



Prevalence of Medication Errors Among Paediatric Inpatients: Systematic Review and Meta-Analysis

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Abstract

Introduction The risk of medication errors is high in paediatric inpatient settings. However, estimates of the prevalence of medication errors have not accounted for heterogeneity across studies in error identification methods and definitions, nor contextual differences across wards and the use of electronic or paper medication charts.

Objective Our aim was to conduct a systematic review and meta-analysis to provide separate estimates of the prevalence of medication errors among paediatric inpatients, depending on hospital ward and the use of electronic or paper medication charts, that address differences in error identification methods and definitions.

Methods We systematically searched five databases to identify studies published between January 2000 and December 2018 that assessed medication error rates by medication chart audit, direct observation or a combination of methods.

Results We identified 71 studies, 19 involved paediatric wards using electronic charts. Most studies assessed prescribing errors with few studies assessing administration errors. Estimates varied by ward type. Studies of paediatric wards using electronic charts generally reported a reduced error prevalence compared to those using paper, although there were some inconsistencies. Error detection methods impacted the rate of administration errors in studies of multiple wards, however, no other difference was found. Definition of medication error did not have a consistent impact on reported error rates.

Conclusions Medication errors are a frequent occurrence in paediatric inpatient settings, particularly in intensive care wards and emergency departments. Hospitals using electronic charts tended to have a lower rate of medication errors compared to those using paper charts. Future research employing controlled designs is needed to determine the true impact of electronic charts and other interventions on medication errors and associated harm among hospitalized children.

1 Introduction

In highlighting that medication errors were the cause of up to 98,000 deaths annually in American hospitals, the landmark 1999 report by the Institute of Medicine (IoM), ‘To Err is Human’, increased awareness of the impact of medication

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Key Points

Prescribing errors are the most frequent type of medication error in paediatric inpatient settings. Multiple ward studies in hospitals using paper medication charts report an approximate prescribing error rate of one per seven orders.

Multiple ward studies using electronic medication charts reported a reduced number of medication errors compared to those using paper charts. However, too few studies were available to provide a pooled prevalence estimate.

Error detection methods had a direct impact on reported error rates, though infrequently statistically significant. Reported error rates did not differ significantly by the number of error sub-categories that were assessed.

errors (defined as unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient [1]) and resulted in an increased focus on their prevention [2]. For example, the World Health Organisation launched the World Alliance for Patient Safety in 2004, and in 2006 the International Medication Safety Network was founded [3]. These organisations share the patient safety priority goals of reducing the prevalence of medication errors, and monitoring the progress of methods towards achieving this goal [3]. Yet medication errors remain one of the main contributors to preventable harm from medical error [4, 5], which as a whole is estimated to be the third leading cause of death in the US [6]. According to the Institute of Medicine, on average every hospital patient is subjected to at least one medication error each day [7]. This is particularly the case for paediatric inpatients who have been identified to be at a higher risk of experiencing a medication error compared with adults [8–20].

Despite increased focus on medication safety, there have been no comprehensive estimates of the prevalence of medication errors among paediatric inpatients. That is, the estimate published by the IoM, and those reported in previous literature reviews that focused on paediatric inpatients [8–20], all suffer from significant limitations. The highly publicised IoM estimate is based on three outdated heterogeneous studies: one observational 2002 study of 36 different care facilities, which reported substantial variation in errors by site and region [21], and two chart review studies—the first a 1995 study conducted in two adult hospitals [22], and the second a 2001 study conducted in two children’s hospitals [23]. The IoM estimate of medication error prevalence is based on descriptive analysis and is not as comprehensive as an estimate that is based on an in-depth analysis that pools multiple studies and adjusts for the heterogeneity across studies. A study that adopted this latter approach was a 2014 review by Koumpagioti et al., which included studies conducted in paediatric hospitals published between 2000 and 2010 [24]. These authors calculated a pooled prescribing error rate of 17.5% of orders (95% confidence interval [95% CI] 10.8–27.0, based on 18 studies), and a medication administration error rate of 0.2 errors per administration (95% CI 0.2–0.3, based on six studies) [24]. However, none of these previous medication error rate estimates, including Koumpagioti et al.’s meta-analysis, have accounted for aspects of heterogeneity including different error identification techniques and definitions of error, and differences in hospital settings and wards.

There are significant differences in the number and types of medication errors that are identified by medication chart review, trigger tools, direct observation, staff or patient survey, and voluntary reporting [25–27]. When estimating medication error rates, those methods that are likely to under-report the overall error rate, such as voluntary reporting [27], should be excluded as the sole source of data, in favour of the gold-standard methods of chart

review for prescribing errors [28], and direct observation for administration errors [29]. Similarly, estimates must account for differences in the definition of medication error used and sub-categories adopted across studies. Large inconsistencies have been observed in the number of error sub-categories (such as wrong dose or wrong patient errors) used across studies [30], and there appears to be no standard approach for the types of error sub-categories included [31]. It is likely that the variable number and type of error sub-categories included may influence the overall reported medication error rate (e.g. a greater number of error sub-categories is likely to result in a greater incidence of overall medication error). Finally, estimates of error rates must account for contextual differences across individual hospital wards and whether they are using paper records or health information technology (HIT). For example, it is known that medication use within intensive care units (ICUs) is more complex than in general wards, which is likely to increase medication error rates, and that the risks of a medication error are exaggerated among neonatal patients [12]. Similarly, wards with computerised provider order entry (CPOE) with clinical decision support (CDS) are likely to report lower medication error rates than those using paper-based medication charts [9, 11, 14, 32–40].

The purpose of this review was to provide comprehensive estimates of medication error prevalence (i.e. overall medication errors, prescribing errors, and medication administration errors) among paediatric inpatients. Specifically, we provide the first estimates that address the impact of (1) study quality (a detailed assessment of error identification methods); (2) study definition of medication error; (3) different hospital wards; and (4) use of HIT (including CPOE with and without CDS).

2 Methods

2.1 Eligibility and Search Strategy

Studies published from January 1, 2000 to December 31, 2018 were identified by searching five electronic bibliographic databases (CINAHL, MEDLINE, Scopus, the Cochrane Library, and EMBASE). The search strategy (see Electronic Supplementary Material 1) was conducted in April 2019 and included terms for *medication* adjacent to terms for *error*. Due to known variations in study definitions of medication errors [30], we also included terms for *preventable adverse drug events*. Results were limited to paediatric hospital inpatients (at least 90% of the sample was aged < 19 years) in hospital wards using paper medication charts, CPOE, or CPOE with CDS. Included

paediatric hospital wards were emergency departments (ED), ICUs, and general wards (paediatric wards from general hospitals and general wards from paediatric hospitals). Studies had to be in the English language, have used chart review or observation to detect medication errors, and report the rate of medication errors. Studies with reduced generalisability, such as those that focused only on a specific patient condition (e.g. oncology patients) or medication type (e.g. injectable medications) were excluded. Results from applying the exclusion criteria are presented in a PRISMA flow diagram (Fig. 1). Three reviewers (PG, SM and MR) independently conducted the literature search, completed title and abstract review, assessed all potential full-text articles and determined eligibility. Two reviewers (PG and SM) conducted data extraction on included studies, and rated study quality. Duplicate papers were identified using Endnote X8 software. Authors of published papers were contacted for additional details when required. Multiple reports of the same study were included and assessed for unique data; no single report of multiple studies was found.

2.2 Elements Considered to Impact the Value of Comparisons, Using Medication Error Rates, Across Studies

2.2.1 Study Quality

Quality ratings were determined by adapting the Newcastle–Ottawa Scale (NOS) for nonrandomised studies [41], the Critical Appraisal Skills Programme (CASP) Cohort Study Checklist [42] and the Checklist Assessment of Medication Error Audits (CAMEA) [43, 44], as detailed in the Electronic Supplementary Material 2. Studies identified as ‘good’ by the NOS received one point on the overall quality rating, as did those achieving an above average score on the CASP and the CAMEA (for a possible total quality score of three out of three). Studies were rated as ‘excellent’ quality (three points), ‘good’ (two points), ‘fair’ (one point) and ‘poor’ (no points). Disagreements between reviewers were resolved by discussion. For each meta-analysis, two estimates were provided to assess the impact of study quality when appropriate: one calculated from studies with ‘poor’ or ‘fair’ quality ratings, and one from those with ‘good’ or ‘excellent’ quality ratings.

2.2.2 Study Definition of Medication Error

We assessed the impact of error definition by noting the number of error sub-categories included in each study. For ‘prescribing error’ definitions, the average number of sub-categories assessed across studies was six (including both clinical and procedural errors). For ‘administration error’

definitions, the average number of sub-categories was also six. When performing the meta-analyses for prescribing and administration errors, we grouped studies into those that included below and those that included equal to or above the average number of error sub-categories when appropriate. When performing the meta-analyses for studies reporting ‘medication error’ rates, we assessed the number of error types that were included (i.e. prescribing, transcribing, dispensing, administration, and/or monitoring errors). That is, we provided two estimates where appropriate: one estimate for those studies that included only prescribing and administration error types, and one estimate for those that also included transcribing, dispensing or monitoring error types.

2.2.3 Hospital Ward and Use of Electronic Charts

We provide separate estimates based on hospital ward and use of paper medication chart or HIT. Separate estimates are also provided for studies that were conducted in a combination of general and ICU or ED wards (referred to as ‘multiple ward’ studies). Separate estimates are provided for error rates for hospitals using paper medication charts, those using CPOE with CDS, and those using CPOE alone. As a result, for each ward and hospital setting, up to four estimates calculated by meta-analyses could be potentially derived, two by study quality grouping, and two by error definition grouping.

2.3 Meta-Analysis

The rates of medication errors, prescribing errors, and administration errors are reported according to the denominators used in the individual studies. Denominators included errors per 100 orders, per 100 medications administered, per 100 admissions and/or per 1000 patient-days. To provide a more accurate estimate of error rates, adjusted for study sample size, we calculated pooled estimates of the mean error rate (where data from at least three studies were available) using meta-analysis random effects models with 95% CIs. The Q statistic is reported to show estimate precision [45]. Heterogeneity is shown by use of I^2 statistic and Tau^2 [46]. A p value of < 0.05 was used to indicate statistical significance. Forest plots and results for all meta-analyses are provided in Electronic Supplementary Material 3. In cases where the Q statistic was not significant, pooling was not appropriate and individual study results are reported separately. Sub-group analysis (by study quality and error definition) was considered appropriate when there were at least two studies contributing data to each estimate and the p value corresponding to the Q value for the mixed effects analysis was statistically significant (< 0.05). Publication bias was tested statistically with Egger’s test and found to be not significant. Analyses were performed using the Comprehensive Meta-Analysis software (CMA; Biostat, Inc.).

PRISMA 2009 Flow Diagram

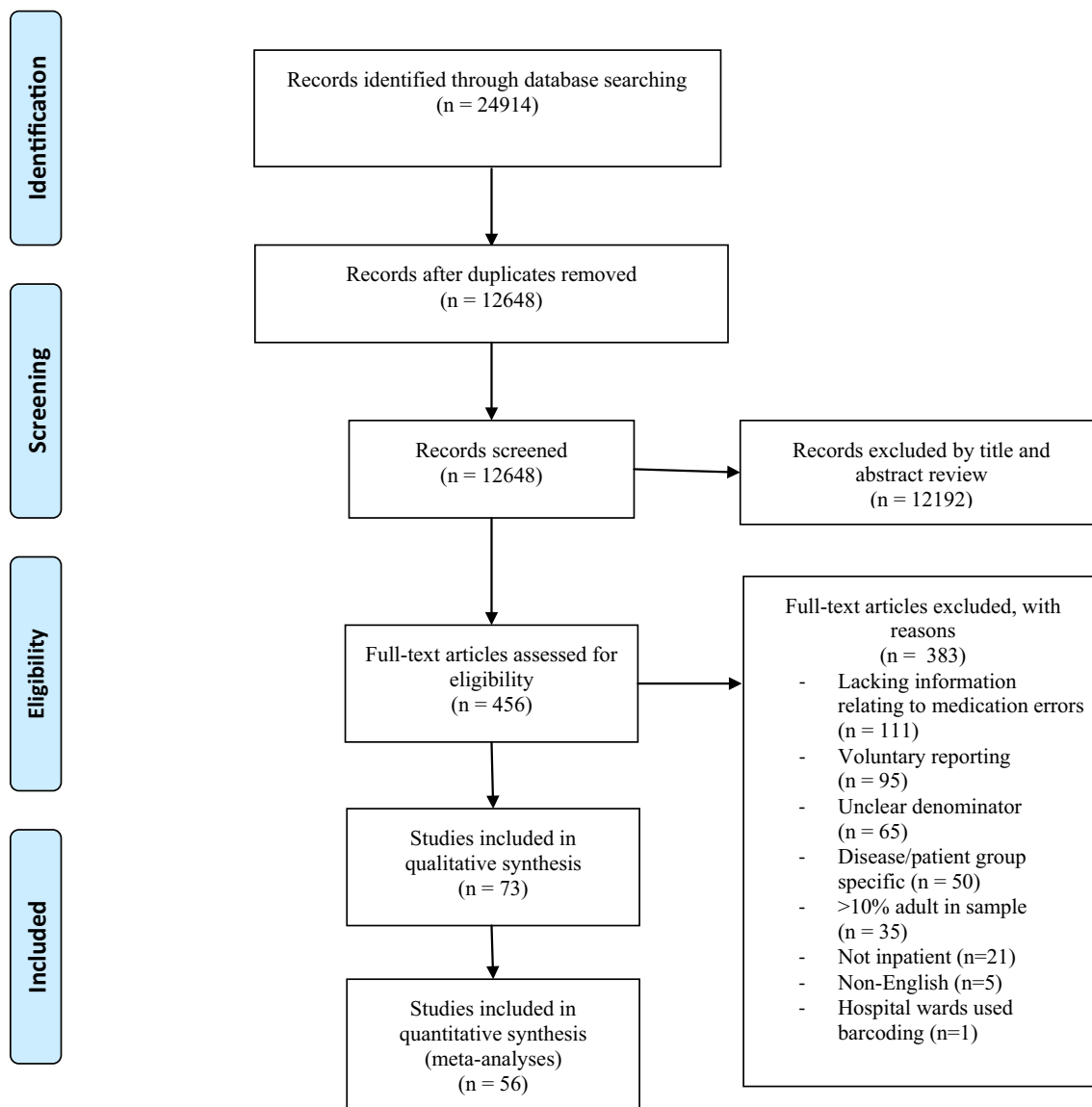


Fig. 1 PRISMA 2009 Flow Diagram

3 Results

Seventy-three articles met the inclusion criteria, representing 71 unique studies, of which 14 were rated to be of excellent quality [18, 23, 47–58], 20 good quality [13, 59–77], 19 fair [78–96], and 18 poor quality [97–114]. Full study details are provided in Electronic Supplementary Material 4. Individual study error rates are provided in Electronic Supplementary Material 5. Fifteen studies provided data that was collected after January 2014 [13, 55, 59, 69, 74, 79, 91, 93, 95, 97, 107, 108, 112–114], ten

of which were conducted in hospitals using paper medication charts [13, 69, 74, 79, 93, 97, 107, 108, 112, 113].

3.1 Error Definitions

Definitions of medication error, prescribing error and administration error varied across studies. The definitions and sub-categories of errors used by each study for these are provided in Electronic Supplementary Material 6. Although there was some variability in the definitions

of medication errors used, in all cases medication errors included both prescribing and administration errors, and included errors that may or may not have been corrected before reaching the patient. One exception was the then American Society of Hospital Pharmacists definition, which stated that medication errors exclude errors that were corrected before reaching the patient [115]. Most studies assessing prescribing errors included both clinical and procedural errors. The number of error sub-categories included within these two categories varied across studies. The clinical error sub-categories most frequently assessed were wrong dose, drug and frequency errors. The procedural error sub-categories most frequently assessed were unclear and incomplete order errors. Sub-categories of administration errors also differed across studies. The most frequently assessed error sub-categories were omission errors, wrong dose and timing errors.

3.2 Summary of Medication Error Rates by Hospital Ward and Hospital Setting

Prescribing errors made up the greatest proportion of medication errors and were the focus of most studies. There were few studies on administration errors conducted in individual hospital wards, although in multiple ward studies the overall rate of administration errors was substantially lower than the rate of prescribing errors. A summary of the differences in medication error rates between hospital wards and hospital settings is illustrated in Table 1. Meta-analyses results are provided where possible in this summary table, and when meta-analysis was inappropriate, the range of error rates reported across studies is shown. Full meta-analyses results are provided in Electronic Supplementary Material 3. In the sections below we present the rates of medication errors by study ward, separating hospitals that used paper medication charts from those that used electronic medication charts.

3.3 Rate of Medication Errors Among Paediatric Inpatients in Multiple Paediatric Wards Using Paper Medication Charts

Nine studies assessed medication errors in multiple paediatric wards using paper medication charts [23, 47, 52, 58, 65, 68, 71, 79, 107]. Seven studies were rated to be of good or excellent quality [23, 47, 52, 58, 65, 68, 71]. Across all studies, the rate of medication errors was 8.9–56.1 per 100 orders (seven studies); 6.6 per 100 doses administered (one study); 24.3–71 per 100 admissions (four studies); and 44.7–167 per 1000 patient-days (four studies).

Fourteen studies assessed prescribing errors in multiple paediatric wards using paper medication charts [18, 23, 52, 58, 59, 68, 79, 89, 92, 96, 102, 107, 109, 110]. Six studies were rated to be of good or excellent quality [18, 23, 52, 58, 59, 68]. Across all studies, the rate of prescribing errors was 2.7–78.3 per 100 orders (12 studies); 18.8–45.2 per 100 admissions (four studies); and 74 per 1000 patient-days (one study).

Eleven studies assessed administration errors in multiple paediatric wards using paper medication charts [18, 23, 47, 52, 58, 68, 71, 79, 99, 103, 107]. Seven studies were rated to be of good or excellent quality [18, 23, 47, 52, 58, 68, 71]. Sub-group meta-analysis showed that these higher quality articles reported significantly lower rates of administration errors compared with poor and fair quality studies (Table 5). Across all studies, administration errors were 0.5–33.7 per 100 orders (five studies); 0.2–89.9 per 100 doses administered (six studies); 6.3–32.0 per 100 admissions (three studies); and 27.0–54 per 1000 patient-days (two studies).

3.4 Rate of Medication Errors Among Paediatric Inpatients in Multiple Paediatric Wards Using Computerised Provider Order Entry (CPOE)

Three studies assessed medication errors in multiple paediatric wards using CPOE. The first was conducted in a US teaching hospital and rated to be of good quality [65]. That study assessed the introduction of CPOE and reported 44.7 medication errors per 1000 patient-days 7 months prior to system introduction and 29.5 medication errors per 100 admissions or 50.9 per 1000 patient-days 9 months after introduction. This represented a non-significant increase in medication errors. The second study was rated to be of excellent quality and assessed adverse drug events in two Japanese teaching hospitals using CPOE systems [53]. That study reported 65.1 medication errors per 100 admissions or 69.5 per 1000 patient-days. The third study was rated to be fair quality and was conducted in the paediatric wards of a Danish hospital and reported that 8 per 100 medication administrations involved a medication error [91].

One study rated to be of good quality assessed the rate of prescribing errors in multiple paediatric wards using CPOE in Malaysia [59]. That study included three hospitals using CPOE and reported a rate of 16.9 prescribing errors per 100 orders.

One study rated to be of good quality assessed administration errors in multiple paediatric wards of a French hospital using CPOE [64]. That study reported 31.3 administration errors per 100 doses administered or 43.0 per 100 admissions.

Table 1 Medication error rates by hospital ward and hospital setting

	Multiple ward, paper	Multiple ward, CPOE	General ward, paper	General ward, CPOE	PICU, paper	PICU, CPOE	NICU, paper	NICU, CPOE	ED, paper	ED, CPOE
Medication errors										
Per 100 orders	13.5 (5.7–28.7) ^a	ND	15.0 (3.1–49.4) ^a	ND	7.7 (2.0–25.4) ^a	ND	5.5–9.5	ND	16.7 ^b	ND
Per 100 administrations	49.6 (24.4–75.1) ^a	29.5–66.9	75.1–75.8	62.5 ^b	ND	5.6–94.9	70.0–91.0	87.6 ^b	0.9–51.1	ND
Per 100 dose administrations	6.6 ^b	8.0 ^b	ND	ND	19.8 ^b	ND	7.0–49.0	ND	ND	ND
Per 1000 patient-days	113.4 (82.4–154.1) ^a	50.9–58.7	514 ^b	62.8 ^b	6.0–7.7	6.4 ^b	35.1–90.0	35.1 ^b	600.0 ^b	ND
Prescribing errors										
Per 100 orders	14.7 (6.1–31.6) ^a	16.9 ^b	16.0 (5.6–38.0) ^a	9.9 (9.0–57.3) ^a	25.9 (17.3–36.7) ^a	1.0–7.8	16.7 (9.1–28.6) ^a	4.0 ^b	22.1 (4.6–62.7) ^a	14.0–16.0
Per 100 administrations	30.7 (18.8–45.8) ^a	ND	18.7–43.8	ND	25.0–46.3	ND	38.5 (27.1–51.4) ^a	ND	15.1 (10.3–21.6) ^a	ND
Per 100 dose administrations	ND	ND	ND	ND	ND	ND	36.7 ^b	ND	8.8 ^b	ND
Per 1000 patient-days	74 ^b	ND	347.0–460.0	ND	892 ^b	ND	ND	ND	ND	ND
Administration errors										
Per 100 orders	2.3 (0.3–15.6) ^a	ND	6.5 ^b	60.0 ^b	ND	ND	ND	ND	ND	ND
Per 100 administrations	13.3 (3.6–38.9) ^a	31.3 ^b	ND	ND	ND	ND	77.9 ^b	ND	3.9 ^b	ND
Per 100 dose administrations	3.1 (0.4–19.5) ^{a,c}	43.0 ^b	27.2 (18.8–37.5) ^a	ND	8.2 ^b	ND	18.3 (9.3–32.9) ^a	11.6 ^b	ND	ND
Per 1000 patient-days	27.0–54.0	ND	ND	ND	ND	ND	ND	ND	ND	ND

CPOE computerised provider order entry, ED emergency department, ND no data available, NICU neonatal intensive care unit, PICU paediatric intensive care unit

^aMeta-analysis results are presented

^bData provided by one study

^cData from studies rated to be of good or excellent quality

3.5 Rate of Medication Errors Among Paediatric Inpatients in General Wards Using Paper Medication Charts

Five studies assessed medication errors in paediatric general wards using paper medication charts [13, 23, 48, 52, 105], four of which were rated to be of good or excellent quality [13, 23, 48, 52]. Across all five studies, medication errors were 4.5–46.0 per 100 orders (four studies); 75.1–75.8 per 100 admissions (two studies); and 514 per 1000 patient-days (one study).

Seven studies assessed prescribing errors in paediatric general wards using paper medication charts [48, 52, 70, 83, 101, 106, 109, 110], three of which were rated to be of good or excellent quality [48, 52, 70]. Across all seven studies, the rate of prescribing errors was 4.1–58.1 per 100 orders (six studies); 18.7–43.8 per 100 admissions (two studies); and 347.0–460 per 1000 patient-days (two studies).

Five studies assessed administration errors in paediatric general wards using paper medication charts [52, 78, 80, 88, 97], one of which was rated to be of good or excellent quality [52]. Across all five studies, the rate of administration errors was 6.5 per 100 orders (one study); and 8.6–44.3 per 100 doses administered (four studies).

3.6 Rate of Medication Errors Among Paediatric Inpatients in General Wards Using CPOE

One study rated to be of excellent quality assessed medication errors in paediatric general wards using CPOE [53]. That study was conducted in two Japanese hospitals and reported 62.5 (56.7–68.3) medication errors per 100 admissions and 62.8 (56.9–68.7) medication errors per 1000 patient-days.

Three studies assessed the rate of prescribing errors in paediatric general wards using CPOE, none were rated to be of good or excellent quality [81, 83, 114]. These studies reported a prescribing error rate of 14.8 to 47.0 errors per 100 orders.

One study rated to be of poor quality assessed the rate of administration errors in a paediatric general ward of a children's hospital in Saudi Arabia that used electronic charts [114]. That study reported an administration error rate of 60.0 errors per 100 orders.

3.7 Rate of Medication Errors Among Paediatric Inpatients in Paediatric Intensive Care Wards Using Paper Medication Charts

Six studies assessed medication errors in paediatric intensive care wards [23, 50, 52, 66, 69, 116], five of which were rated to be of good to excellent quality [23, 50, 52,

66, 69]. Across all six studies, the rate of medication errors was 2.3–14.6 per 100 orders (four studies); 5.6–94.9 per 100 admissions (two studies); 19.8 per 100 doses administered (one study); and 6.0–9.1 per 1000 patient-days (three studies).

Twelve studies assessed prescribing errors in paediatric intensive care wards using paper medication charts [49, 52, 62, 76, 77, 93, 94, 98, 100, 109–111], of which five studies were rated to be of good to excellent quality [49, 52, 62, 76, 77]. Across all twelve studies, the rate of prescribing errors was 8.2–39.1 per 100 orders (eight studies); 25.0–46.3 per 100 admissions (four studies); and 892 (95% CI 765–1019) per 1000 patient-days (one study).

One study assessed administration errors in the paediatric intensive care unit (PICU) of a children's hospital in Argentina [52]. That study was rated to be of excellent quality and reported an administration error rate of 8.2 per 100 doses administered.

3.8 Rate of Medication Errors Among Paediatric Inpatients in Paediatric Intensive Care Wards Using CPOE

Two studies assessed medication errors in paediatric intensive care wards using CPOE [53, 95]. The first study was conducted in two Japanese hospitals and was rated to be of excellent quality [53]. That study reported 5.6 (95% CI 0.1–31.0) medication errors per 100 admissions and 6.4 (95% CI 0.2–35.5) medication errors per 1000 patient-days. The second study was conducted in a South African PICU and was rated to be of fair quality [95]. That study reported that 94.9 per 100 admissions experienced a medication error.

Four studies assessed prescribing errors in paediatric intensive care wards using CPOE [49, 55, 76, 111], each evaluating the impact of introducing CPOE to a paper medication chart system. The first study was rated to be of good quality and was conducted in a US PICU [76] and the second study was conducted in a UK PICU and was rated to be of poor quality [111]. These studies reported a significant reduction in the rate of prescribing errors, from 39.1 to 1.6 per 100 orders following 1 month of using CPOE [76]; and from 8.8 to 4.6 per 100 orders following 1 week of operation [111]. Two studies were conducted in an Israeli PICU and were each rated to be of excellent quality [49, 55]. These studies reported a reduction in the rate of prescribing errors from 8.2 to 7.8 per 100 medication orders following 1 year of using CPOE [49], and then 11 years later reported a further reduced rate at 1.0 prescribing error per 100 medication orders after 1 year of using CPOE with CDS [55].

3.9 Rate of Medication Errors Among Paediatric Inpatients In Neonatal Intensive Care Wards Using Paper Medication Charts

Seven studies assessed medication errors in neonatal intensive care wards [23, 52, 63, 72, 85, 105, 116], four of which were rated to be of good to excellent quality [23, 52, 63, 72]. Across all seven studies, the rate of medication errors was 5.5–9.5 per 100 orders (three studies); 7.0–49.0 per 100 doses administered (two studies); 72.6–91.0 per 100 admissions (two studies); and 4.0–90.0 per 1000 patient-days (two studies).

Eight studies assessed prescribing errors in neonatal intensive care wards [52, 57, 67, 104, 108–110, 117], four of which were rated to be of good to excellent quality [52, 56, 57, 67]. Across all eight studies, the rate of prescribing errors was 11.6–58.2 per 100 orders (five studies); 36.7 per 100 doses administered (one study); and 25.7–46.9 per 100 admissions (three studies).

Four studies assessed administration errors in neonatal intensive care wards [52, 73, 82, 112], two of which were rated to be of good or excellent quality [52, 73]. Across all four studies, the rate of administration errors was 8.4–31.4 per 100 doses administered (three studies); and 77.9 per 100 admissions (one study).

3.10 Rate of Medication Errors Among Paediatric Inpatients in Neonatal Intensive Care Wards Using CPOE

One study rated to be of excellent quality assessed medication errors in the neonatal intensive care wards of two Japanese hospitals using CPOE [53]. That study reported a medication error rate of 87.6 (95% CI 73.5–101.7) per 100 admissions and 35.1 (95% CI 29.5–40.8) per 1000 patient-days.

One study rated to be of poor quality assessed prescribing errors in neonatal intensive care wards using CPOE [104]. That study was conducted in a US neonatal intensive care unit (NICU) and reported a significant reduction in the rate of prescribing errors from 58.2 to 4.0 per 100 orders immediately following the introduction of CPOE.

One study rated to be of fair quality assessed administration errors in a neonatal intensive care ward using CPOE [82]. That study assessed the impact of introducing CPOE in a US NICU and reported a significant reduction in the medication administration error rate from 19.8 to 11.6 per 100 doses administered following 1 month of using CPOE.

3.11 Rate of Medication Errors Among Paediatric Inpatients in Emergency Departments Using Paper Medication Charts

Three studies assessed medication errors in emergency departments using paper medication charts [61, 74, 85]. The first study was rated to be of good quality and was conducted in four rural US children's emergency departments and reported a medication error rate of 51.1 per 100 admissions [61]. The second study was rated to be of fair quality and was conducted in an Indian paediatric emergency department for neonates and reported a medication error rate of 16.7 per 100 orders, and 600.0 per 1000 patient-days [85]. The third study was rated to be of good quality and was conducted in the paediatric department of a French hospital and reported a medication error rate of 0.9 per 100 admissions [74].

Six studies assessed prescribing errors in emergency departments using paper medication charts [51, 60, 61, 75, 86, 90], four of which were rated to be of good to excellent quality [51, 60, 61, 75]. Across all six studies, the rate of prescribing errors was 9.8 to 59.2 per 100 orders (three studies); 8.8 per 100 doses administered (one study); and 10.1 to 19.4 per 100 admissions (four studies).

One study rated to be of excellent quality assessed the rate of administration errors in a Canadian emergency department [51]. That study reported an administration error rate of 3.9 per 100 admissions.

3.12 Rate of Medication Errors Among Paediatric Inpatients in Emergency Departments Using CPOE

Two studies assessed the rate of prescribing errors in paediatric emergency wards [54, 87]. The first was rated to be of excellent quality and assessed the impact of adding CDS to an existing CPOE system used in the paediatric emergency department in a US hospital [54]. That study reported a significant reduction in the rate of prescribing errors from 31.0 to 14.0 per 100 orders 2 months after the introduction of the CDS. The second was rated to be of fair quality and assessed the rate of prescribing errors in a separate US emergency department, which used a CPOE system [87]. Of the paediatric inpatients assessed, a prescribing error rate of 16.0 per 100 orders was reported, which represented an 80% reduction in the number of errors that occurred before the CPOE system was introduced (unpublished data).

4 Discussion

This systematic review and meta-analysis is the first to provide pooled estimates of medication errors, prescribing errors and administration errors among paediatric inpatients differentiated by hospital ward and use of HIT. Prescribing errors made up the greatest proportion of medication errors and were the focus of most studies. The few multiple ward studies on administration errors reported rates of administration errors that were substantially lower than the reported rates of prescribing errors. Similarly, there were limited studies of hospital wards with CPOE. This may reflect a lag in the implementation of such systems in paediatric hospitals, particularly smaller teaching and nonteaching hospitals [118], possibly due to a lack of paediatric-centric HIT as system development is chiefly adult orientated [119]. Our estimates support previous reports that the prescribing error rate is higher in NICUs, EDs and PICUs than general wards [120]. Multiple factors are likely to contribute to this difference, such as greater complexity of medication therapy in ICUs compared with general wards [12], greater instability of ICU patients requiring frequent changes in therapy, increased staff workloads [121, 122] and higher use of intravenous medications [123].

Using the detailed summary of medication error rates presented in Table 1, and acknowledging that the confidence intervals observed in meta-analyses were large and that most studies focused on prescribing errors, we estimate an approximate medication error rate of one per seven orders in paediatric wards using paper medication charts, with at least one error experienced by every second or third paediatric admission.

Although few studies were conducted in hospitals using CPOE, the rate of prescribing errors was reported to be consistently lower in ICUs using CPOE than those using paper medication charts. This finding was supported by five pre/post studies [49, 55, 76, 104, 111]. In addition, indirect comparisons across studies conducted in wards using paper medication charts and those using CPOE mostly showed a lower error rate in wards using CPOE (see Table 10). However, this finding was not consistent across all studies. That is, two studies conducted in a paediatric general ward [83], and in multiple paediatric wards using CPOE [65], reported a non-significant increase in prescribing and medication errors following CPOE implementation, respectively.

Study quality was found to significantly impact the rate of administration errors reported across multiple ward studies such that studies of higher quality reported significantly lower rates of administration errors. However, subgroup analyses of study quality and error definition could only be performed when there were at least two studies in each sub-group, and this was the case for only eight and

three of 17 analyses, respectively. Given the small number of studies available when broken down by ward, hospital setting, and type of medication error (prescribing, administration, or both), this was a significant limitation of this review. Small study numbers also did not allow us to identify which aspects of study quality contributed to differences in reported error rates. However, our analysis of study quality highlighted some key methodological problems in studies. First, approximately half of the studies did not use trained chart reviewers or observers to identify and evaluate medication errors, and only 17 employed multiple data sources and methods of error identification. This is important as reviewer training and using multiple data sources and reviewers is known to improve the reliability and validity of error identification and classification [124]. In addition, reviewers were typically reported to be clinical pharmacists, limiting the input received from other professions. Moreover, although undertaken in paediatric settings, studies rarely specified that reviewers had specific paediatric experience. Third, medication chart reviewers were frequently aware of the hospital staff responsible for prescribing and administering the medication reviewed, and hospital staff were also frequently reported to be aware that they were participating in a study on medication errors. This may introduce bias consistent with the Hawthorne effect, particularly for observational studies [125]. However, measurement of this effect has suggested that its impact on medication error rates is likely to be minimal [126, 127], and lessened with proper observer training [29].

Our findings did not support previous suggestions that differences in the error sub-categories assessed may significantly impact reported error rates across studies [30]. Although the number of sub-categories of prescribing or administration errors were variable across studies, we found that certain core error sub-categories were consistently assessed. For example, dose errors, which are likely to make up the greatest proportion of medication errors [44], were consistently assessed across studies. However, the small number of studies with different numbers of error sub-categories when stratified by hospital ward and setting limited our analyses, and a further confirmatory study is needed.

This review had some limitations. First, we combined specialist paediatric hospitals with general hospitals focusing on paediatric inpatients. A recent study of multiple specialist and general hospital wards has found significant differences in medication error rates across ward types, though it was unclear if actual error rates differed as each ward detected errors by a separate individual pharmacist [18]. We also combined studies using prospective and retrospective chart review methods, and there may be differences in the number and type of errors identified between studies undertaking retrospective and prospective audits [26]. We also collapsed studies reporting error rates as percentages

(number of errors found over number of orders reviewed) and those reporting errors per 100 orders/drugs/admissions. That is, we collapsed studies that may or may not have recorded more than one error per order. Although a 2001 study reported that identifying more than one error per order is extremely rare [23], it was out of the scope of this review to determine how this impacted on error rates. Finally, the review is limited by the representativeness of the included studies and caution should be exercised in generalising the findings of this review to other settings (such as primary care) or contexts. That is, approximately one third of the studies were conducted in the US, and approximately one half of the studies were conducted in teaching hospitals. Moreover, most studies were undertaken at single sites with the notable exception of a recent study conducted in 17 Malaysian hospitals [59].

This review highlights that medication errors occur at all stages of the medication use process. Although most studies conducted in paediatric inpatient settings focus on prescribing errors, the few that focused on administration errors also found them to be a frequent occurrence. There are few studies that have investigated the effectiveness of HIT in reducing medication errors outside of paediatric intensive care wards, and studies evaluating harm outcomes concurrently are scarce. Future investors into such technologies should be aware that introducing these technologies into a paediatric setting may require significant work practice changes and can introduce new or unanticipated errors or harms [128]. More systematic and comprehensive evaluation of the impact of such technology on medication safety in various paediatric patient sub-groups and settings is needed given the investments being made in these technologies and their expected effects on safety demonstrated in studies of adult hospitals using electronic medication systems [129, 130]. A similar approach should be taken with all proposed interventions for improving paediatric medication safety, including non-technological approaches [36, 131, 132], and ideally also encompass a cost-effectiveness analysis. Such data will be extremely useful for enabling more evidence-based clinical and policy decisions about optimal approaches for improving medication safety in paediatric inpatients.

5 Conclusion

The rate of medication errors occurring in paediatric hospital wards using paper medication charts is high. Every two to three inpatients can expect to experience at least one medication error with an error occurring in approximately every seven orders. Notably, the prescribing error rate was higher in ICUs and EDs where patients are more vulnerable to harm. Studies on medication error predominantly focused on prescribing errors rather than administration errors, with

sub-categories of dispensing, monitoring and transcribing errors very rarely assessed. Hospital wards using CPOE tended to have lower rates of medication errors, particularly in ICUs, though there are some inconsistencies and few studies have directly assessed the impact of CPOE on medication error rates in paediatric settings. Further study of medication errors in paediatric settings is required to more accurately delineate the extent and nature of the problem in this vulnerable population. A greater focus on administration errors, and on hospital wards using HIT is needed. Increased efforts are also needed to accurately measure harm associated with medication errors across all studies.

Compliance with Ethical Standards

Conflict of interest Peter Gates, Melissa Baysari, Madlen Gazarian, Magdalena Raban, Sophie Meyerson, and Johanna Westbrook have no conflicts of interest that are directly relevant to the content of this study.

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