-related patient harm. The proactive role of the clinical pharmacist resulted in recommendations with a high acceptance rate.

We identified only 1 previous high-quality study that investigated interventions by a clinical pharmacist on a PICU.\(^{14}\) This study of Kaushal et al reported a reduction of serious MEs on a PICU from 29 to 6 per 1000 patient days after the introduction of a clinical pharmacist. However, in that study, the definition of MEs differed from our broader definition. In addition, the clinical pharmacist was present full time on the PICU, while in our study the pharmacist spent

**TABLE 2** Interrupted time series analysis

| MEs Per 100 Prescriptions | $\beta$ (SE) | 95% CI | P Value |
|----------------------------|-------------|--------|---------|
| Intercept ($B_0$)          | 1.92        |        |         |
| Slope preintervention ($B_1$) | .10 (0.05)  | -0.03 to 0.23 | .11 |
| Slope postintervention     | -.11 (0.06) | -0.25 to 0.02 | .08 |
| Slope differences ($B_3$)  | -.21 (0.07) | -0.41 to -0.02 | .04 |
| Level change directly after intervention ($B_2$) | -.61 (0.28) | -1.31 to 0.08 | .07 |
| Relative effect directly after intervention | 23% |

Abbreviation: ME, medication error. $B_1$ estimates the preintervention slope. $B_2$ estimates the difference between the observed level just after the intervention started and that predicted by the preintervention slope. $B_3$ estimates the difference in slopes between the preintervention and postintervention periods.
approximately 3 h/day on the PICU. Our study demonstrates that a comparable decrease in the incidence of MEs after the introduction of a clinical pharmacist can be achieved also with a more cost-effective protocol. Other studies that have investigated the effect of the presence of a clinical pharmacist on a PICU involved single-arm designs without a control group and focused on the recommendations and their acceptance by doctors and nurses rather than on the reduction of MEs.19-23 Our finding that most recommendations of the clinical pharmacist concerned dosages is in accordance with the aforementioned studies, but the acceptance rates of the recommendations of 95% and 98% were higher than the 63% acceptance rate in our study.19,20,23

In our study, the clinical pharmacist was actively involved in the medication process of 1 to 2 patients per day, who were considered most at risk for MEs. We performed a post hoc analysis to explore differences in the prevalence of MEs between patients whose medications were audited and discussed in the PICU team and patients without the medication audit. This analysis showed a significant difference between the 2 groups (mean difference = −1.71; 95% CI, −3.13 to −0.28; P = .03), meaning the prevalence of MEs per 100 prescriptions is significantly lower in patients with medication audit than those without. This result suggests that the intervention has no effect (or a delayed effect) in the nonaudited patients, but this hypothesis must be investigated in future research.

We found no significant effect of the interventions of the clinical pharmacist on patient harm. This might be explained by the low baseline rate of harmful MEs, and our study may have been underpowered to detect a difference. Although the low number of harm incidents is consistent with previous studies (6.9), these results may be underestimated as we studied patient harm during the stay on the PICU only, and we did not perform a follow-up after transfer or discharge.

It can be expected that in the future computerized physician order entry systems will increasingly support the medication prescription process, possibly marginalizing the role of the clinical pharmacist. Although a computerized physician order entry reduces MEs in children,24,25 it is important to note that information technology introduces new errors.26 Ongoing research is necessary to determine
if participation of a clinical pharmacist within the setting of a multidisciplinary team remains effective when the context changes. Also, future research might focus on the role of pharmacists in chronic disease management and medication therapy management. Economic evaluations suggest a cost avoidance effect of interventions by a clinical pharmacist, but robust comparative economic analyses are lacking. Therefore, future research should focus on the economic costs and benefits of the participation of a clinical pharmacist on PICUs. Another direction for future research should focus on the risk factors that lead to MEs and related harm in critically ill children. Several risk factors have been studied, such as age, severity of illness, and surgery, but the existing studies are limited and report nonconclusive results. Only the number of prescriptions seems to be an independent risk factor for MEs.

Our study was designed as a single-center study. In such a setting and anticipating that the study intervention would influence behavior of the professionals and the organization of care, an ITS design is the recommended approach. The optimal number of data collection points is still under debate, with recommendations that vary from 3 to 12 points. We collected data at 6 points before and 6 points after the intervention, which is in line with the Cochrane Collaboration guidelines. An ITS does not provide protection against the effect of other events occurring at the same time as the study intervention. A comparable patient group that could be used as a control group was not available at our hospital. To increase the confidence in the study results, we studied the rate of safety incidents during the study periods as a control variable. This analysis shows no significant differences between the preintervention and postintervention periods (β2 = .16; 95% CI, −0.03 to 0.36; P = .11 and β3 = .03; 95% CI, −0.02 to 0.08; P = .18). Also, the capacity of both nursing and medical staffing, a known risk factor for adverse events, was stable.

We recognize several limitations in our study. First, because of limited resources, the clinical pharmacist was present from Monday to Friday. We are aware that patients on a PICU may be instable and that relevant changes in medications are to be expected also during the weekends. The inclusion of patients that were admitted to the PICU during the weekends might have resulted in an underestimation of our results. Second, we retrospectively reviewed clinical records to detect potential MEs (harmful or otherwise). The results of this method depended on the information documented by doctors and nurses, which might have introduced an underestimation of MEs. Third, blinding of the researchers was not complete during the process of identification of MEs, since the researchers knew whether the patient had been admitted during the preintervention or postintervention period. However, both researchers and experts were completely blinded for the presence of an audit by the clinical pharmacist. Finally, this research was performed in a single-center study. Although generalizability of the results might be limited, our study clearly shows an increase in drug safety in our setting after the introduction of a medication audit by a clinical pharmacist. The authors are aware that some excellent institutions already have 24/7 coverage by a clinical pharmacist. However, depending on existing local prescription procedures, patient population, resources, and pharmacological staffing, our results may be of interest for other health care settings around the globe that are similar to our situation.

CONFLICT OF INTERESTS
The authors declare no conflict of interest.

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REFERENCES
1. Kale A, Keohane CA, Maviglia S, Gandhi TK, Poon EG. Adverse drug events caused by serious medication administration errors. BMJ Qual Saf. 2012;21:933-938.
2. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care. 2008;17:216-223.
3. Zegers M, de Bruijne MC, Wagner C, et al. Adverse events and potentially preventable deaths in Dutch hospitals: results of a retrospective patient record review study. Qual Saf Health Care. 2009;18:297-302.
4. Choi I, Lee S, Flynn L, et al. Incidence and treatment costs attributable to medication errors in hospitalized patients. Res Social Adm Pharm. 2016;12:428-437.
5. Glanzmann C, Frey B, Meier CR, Vonbach P. Analysis of medication prescribing errors in critically ill children. Eur J Pediatr. 2015;174:1347-1355.
6. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA. 2001;285:2114-2120.
7. Marino BL, Reinhardt K, Eichelberger WJ, Steingard R. Prevalence of errors in a paediatric hospital medication system: implications for error proofing. Outcomes Manag Nurs Pract. 2000;4:129-135.
8. Maaskant JM, Bosman D, van Rijn-Bikker P, van Alderen W, Vermeulen H. Preventable errors with non-opioid analgesics and antiemetic drugs increase burden in hospitalized children. Eur J Pediatr Surg. 2014;24:381-388.
9. Rashed AN, Neubert A, Tomlin S, et al. Epidemiology and potential associated risk factors of drug-related problems in hospitalised children in the United Kingdom and Saudi Arabia. Eur J Clin Pharmacol. 2012;68:1657-1666.
10. Manias E, Kinney S, Cranwick N, Williams A, Borrott N. Interventions to reduce medication errors in pediatric intensive care. Ann Pharmacother. 2014;48:1313-1331.
11. Rinke ML, Bundy DG, Velasquez CA, et al. Interventions to reduce paediatric medication errors: a systematic review. Pediatrics. 2014;134:338-360.
12. Sanghera N, Chan P, Kakhi ZF, et al. Interventions of hospital pharmacists in improving drug therapy in children. Drug Saf. 2006;29:1031-1047.
13. Maaskant JM, Vermeulen H, Apampa B, et al. Interventions for reducing medication errors in children in hospital. Cochrane Database Syst Rev. 2015;(3): Art. No: CD006208

14. Kausral R, Bates DW, Abramson EL, Soukup JR, Goldmann DA. Unit-based clinical pharmacists’ prevention of serious medication errors in pediatric inpatients. Am J Health Syst Pharm. 2008;65:1254-1260.

15. National Coordinating Council for Medication Error Reporting and Prevention. Available: www.nccmerp.org. (accessed May 2014).

16. Maaskant JM, Eskes A, van Rijn-Bikker P, Bosman D, van Aalderen W, Vermeulen H. High-alert medications for pediatric patients: an international modified Delphi study. Expert Opin Drug Saf. 2013;12:805-814.

17. De Boer M, Kiewiet JJS, Boeker EB, et al. A targeted method for standardized assessment of adverse drug events in surgical patients. J Eval Clin Pract. 2013;19:1073-1082.

18. Dutch paediatric formulary, Dutch Knowledge Centre for Paediatric Pharmacotherapy. www.kinderformularium.nl. (assessed July 2014 to April 2015).

19. Echarri-Martínez L, Fernández-Llamaras MC, Manrique-Rodríguez S, García-López I, López-Herce J. Sanjurjo-Sáez M. Pharmaceutical care in paediatric intensive care unit: activities and interdisciplinarity learning in a Spanish hospital. European Journal of Hospital Pharmacy. 2011;19:416-422.

20. Krupicha ML, Bratton SL, Sonnenthal K, Goldstein B. Impact of a pediatric clinical pharmacist in the paediatric intensive care unit. Pediatr Med. 2002;30:919-921.

21. LaRochelle JM, Ghaly M, Creel AM. Clinical pharmacy faculty interventions in a pediatric intensive care unit: an eight-month review. J Pediatr Pharmacol Ther. 2012;17:263-269.

22. Maat B, Au YS, Bollen CW, van Vught AJ, Egberts TCG, Rademaker CMA. Clinical pharmacy interventions in paediatric electronic prescriptions. Arch Dis Child. 2013;98:222-227.

23. Tripathi S, Crabtree HM, Fryer KR, Graner KK, Arteaga GM. Impact of clinical pharmacist on the paediatric intensive care practice: an 11-year tertiary center experience. J Pediatr Pharmacol Ther. 2015;20(4):290-298.

24. Radley DC, Wasserman MR, Olsho LE, Shoemaker SJ, Spranca MD, Bradshaw B. Reduction in medication errors in hospitals due to adaption of computerized provider order entry systems. J Am Med Inform Assoc. 2013;20:470-476.

25. Nuckols TK, Smith-Sprangler 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. Systematic Reviews. 2014;3:56. https://doi.org/10.1186/2046-4053-3-56

26. Cheung KC, Veen van der W, Bouvy ML, Wensing M, van den Bemt PM, de Smet PA. Classification of medication incidents associated with information technology. J Am Med Inform Assoc. 2014;21: e63-e70.

27. Gallagher J, Byrne S, Woods N, Vonbach P. Cost-outcome description of clinical pharmacist interventions in a university teaching hospital. BMC Health Serv Res. 2014;14:177. https://doi.org/10.1186/1472-6963-14-177

28. Etchells E, Koo M, Daneman N, et al. Comparative economic analyses of patient safety improvement strategies in acute care: a systematic review. BMJ Qual Saf. 2012;21:448-456.

29. Starvroudis TA, Shore AD, Morlock L, Hicks RW, Bundy D, Miller MR. NICU medication errors: identifying a risk profile for medication errors in the neonatal intensive care unit. J Perinatol. 2010;30:459-468.

30. Agerwal S, Classen D, Larsen G, et al. Prevalence of adverse events in pediatric intensive care units in the United States. Pediatr Crit Care Med. 2010;11:568-578.

31. Holdsworth MT, Fichtl RE, Behta M, et al. Incidence and impact of adverse drug events in pediatric inpatients. Arch Pediatr Adolesc Med. 2003;157:60-65.

32. Fan E, Laupacis A, Pronovost PJ, Guyatt GH, Needham DM. How to use an article about quality improvement. JAMA. 2010;304:2279-2287.

33. Jandoc R, Burden AM, Mamdani M, Lévesque LE, Cadarette SM.Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. J Clin Epidemiol. 2015;68:950-956.

34. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther. 2002;27:299-309.

35. Effective Practice, Organisation of Care (EPOC): Suggested risk of bias criteria for EPOC reviews. EPOC resources for review authors. Vol. Oslo: Norwegian Knowledge Centre for the Health Services;2014. http://epoc.cochrane.org/epoc-specific-resources-review-authors (accessed May 2014).

36. Wilson S, Bremner A, Hauck Y, Finn J. The effect of nurse staffing on clinical outcomes of children in hospital: a systematic review. Int J Evid-Based Healthc. 2011;9:97-121.

37. Wilcox ME, Chong CA, Niven DJ, et al. Do intensivist staffing patterns influence hospital mortality following ICU admission? A systematic review and met-analyses. Crit Care Med. 2013;41:2253-2274.

38. Meyer S, Massetti C, Cheng CM, Schwappach DL, et al. Systematic review of medication safety assessment methods. Am J Health Syst Pharm. 2011;68:227-240. SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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