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ORIGINAL RESEARCH ARTICLE

A Mixed-Methods Analysis of Medication Safety Incidents Reported in Neonatal and Children's Intensive Care

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Abstract

Background Critically ill neonates and paediatric patients may be at a greater risk of medication-related safety incidents than those in other clinical areas.

Objective This study aimed to examine the nature of, and contributory factors associated with, medication-related safety incidents reported in neonatal and paediatric intensive care units (ICUs).

Methods We carried out a mixed-methods analysis of anonymised medication safety incidents reported to the National Reporting and Learning System that involved children (aged ≤ 18 years) admitted to ICUs across England and Wales over a 9-year period (2010–2018). Data were analysed descriptively, and free-text descriptions of harmful incidents were examined to explore potential contributory factors associated with incidents.

Results In total, 25,567 eligible medication-related incident reports were examined. Incidents commonly occurred during the medicines administration ($n = 13{,}668$ [53.5%]) and prescribing stages ($n = 7412$ [29%]). The most commonly implicated error types were drug omission ($n = 4812$ [18.8%]) and dosing errors ($n = 4475$ [17.5%]). Neonates were commonly involved in reported incidents ($n = 12{,}235$ [47.9%]). Anti-infectives ($n = 6483$ [25.4%]) were the medications most commonly associated with incidents and commonly involved neonates. Incidents that were reported to have caused patient harm accounted for 12.2% ($n = 3129$) and commonly involved neonates ($n = 1570/3129$ [50.2%]). Common contributing factors to harmful incidents included staff-related factors (68.7%), such as failure to follow protocols or errors in documentation, which were often associated with working conditions, inadequate guidelines, and design of systems and protocols.

Conclusions Neonates were commonly involved in medication-related incidents reported in children's intensive care settings. Improvements in staffing and workload, design of systems and processes, and the use of anti-infective medications may reduce this risk.

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1 Introduction

Medication-related safety incidents are commonly reported as the most frequent incident type in hospitals and may be more likely to cause harm in children than in adults [1, 2]. The risk of experiencing these incidents may be greater for neonates and children admitted to intensive care units (ICUs) than for those on general wards because of factors such as the use of medicines associated with a high risk of harm, complicated and severe illnesses, complex weight-based dosing calculations, and heavy staff workload [3–5]. In addition, neonates and children admitted to ICUs may be pre-verbal or sedated, and this will affect their ability to prevent errors themselves [6].

Our recent systematic review indicated that the median prevalence of medication errors in paediatric ICUs was 14.6% of medication orders (interquartile range 5.7–48.8; three studies) and ranged from 5.5 to 77.9 per 100 medication orders in neonatal ICUs (two studies) [7]. However,

Key Points

An understanding of the type of, and factors contributing to, medication safety incidents in neonatal and children's intensive care settings is essential to inform the planning of interventions to improve medication safety.

Incidents involving medication administration and prescribing stages, medication omissions, wrong doses, and anti-infective medications were most commonly reported. Incidents involving neonates were most frequently reported, and most harmful incidents involved this patient population.

Redesign of systems and policies may improve medication safety. The use of anti-infective medications is also a clear target for medication safety interventions. Improvements in working conditions will help with the effective implementation of medication safety interventions in neonatal and children's intensive care settings.

data concerning the nature of medication errors and related adverse drug events in these settings were limited [7], as was research exploring the factors contributing to medication errors and related harm involving this high-risk patient population [8].

Detailed analysis of medication safety incident reports submitted to national reporting systems is important as greater understanding of their underlying antecedents helps guide the creation of improvement strategies and prioritisation of high-risk areas [9–11]. This would support international efforts to reduce preventable medication-related harm, as highlighted in the third World Health Organization (WHO) global patient safety challenge [12]. The strategic framework of this challenge includes incident reporting and learning as a key component.

Several countries, including the UK, the Netherlands, Denmark, and Australia, have established national incident reporting systems [13], with the National Reporting and Learning System (NRLS) in England and Wales being the largest and most comprehensive worldwide [14]. The NRLS receives around 65,000 incident reports involving paediatric patients every year [9]. The NRLS is a good example of reporting systems that include the checklist of *WHO Draft Guidelines for Adverse Event Reporting and Learning Systems* [15, 16] and gather necessary information about incidents to enable success analysis and results dissemination with recommendations for safety improvements in healthcare systems. Incident reports submitted to the NRLS have been a source of information for those creating national patient safety alerts, rapid response reports, and medication safety guidance and research that aimed to reduce medication errors and related adverse drug events across different healthcare settings [5, 9, 17–19].

To our knowledge, no systematic analysis has yet examined the frequency and nature of, and factors contributing to, medication-related safety incidents reported from neonatal and children's intensive care settings in UK national health service (NHS) hospitals. Previous studies have analysed incidents affecting paediatric primary care [9], adult critical care [20], and specific children's inpatient units (e.g. neonatal units) [21]. These studies did not focus specifically on children in ICUs [22]. This study therefore aimed to examine the nature of, and factors contributing to, reported medication safety incidents in children's intensive care settings across England and Wales over a 9-year period.

2 Methods

2.1 Study Design, Settings, and Data Source

We carried out a retrospective mixed-methods study. This included analysis of data from medication-related incidents involving children (aged ≤ 18 years) admitted to hospital intensive care settings and submitted to the NRLS database from NHS organisations in England and Wales over a 9-year period (1 January 2010 to 31 December 2018). This period was chosen as it provides a sufficiently large dataset from recent years [23] and represents the period since mandatory reporting of serious harm and death incidents in NHS organisations was implemented (June 2010) [14].

Intensive care services for children can be divided into two fields: neonatal intensive care and paediatric critical care. In England and Wales, these are advanced and mature services providing critical care for both neonates (aged ≤ 28 days) and children (aged ≤ 18 years) with severe illnesses. There is substantial crossover between neonatal and paediatric intensive care because some services (e.g. congenital cardiac surgery) are provided on a national basis by specialised units. Critical care units provide care at a regional level, and annual admission rates have increased dramatically in recent years, partly because of an increased number of children being born prematurely or with complex medical conditions requiring intensive care [24]. Medication prescribing systems in these units are still largely paper based [25].

The NRLS defines a patient safety incident as "any unintended or unexpected incident that could have [led] or did lead to harm for one or more patients receiving healthcare" [26]. Anonymised incident reports related only to the use of medication in hospital paediatric critical care settings (paediatric/neonatal ICU or high-dependency units) were obtained from the NRLS. Because of the way the incident data from neonatal and paediatric intensive care are coded

in the NRLS, it was impractical to separate the data into separate groups (neonatal and paediatric ICU) reliably, so the data were processed together.

2.2 Screening Process and Descriptive Analysis

Patient safety incidents are mostly reported by healthcare professionals in NHS organisations to their local risk management system using existing coding frameworks. The NHS organisations analyse, investigate, and anonymise incident reports and then submit them to the NRLS. All incidents reported by NHS organisations are aligned to the NRLS classification system [27]. In this study, we utilised the final codes recorded in the NRLS classification system without amendments by the research team, as described in Table 1 in the electronic supplementary material (ESM).

Two authors (AA and AS) independently screened all incidents and excluded those that were not medication related. In the first stage of data analysis, authors AA and AS coded medication(s) within each report using the British National Formulary for Children (BNF-C) categorisation system for medication classes [28]. Existing coded data from the NRLS framework for patient age, harm level, stage of medication use, and error category were extracted by AA and AS independently [27].

2.3 Contributory Factors Associated with Incidents Resulting in Patient Harm

In the second phase of the study, we reviewed all incidents reported to have caused patient harm (low harm, moderate harm, severe harm, and death) and conducted a content analysis of free-text incident descriptions (what happened, contributory factors, planned actions preventing reoccurrence) to understand potential contributory factors.

The contributory factors framework within the PISA (PatIent SAfety classification) system was applied to the selected incident reports [29]. This has been successfully used in studies examining NRLS medication incident data in primary care and mental health hospitals [9, 30–33]. To assess the feasibility of using the PISA system in our study, we applied the framework to a sample of the incidents and found that it captured all factors reported in the reports. One author (AA) then applied the PISA framework to each incident, and another author (AS) independently coded a random sample of 500 reports. Any disagreements between the reviewers were discussed until consensus was reached.

2.4 Data Analysis

2.4.1 Descriptive Analysis

Descriptive analyses were conducted using STATA v15® [34]. We used frequency distributions and cross-tabulations to assess relationships between categories. As specific information about the location or speciality in which each incident occurred was lacking, the data were analysed according to age groups (Fig. 1).

We generated cross-tabulations between three patient age groups (age < 28 days, 1 month to 1 year, and 2–18 years), medication use process stage (supply, prescribing, advice, preparation/dispensing, administration, and monitoring), degree of harm (severity), and error type (Table 1 in the ESM). Further analysis explored the three most common BNF-C medication sub-classes involved across the medication use process stages. We also generated cross-tabulations between medications involved in reported incidents and the degree of harm to identify medication classes commonly involved with harmful events.

2.4.2 Content Analysis of Incidents Reported to have Caused Patient Harm

We applied the four main domains of the PISA classification system contributory factors list (patient, staff/individual, equipment, and organisation) and their sub-categories to the subset of incidents associated with harm. We also used Reason's theoretical model of accident causation [35] to classify and present emerging contributory factor categories as (1) active failures (proximal causes of incidents) associated with individuals and (2) organisational (latent) systems failures as described in the reports. Information in the incident reports was insufficient to allow further categorisation of these failures (e.g. slips or lapses for active failures).

3 Results

3.1 Descriptive Findings

A total of 25,612 incident reports were obtained from the NRLS database. Of these, 25,567 (99.8%) were medication related and deemed eligible for inclusion. The remainder (0.2%) were excluded as they were not associated with the use of medication (e.g. infant feeds [breast milk, formula]). Figure 1 illustrates the screening process, including the capture of key information with each report.

Most incident reports involved infants aged < 28 days (n = 12,235 [47.9%]) and children aged between 1 month and 1 year (n = 9337 [36.5%]). Most reported incidents related to medicines administration (n = 13,668 [53.5%])

Table 1 Descriptive statistics of the incident reports dataset, including age groups, common stages of medication use process, common error types, severity, and medication classes

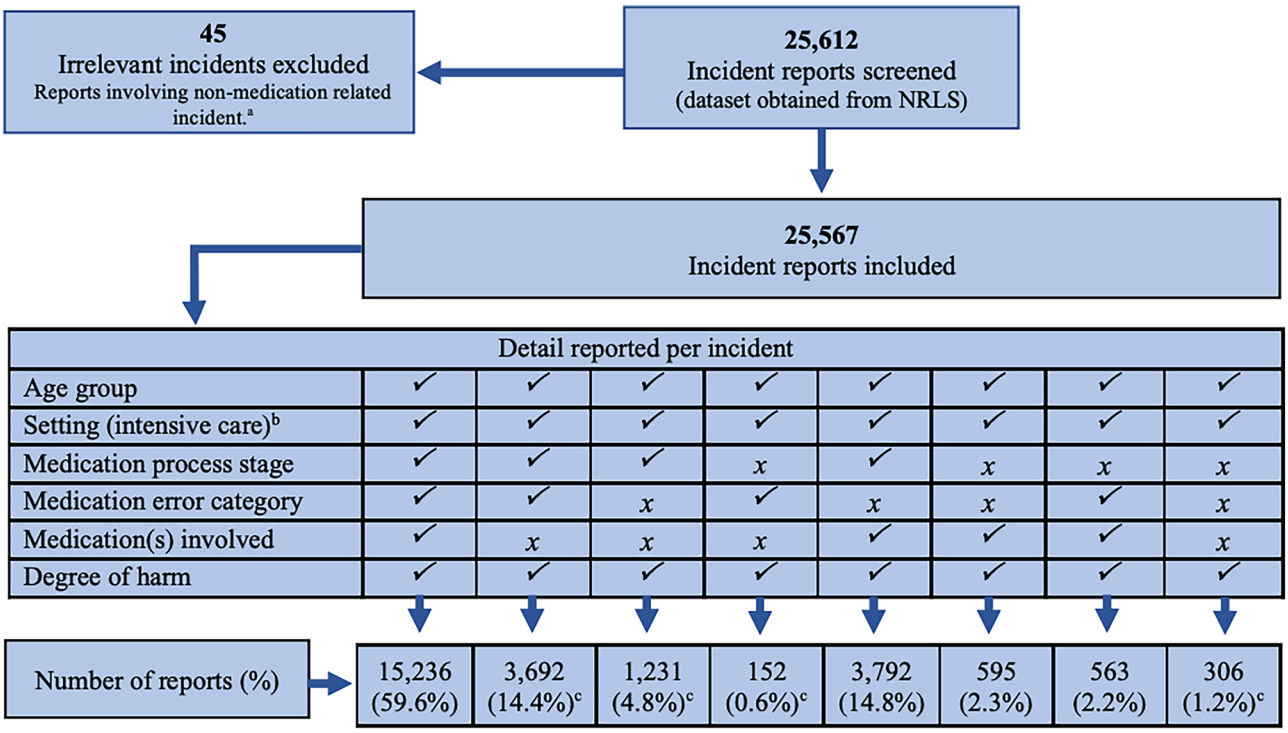
Category			Number of incidents
Incident reports per age group			
< 28 days			12,235 (47.9)
1 month to 1 year			9337 (36.5)
2–18 years			3995 (15.6)
Commonly involved stages of medication use process		Commonly reported error category per stage	Number of incidents
Administration	13,668 (53.5)	Omitted medicine	3590 (26.3)
		Wrong frequency	1810 (13.2)
		Wrong dose	1674 (12.2)
Prescribing	7412 (29)	Wrong dose	2450 (33.1)
		Wrong frequency	1156 (15.6)
		Wrong quantity	614 (8.3)
Incident reports per degree of harm (severity)			
No harm			22,438 (87.8)
Low			2833 (11.1)
Moderate			286 (1.1)
Severe/death			10 (0.04)

Category (British National Formulary—Children)	Degree of harm (severity) per drug class				Number of incidents
	No harm	Low	Moderate	Severe/death	
Medication classes involved with reported incidents and degree of harm per drug class					
Gastrointestinal system	790 (89.2)	90 (10.2)	6 (0.7)	0	886 (3.5)
Cardiovascular system	2144 (86.8)	297 (12)	28 (1.1)	0	2469 (9.7)
Respiratory system	770 (89.4)	84 (9.8)	7 (0.8)	0	861 (3.4)
Central nervous system	2283 (87.4)	301 (11.5)	29 (1.1)	0	2613 (10.2)
Infections	5709 (88.1)	728 (11.2)	44 (0.7)	2 (0.03)	6483 (25.4)
Endocrine system	716 (84.7)	118 (13.9)	11 (1.3)	0	845 (3.3)
Obstetrics, gynaecology, and urinary tract disorders	2 (66.7)	1 (33.3)	0	0	3 (0.01)
Malignant disease and immunosuppression	117 (89.3)	12 (9.2)	2 (1.5)	0	131 (0.5)
Nutrition and blood	3948 (87.6)	502 (11.1)	51 (1.1)	4 (0.09)	4505 (17.6)
Musculoskeletal and joint diseases	132 (88.6)	15 (10.1)	2 (1.3)	0	149 (0.6)
Eye	102 (92.7)	7 (6.4)	1 (0.9)	0	110 (0.4)
Ear, nose, and oropharynx	16 (94.1)	1 (5.9)	0	0	17 (0.1)
Skin	130 (90.9)	13 (9.1)	0	0	143 (0.6)
Immunological products and vaccines	150 (88.8)	15 (8.9)	4 (2.4)	0	169 (0.7)
Anaesthesia	696 (89.2)	72 (9.2)	12 (1.5)	0	780 (3.1)
Multiple drug categories involved	18 (81.8)	3 (13.6)	1 (4.5)	0	22 (0.1)
Unknown drugs	4715 (87.6)	574 (10.7)	88 (1.6)	4 (0.1)	5381 (21.1)

Data are presented as *n* (%)

and prescribing ($n = 7412$ [29%]), with the most common error types being drug omission ($n = 4812$ [18.8%]), wrong dose ($n = 4475$ [17.5%]), and wrong frequency ($n = 3193$ [12.5%]) (Table 1).

Most incidents did not cause patient harm ($n = 22,438$ [87.8%]). Of 3129 (12.2%) harmful events, 2833 (90.5%) resulted in low harm, 286 (9.1%) caused moderate harm, and ten (0.31%) led to severe harm/patient death. The medications most commonly involved with incidents were anti-infectives ($n = 6483$ [25.4%]), followed by medications affecting nutrition and blood ($n = 4505$ [17.6%]) and agents acting on the central nervous system ($n = 2613$ [10.2%]). The majority of the 6483 incidents with anti-infectives involved antibacterial agents ($n = 6002$ [92.6%]), and aminoglycosides were the predominant subclass of these ($n = 2470$



NRLS: National Reporting and Learning System.
✓: reported x: not reported
[a] Non-medication incidents reports involving products such as infant feeds (breast milk, formula).
[b] Speciality was specified in 2.2% (565/25,567) and 12.9% (3,322/25,567) of reports as neonatal and paediatric intensive care settings, respectively.
[C] Incidents reports with unknown medication(s): 5,381/25,567 (21.1%).

Fig. 1 Categories of incident reports containing key information

[41.2%]). Table 1 shows the medication classes involved and the level of harm caused by each drug category.

3.1.1 Incidents Reported by Age Group (Age < 28 Days, 1 Month to 2 Years, and 2–18 Years)

The stages of the medication use process most commonly involved with incidents across all age groups was medication administration and prescribing, with drug omissions and wrong doses being the most common error types, as described in Table 2. Half of all harmful incidents (n = 1570/3129 [50.2%]) involved neonates (aged ≤ 28 days). Across both prescribing and administration stages, anti-infectives were the medications most commonly involved with reported incidents in the youngest age groups (< 28 days, n = 3399/9941 [34.2%] and 1 month to 2 years, n = 1427/7819 [18.2%]).

Across all medication use process stages, most of the incidents associated with anti-infective medications involved neonates aged ≤ 28 days (n = 4153/6483 [64.1%]). Aminoglycosides were the most commonly involved anti-infectives in this age group (n = 2007/4153 [48.3%]).

Across all age groups, harmful incidents most frequently occurred during medicines administration (n = 1955/3129 [62.5%]), involved medications commonly used to treat infections (n = 774/3129 [24.7%]), and involved wrong dosing (n = 608/3129 [19.4%]), drug omission (n = 606/3129 [19.4%]), and wrong frequency (n = 454/3129 [14.5%]) error types. Table 2 presents detailed information about the incidents reported in each age group, including commonly involved medication use process stages, levels of harm, drug classes, and error types.

3.2 Contributory Factors for Incidents Reported to have Caused Patient Harm

Of the 12.2% of harmful incidents, 1765 reports (56.4%) were included as they stated explicit contributory factors,

Table 2 Summary of the descriptive analysis of incident reports by age group

Age group	Category	Total incidents	Degree of harm (severity)				Common error types		Commonly involved drug classes in each stage	
			No harm	Low	Moderate	Severe/death				
< 28 days	Reported incidents	12,235 (47.9)	10,665 (87.2)	1402 (11.5)	163 (1.3)	5 (0.04)				
	Commonly involved stages of medication use process									
	Administration	6465 (52.8)	5491 (84.9)	865 (13.4)	104 (1.6)	5 (0.08)	Omitted medicine	1750 (27.1)	Anti-infectives	2146 (33.2)
							Wrong frequency	1067 (16.5)	Nutrition and blood	1206 (18.7)
							Wrong dose	721 (11.2)	Cardiovascular system	381 (5.9)
	Prescribing	3476 (28.4)	3159 (90.9)	285 (8.2)	32 (0.9)	0 (0.00)	Wrong dose	1011 (29.09)	Anti-infectives	1253 (36.1)
							Wrong frequency	667 (19.19)	Nutrition and blood	690 (19.9)
							Wrong quantity	302 (8.69)	Central nervous system	236 (6.8)
	Totals	9941 (81.2)	8650 (87.01)	1150 (11.6)	136 (1.4)	5 (0.05)		5518 (55.5)		5912 (59.5)
1 month to 2 years	Reported incidents	9337 (36.5)	8282 (88.7)	967 (10.4)	84 (0.9)	4 (0.04)				
	Commonly involved stages of medication use process									
	Administration	5082 (54.4)	4419 (86.9)	600 (11.8)	61 (1.2)	2 (0.04)	Omitted medicine	1443 (28.39)	Nutrition and blood	900 (17.7)
							Wrong dose	622 (12.24)	Anti-infectives	869 (17.1)
							Wrong frequency	579 (11.39)	Cardiovascular system	696 (13.7)
	Prescribing	2737 (29.3)	2493 (91.1)	231 (8.4)	12 (0.4)	1 (0.04)	Wrong dose	965 (35.26)	Anti-infectives	558 (20.4)
							Wrong frequency	379 (13.85)	Nutrition and blood	450 (16.4)
							Omitted medicine	208 (7.60)	Central nervous system	376 (13.7)
	Totals	7819 (83.7)	6912 (74.02)	831 (10.6)	73 (0.93)	3 (0.04)		4196 (53.7)		3849 (41.2)
Age >2 years (2–18 years)	Reported incidents	3995 (15.6)	3491 (87.4)	464 (11.6)	39 (1.0)	1 (0.03)				
	Commonly involved stages of medication use process									
	Administration	2121 (53.1)	1803 (85.0)	294 (13.9)	23 (1.1)	1 (0.05)	Omitted medicine	397 (18.7)	Central nervous system	411 (19.4)
							Wrong dose	331 (15.6)	Anti-infectives	302 (14.2)
							Wrong quantity	195 (9.2)	Nutrition and blood	292 (13.8)
	Prescribing	1199 (30.0)	1084 (90.4)	104 (8.7)	11 (0.9)	0 (0.0)	Wrong dose	474 (39.5)	Anti-infectives	253 (21.1)
							Wrong frequency	110 (9.2)	Central nervous system	226 (18.8)
							Omitted medicine	100 (8.3)	Cardiovascular system	152 (12.7)
	Totals	3320 (83.1)	2887 (86.9)	398 (11.9)	34 (1.02)	1 (0.03)		1607 (48.4)		1636 (49.3)

Data are presented as number of incidents (%)

whereas the remaining 1364 reports (43.6%) were excluded because descriptions of reported incidents in the free-text data were lacking.

Three main categories emerged from our content analysis that explored contributory factors: factors related to patients ($n = 62/1765$ [3.5%]), medical staff/individual factors ($n = 1212$ [68.7%]), and organisational factors ($n = 482$ [27.3%]). Some incident reports were related to impractical/faulty equipment or inadequate medication storage ($n = 9$ [0.5%]). Incidents that involved multiple contributory factors were common across the harmful incidents examined, and the most frequent combinations of these were staff- and organisational-related factors. Of the 1212 reported incidents that stated staff-related contributory factors, 807 (66.6%) incidents also involved organisational-related factors. Within these incidents, failures to follow/adhere to protocols or procedures because of a busy environment and work overload were common combinations.

3.2.1 Patient-Related Factors

Patient factors featured in incidents involving dose omissions and extravasation injuries. Challenging venous access in neonates led to dose omissions and consequent delays in treatment (example 1.1, Table 2 in the ESM). Given the undeveloped skin and fragile vasculature in this patient group, extravasation injuries were commonly reported in neonates despite correct cannula management procedures being followed.

3.2.2 Staff-Related Factors

Active failures were also associated with reported incidents. Staff factors included cognitive issues (e.g. perception, memory, or thinking), inadequate skill set/knowledge, and failure to follow/adhere to protocols or procedures. These active failures were frequently reported as being caused by organisational-related factors (latent conditions), such as work pressures and issues related to using paper-based prescribing systems (e.g. design of prescription or illegible handwriting). Figure 2 illustrates multi-directional interactions between active failures and latent conditions.

Failure to follow protocols or procedures (active failures), commonly involving prescribing, administering, or monitoring anti-infective medications, were the most common contributory factors directly involving staff. At times, staff did not monitor drug levels as recommended in protocols or follow safety procedures (e.g. independent double checking) for medication administration (example 2.1, Table 2 in the ESM). Other common contributory factors included cognitive issues, such as distraction, inattention, and oversight (example 2.2, Table 2 in the ESM).

Active failures (such as inappropriate cannula management) were also associated with some incidents. For example, lack of regular monitoring of cannula sites for early signs of extravasation injuries and failure to follow guidelines for administering intravenous medications contributed to some incidents. However, these active failures caused by individuals were commonly associated with medical staff being busy/overloaded by work (example 2.3, Table 2 in the ESM).

Errors (active failures) also occurred commonly during patient transfers between units or at handover between shifts. Most of these failures included poor-quality documentation, such as doses given but not documented or administration records lost during handover or patient transfer to ICU (example 2.4, Table 2 in the ESM). These active failures were notably reported as being associated with latent conditions such as heavy workloads (staff busy with other prioritised commitments) and inadequate patient record documentation systems.

Staff also reported errors in medication administration and monitoring due to inadequate knowledge, such as those with specific safety requirements in dosing or administration processes (e.g. phenytoin).

3.2.3 Organisational-Related Factors

The pressurised work environment within ICUs and a shortage of staff often contributed to medication omissions and failures to follow safety policies (example 3.1, Table 2 in the ESM). Incidents were also associated with errors during shift handovers due to inadequate protocols for this process and poor communication between medical staff (example 3.2, Table 2 in the ESM). Newly qualified staff working in the ICU but lacking training and familiarity with the setting's policies and procedures were also described as a cause of incidents.

It became apparent that, in some cases, children, mostly neonates, were transferred routinely from other hospital areas (e.g. general or post-natal wards) to ICUs for single-dose administration before being returned. Incidents occurring during this process were often reported as being due to poor documentation of doses given in either the ward or the ICU or loss of medicine administration records (example 3.3, Table 2 in the ESM).

Other important contributory factors were categorised under poor continuity of care between ICU and hospital departments such as pharmacy and test laboratories. This involved delays in medicines supply from pharmacies, inadequate dispensing protocols, and delays in delivery of blood test results from laboratories (example 3.4, Table 2 in the ESM), which mainly caused dose omissions.

The design of prescription forms and use of paper-based documentation systems frequently contributed to

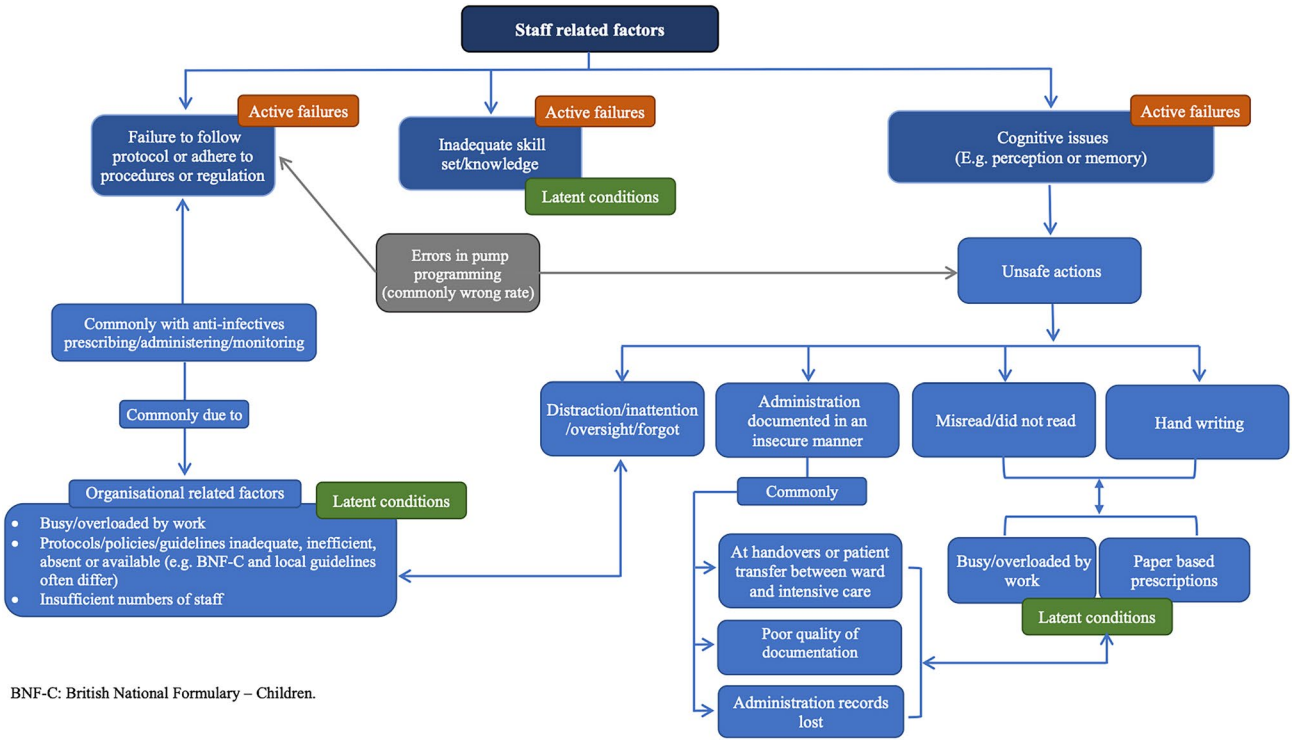


Fig. 2 Contributory factors related to medical staff and interactions with organisational related factors. *BNF-C* British National Formulary—Children

the reported incidents. Ambiguous handwriting and poorly designed prescriptions were caused confusion that led to medication errors (example 3.5, Table 2 in the ESM). The unavailability of protocols and inadequate and variable guidelines were also notable contributory factors (example 3.6, Table 2 in the ESM).

4 Discussion

To our knowledge, this is the first detailed analysis of medication-related incident data reported to a national database from neonatal and children's intensive care settings. We found that incidents relating to medication administration and prescribing stages, and those involving medication omissions, wrong doses, and wrong frequency were the most common across all age groups. Neonates aged < 28 days were associated with most of the reported incidents and affected by most of the harmful incidents. The dominant contributory factors associated with these incidents included the challenging physiology of neonates, working conditions (e.g. heavy workload), variable or inadequate guidelines and systems, and poor continuity of care between ICUs and other hospital departments. Anti-infectives and medications affecting nutrition and blood were the medication classes most frequently involved in harmful and no-harm incidents.

We explored contributory factors for the reported incidents to help facilitate understanding about medication safety in this environment and illuminate the complexity of neonatal and children's intensive care settings. Routine tasks (e.g. securing and monitoring venous access, checking and acting on drug levels, and administration double-checking procedures) were adversely affected by organisational factors such as staff shortages and consequent heavy workload, along with inadequate dosing guidelines and prescribing systems. Indeed, prescribing remains largely paper based in the UK [25]. The introduction of electronic prescribing systems has been associated with significant reductions in certain types of errors, such as illegible prescriptions [36]. Handwriting was one of the factors commonly involved with reported incidents in this study. In addition, clinical decision support is offered primarily in the form of administrative policies and guidelines, many of which are not standardised across interfaces of care. In a recent multi-centre study of the causative factors of prescribing errors in paediatric intensive care in England, a core feature of these decision support systems was their intellectual and physical inaccessibility. Furthermore, the only control against medication error in this setting was identified as the bedside nurse or

unit pharmacist. However, these controls may be constrained by staff shortages and whether pharmacy services are available only during 'office hours' [8].

We found that the use of anti-infective medications is an area of risk to children in the ICU, particularly neonates aged < 28 days, with a high proportion of aminoglycosides implicated in incidents. This class of medicines is widely used to treat infections in neonates [37]. Aminoglycoside dosing and monitoring errors may cause serious and sometimes irreversible injury [38]. National co-ordinated guidance was implemented in 2010 to reduce these incidents with aminoglycosides in neonates [39]; however, the present study shows that incidents persist. As such, the use of safer alternative antimicrobials in critically ill neonates should be evaluated and safety measures in the use of these medications should be improved.

Common error types identified in our study, such as wrong doses and dose omissions, were notably associated with the pressurised ICU work environment, suggesting that improved staffing and workload is an important target. Studies have found that heavy workload and inadequate staffing, and related staff fatigue, were significantly associated with missed care for critically ill children [8, 40–42]. Children's ICUs, including high-dependency beds in England and Wales, routinely exceed the standard limit of bed occupancy (reaching 85–100% occupancy), which should be < 85% and thus are often considered overloaded [43]. A better understanding of safe working conditions, and their influence on the implementation of medication safety improvements in these settings, is needed. The application of principles from the field of human factors and ergonomics could support the redesign of systems and processes to improve safety in complex work settings such as ICUs [44].

A meta-analysis conducted in 2020 [45] found that including pharmacists in hospital clinical areas to intervene in prescribing errors significantly reduced these errors in paediatric inpatients. Clinical pharmacy services are normally provided in hospitals in England and Wales, but the role of these services in medication safety in UK children's intensive care settings is not well understood [45]. In addition, evidence on the clinical effectiveness (mitigating patient harm) of other strategies, such as computerised physician order entry and clinical decision support systems, remains limited [46]. Therefore, future controlled interventional studies are recommended with priority for critically ill neonates and anti-infective medications (particularly aminoglycosides) as high-risk areas.

In this study, we analysed a large dataset covering a 9-year period and generated important evidence of the nature of and factors contributing to medication safety incidents in children's ICUs. This evidence may be used to support efforts to reduce medication errors and related patient harm in this area. The main limitation of this study is that we were unable to calculate the rate of events (e.g. per number of patients or prescriptions) as our data source was a national, fully anonymised, retrospective, and spontaneous incident-reporting data source [47]. Another limitation of this study relates to the poor quality of reporting of the speciality (neonatal or children's ICU) where incidents occurred, which limited our ability to separate data from the two settings and to generate distinct improvement recommendations. Information about the medications involved with reported incidents was also missing. Therefore, the quality of reporting of information about incident location (e.g. neonatal ICU, paediatric ICU, or high-dependency unit) and medications involved could be improved in the NRLS reports to promote learning from incidents in future studies. In addition, we acknowledge that discrepancies may occur between reporter-allocated level of harm and the harm described within reported incidents [48]. This study did not reclassify reported incidents and used the NRLS classification system, so we did not examine variations between described and reported levels of harm in incidents.

5 Conclusion

This is the first exploration of the type, and contributory factors of medication-related safety incidents reported in children's ICUs at a national level. We found that incidents were commonly associated with medication administration and prescribing stages. Most harmful and no-harm incidents involved neonates. Medication incidents occurring in this setting may have origins in challenging venous access in neonates, failure of ICU staff to follow safety protocols, notably, due to ICU excessive workload, inadequate policies or systems, and staff shortages. We identified areas for medication safety improvement in these settings, including transfer-of-care processes between wards and the ICU, medicines prescribing, and patient record documentation systems, as well as the use of anti-infective medications.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40272-021-00442-6.

Declarations

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Conflicts of Interest Anwar A. Alghamdi, Richard N. Keers, Adam Sutherland, Andrew Carson-Stevens and Darren M. Ashcroft have no conflicts of interest that are directly relevant to the content of this study.

Availability of data and material NHS Improvement approved the sharing of the NRLS data with the University of Manchester. As per the data sharing agreement (DSA.5047), access to data is only available after approval by NHS Improvement (https://www.england.nhs.uk/contact-us/contact-nhs-improvement/).

Ethics approval The National Patient Safety Team at NHS England and NHS Improvement approved the study protocol and the sharing of the NRLS data with the University of Manchester (approval reference: DSA.5047).

Consent Data utilised in this study were fully anonymised prior to being made available to the research team under an approved data sharing agreement without individual consent from patients and practitioners described in the incident reports.

Code availability Not applicable.

Authors' contributions Anwar A. Alghamdi contributed to the study design and the analysis and interpretation of data and led the data screening, inclusion and exclusion assessment, data coding and analysis, and manuscript writing. Richard N. Keers and Darren M. Ashcroft contributed to the study design and interpretation of data, critically reviewed and revised the manuscript, and supervised AAA throughout his PhD programme. Adam Sutherland was involved in the data screening, coding, and analysis; inclusion and exclusion assessment; and review and revision of the manuscript. Andrew Carson-Stevens was involved in the data analysis and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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