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What causes prescribing errors in children? Scoping review

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ABSTRACT

Objectives (1) Systematically assemble, analyse and synthesise published evidence on causes of prescribing error in children. (2) Present results to a multidisciplinary group of paediatric prescribing stakeholders to validate findings and establish how causative factors lead to errors in practice.

Design Scoping review using Arksey and O'Malley's framework, including stakeholder consultation; qualitative evidence synthesis.

Methods We followed the six scoping review stages. (1) Research question—the research question was 'What is known about causes of prescribing error in children?' (2) Search strategy—we searched MEDLINE, EMBASE, CINAHL (from inception to February 2018), grey literature and reference lists of included studies. (3) Article selection—all published evidence contributing information on the causes of prescribing error in children was eligible for inclusion. We included review articles as secondary evidence to broaden understanding. (4) Charting data—results were collated in a custom data charting form. (5) Reporting results—we summarised article characteristics, extracted causal evidence and thematically synthesised findings. (6) Stakeholder consultation—results were presented to a multidisciplinary focus group of six prescribing stakeholders to establish validity, relevance and mechanisms by which causes lead to errors in practice.

Results 68 articles were included. We identified six main causes of prescribing errors: *children's fundamental differences* led to *individualised dosing and calculations; off-licence prescribing; medication formulations; communication with children*; and *experience working with children*. Primary evidence clarifying causes was lacking.

Conclusions Specific factors complicate prescribing for children and increase risk of errors. Primary research is needed to confirm and elaborate these causes of error. In the meantime, this review uses existing evidence to make provisional paediatric-specific recommendations for policy, practice and education.

Strengths and limitations of this study

- ► This study used systematic methods to provide a comprehensive review of causes of prescribing errors in children.
- ► We consulted prescribing stakeholders to add key contextual information on how errors happen in practice.
- ► Risk of overemphasising expert opinion was introduced by the decision to include secondary evidence.
- ► Article selection was made potentially subjective because of the study's inclusive approach, bringing together all evidence that could contribute information on causes of errors.

INTRODUCTION

Thirteen per cent of prescriptions written for children contain errors.[1] These lead to harm, which can be catastrophic,[2] and increase costs.[3] Recent research has clarified the extent of the problem[1 4 5] but the causes of errors are still poorly understood. Research in adults[6–8] is of limited value because paediatric prescribing errors are different. Potentially harmful errors are three times more common in children.[9] The youngest patients are most affected, which suggests that something specific to children causes errors.[9] Dosing errors are by far the leading error type,[4] including potentially lethal tenfold dosing errors, to which children are much more susceptible.[10]

There have been limited attempts to synthesise existing evidence about the causes of prescribing errors in children.[11] Authors have discussed how prescribing for children differs. But what we know less about is *how and why* those differences lead to errors. This information is essential for clinicians and educators trying to improve medication safety in children. This article reports a scoping review that, first, systematically assembled and analysed published evidence about the causes of paediatric prescribing errors and, second, presented the findings to a multidisciplinary group of stakeholders to validate findings and provide details of how causative factors lead to errors.

METHODS

We chose scoping review methodology[12 13] because it 'identifies key concepts, research gaps, and evidence to inform

Table 1 STARLITE[17] summary of search strategy

Sampling strategy	Comprehensive—attempting to identify all published materials
Type of study	Any study contributing to research question: all study designs, quantitative, qualitative or mixed; primary or secondary sources
Approaches	Electronic database searching; Google Scholar; reference lists hand searching; articles found opportunistically
Range of years	From database inception to February 2018
Limits	English language articles; children aged 0–18 years
Inclusion/exclusion criteria	See box 1
Terms used	See online supplementary file 1
Electronic databases	Ovid MEDLINE; EMBASE; CINAHL; PubMed; Google Scholar

practice, policymaking and research.'[14] Scoping reviews use rigorous and transparent methods to identify and analyse relevant literature[15] with the added advantage of including heterogeneous, methodologically diverse evidence, and a stakeholder consultation to validate this evidence. These steps are key to understanding complex topics of this sort. A medical student (OK), an endocrinologist and senior medical education researcher (TD), a paediatric specialty trainee undertaking a PhD in medical education (RLC), a professor of child health (MDS) and an academic pharmacist (MPT) conducted the review. We used the six scoping review stages, as laid out by Arksey and O'Malley,[12] to provide a structure for the methods, and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines.[16]

Identifying the research question

The review question was '*What is known about causes of prescribing error in children?*' Since preliminary searching had found little explanatory evidence, we defined 'causes' to include contributors, predictors, risk factors and correlates of errors.

Identifying relevant studies

We designed the search strategy to find all articles about factors contributing to errors (table 1),[17] combining the concepts 'prescribing', 'error', 'cause' and relevant synonyms, limited to children aged 0–18 years. A specialist librarian reviewed the search syntax and applied it to MEDLINE, EMBASE and CINAHL (MEDLINE search terms are shown in online supplementary file 1). We also searched PubMed for articles not yet indexed for MEDLINE, and Google Scholar and EThOS (British Library thesis database) for grey literature. We hand searched reference lists of all included articles to complement database searching, which may miss heterogeneous evidence.[18]

Screening and selection procedures

We tabulated search results in Microsoft Excel (Microsoft, Redmond, USA), removed duplicates manually and applied the following inclusion and exclusion criteria (summarised in box 1): prescribing error (according to Ghaleb *et al*.'s definition of clinically important paediatric prescribing errors,[19] using handwritten or electronic prescriptions, by doctors, for children and young people aged 0–18). We included drug choice and communication with patients,[20] though most errors were reported in prescription writing.

In order to refine and then apply the inclusion and exclusion consistently,[13] RLC and OK jointly reviewed 100 results. OK then screened all titles and abstracts and recorded reasons for excluding ineligible articles. RLC and OK discussed articles where decisions were unclear, retrieving full texts if necessary. To validate the accuracy of the selection process, all members of the research team independently reviewed 20 abstracts, reaching the same decision in 19/20 cases. OK and RLC then jointly reviewed abstracts or full texts of all remaining articles.

We included 'primary evidence' (empirical research) as well as 'secondary evidence' from review articles, whose

Box 1 Eligibility criteria for article selection

Inclusion criteria

- All studies contributing information on causes of medication prescribing errors ('as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice'[19]) of all types in children aged 0–18.
- Handwritten or electronic prescriptions.

Exclusion criteria

- Did not specifically address children.
- Did not contribute information on causes, risk factors, associations or predictors of error.
- Study involving adult patients and not possible to discern causes relating to children specifically.
- Study investigating medication errors and not possible to discern causes of prescribing errors specifically.
- Related to prescribing errors made by non-medical prescribers.
- Related to non-drug prescribing, such as prescribing eyeglasses.
- Articles not available in English language.
- Full-text article could not be retrieved.

authors advanced well-reasoned arguments for causes of errors based on referenced evidence, experience or authoritative opinion. We included secondary evidence because it contributed understanding of the topic and our methodology included an extra 'filter': a consultation exercise, to validate relevance of findings to practice. As is customary in scoping reviews, we did not exclude articles based on quality or design.[15] Table 2 allows readers to form opinions on the strength of evidence by linking identified causes of error with types of articles and study methodologies.

Charting the data

Using Microsoft Excel, we created a custom data charting form including study demographics, methodology and error causes. OK charted all study details; RLC read all articles and checked the accuracy of her data extraction.

Collating, summarising and reporting results

We tabulated key information from included studies and quantified their characteristics. We then synthesised research findings thematically.[21] First, OK and RLC independently coded causes of error in a subset of 20 articles. By discussing their coding, they developed a thematic framework, which OK applied to the remaining articles. RLC checked the accuracy of coding in all articles. We quantified codes, giving a sense of the relative importance attached to the causes of prescribing error described in literature. We then developed themes, which were agreed by all authors.

Stakeholder consultation

We purposefully sampled key prescribing stakeholders from a range of backgrounds to participate in a multidisciplinary focus group. RLC presented the findings of the literature review and asked participants to discuss how, in their experience, these factors led to errors. The focus group protocol is included as online supplementary file 2. RLC recorded the discussion and transcribed it verbatim. We analysed the transcript by coding information within the themes from the literature review and then identifying details of how causes led to errors in practice ('error mechanisms'). Stakeholder evidence is presented within the main text and in a table. Quotations which support findings in the main text are linked by numbers, for example, (3PP1).

Patient and public involvement

We did not involve patients or families in the conduct of this research.

RESULTS

Included and excluded articles

Figure 1 summarises study selection. From 1735 identified articles, 228 were considered potentially contributory after initial exclusions. A further 185 were excluded after two-person review of abstract or full text, as required; this was mainly because they studied error epidemiology (81 articles) or interventions to prevent errors (48 articles) but did not contribute information on errors' causes. We identified a further 25 articles through reference list searching (22 articles) and by finding relevant studies opportunistically during searching and article retrieval (three articles). Sixty-eight articles were included in the review (n=68) (table 2).

Article characteristics

Of the 68 included articles, 59 (87%) were published since 2000 (table 3). The majority were from North America (35 articles; 51%) or the UK (18 articles; 26%). Forty-four (63%) articles reported primary research; of these, 39 were observational studies in clinical settings. These typically identified errors using drug chart/medical record review (21 studies; 42%) or incident reporting (13 studies; 26%). In 20 of the 44 primary studies (45%), factors associated with errors were supported with statistical analysis. Twenty-four (35%) reported secondary evidence, of which 19 were review articles (table 4).

Stakeholder consultation

A consultant paediatrician, two paediatric trainees, a paediatric pharmacist/independent prescriber, an advanced paediatric nurse practitioner/independent prescriber and a nurse educator participated in the stakeholder focus group. Four were female and two were male. Their experience working in paediatrics ranged from 3 to 30 years. Stakeholder evidence is presented within the main text and, with direct quotations, in table 5. Quotations are linked to the main text using participant identifiers, for example, (3PP1).

Causes of errors

As in adults, 'generic' factors such as prescriber characteristics, organisational problems, working conditions and interprofessional communication caused errors. Table 2 reports these findings in detail. Most articles, however, focused on causes of errors that were specific to children, resulting in six major themes.

Children's fundamental differences

Fundamental differences between children and adults (16 references) were: rapidly changing, highly variable size and weight[22–29]; physiology and metabolism[22–24 29–31]; pharmacokinetics and pharmacodynamics[22 23 25–28 31–36]; disease states and prematurity[24 32 36 37]; development (including puberty) and cognition.[23 26 29 31] These differences led to five major causes of errors. Growth and changing size necessitate *individualised dosing*, typically based on weight, age or body surface area, requiring prescribers to perform *calculations* (45 references). Differences in drug handling mean that pharmacokinetic-pharmacodynamic research conducted in adults does not apply in children, contributing to the practice of *off-licence prescribing* (14 references).[32] The non-standard nature of off-licence treatments, along with developmental differences such as inability to swallow tablets, leads to use of different *medication formulations* in children (15

Table 2 Summary of included studies

Study details			Design				Causes						
First author	Year	Country	Context	Specific focus	Data source	Outcome	CFD	IDC	OLP	MF	CC	EWC	Other
Prospective observational studies in clinical settings													
Zhang[78]	2017	China	NICU	–	Incident reports	Other statistics							Lack of education, staffing problems, workload, missing patient information, inadequate communication within healthcare team
Coffey[61]	2009	Canada	Paediatric wards	Medicines reconciliation	Drug chart review	Logistic regression							Multiple medications
Rashed[62]	2012	UK; Saudi Arabia	Paediatric wards; PICU; NICU	–	Medical record review; drug chart review	Logistic regression; researcher inference		✓					Multiple medications, transferred admission
Wilson[44]	1998	UK	Paediatric cardiac ward; paediatric cardiac ICU	–	Incident reports	Hypothesis testing		✓				✓	Patient complexity, multiple medications, distractions, workload
Honey[56]	2015	USA	Paediatric outpatients	Effect of resident training programme	Drug chart review	Hypothesis testing						✓	
Butler[63]	2013	Ireland	Paediatric wards	Medicines reconciliation	Medical record review; drug chart review; other	Descriptive statistics							Multiple medications, drug type
Kirk[43]	2005	Singapore	Paediatric wards; outpatients; ED	Computer calculated dosing	Drug chart review	Logistic regression						✓	Drug type
Fahrenkopf[79]	2008	USA	Paediatric wards	Effect of resident burnout and depression	Drug chart review; incident reports	Hypothesis testing							Depression in prescriber
Buckley[80]	2007	USA	PICU	PICU setting	Direct observation	Descriptive statistics							Memory lapses, lack of knowledge, procedural violations, organisational issues
Al-Ramahi[81]	2017	Palestine	Paediatric wards	Dosing errors	Medical record review	Hypothesis testing		✓					Younger patient age, lower patient body weight, multiple medications, longer hospital stay
Lesar[10]	2002	USA	Paediatric wards; NICU, PICU	Ten-fold dose prescribing errors	Drug chart review	Descriptive statistics		✓					
Retrospective observational studies in clinical settings													
Yeh[82]	2010	Taiwan	Outpatients	Methylphenidate overprescribing in ADHD	Medical record review	Logistic regression							Patient lower socioeconomic status, younger prescriber age, increasing duration of prescription
Shaw[46]	2013	USA	ED	ED setting	Incident reports	Descriptive statistics		✓					Human factors, inadequate supervision, procedural violations, inadequate communication within healthcare team, working environment

Continued

Table 2 Continued

Study details			Design				Causes						
First author	Year	Country	Context	Specific focus	Data source	Outcome	CFD	IDC	OLP	MF	CC	EWC	Other
McPhillips[83]	2005	USA	Outpatients	Dosing errors in outpatients	Drug chart review; other database	Logistic regression							Drug type, as required drug use, patient age, patient complexity, multiple medications
Lobaugh[84]	2017	USA	Anaesthesia	Paediatric anaesthesia	Incident reports	Descriptive statistics; researcher inference		✓					Human error, lack of knowledge, workplace conditions
Conn[58]	2017	UK	Paediatric secondary care	Intravenous fluid prescribing errors	Incident reports	Qualitative analysis		✓				✓	Working out of hours, conflicting protocols, patient complexity, inadequate communication within healthcare team, lack of knowledge
Conroy[47]	2011	UK	Paediatric wards; NICU	Off-licence medication use	Incident reports	Hypothesis testing			✓	✓			
Conroy[85]	2009	UK	Paediatric hospital—all settings	Off-licence medication use	Incident reports	Descriptive statistics			✓				
Pacheco[86]	2012	USA	ED	Effect of resident level of training	Drug chart review	Descriptive statistics							Workload, fatigue, distractions, complacency
Chen[64]	2012	Taiwan	Outpatients	Stimulant prescribing errors in ADHD	National database	Logistic regression							Changing physicians, patient condition, patient rural residence, prescriber increasing age
Rinke[55]	2008	USA	ED	Paediatric ED setting	Medical record review; drug chart review	Descriptive statistics		✓				✓	
Taylor[57]	2005	USA	ED	Paediatric ED setting; effect of resident specialty/ level of training	Medical record review; drug chart review	Descriptive statistics		✓				✓	Working environment, stress, distractions, workload, inadequate supervision
Wingert[87]	1975	USA	ED	Paediatric ED setting	Medical record review; drug chart review	Hypothesis testing		✓					Distractions, workload
Selbst[45]	1999	USA	ED	Paediatric ED setting	Incident reports; medical record review	Descriptive statistics		✓					Nights and weekends, soundalike medications, working environment, stress, distractions, verbal drug ordering, fatigue, staffing levels
Kozer[54]	2002	Canada	ED	Paediatric ED setting	Drug chart review	Hypothesis testing						✓	
Vila-de-Muga[88]	2011	Spain	ED	Paediatric ED setting	Drug chart review	Hypothesis testing							Weekends, nights, holidays
Pichon[89]	2002	Switzerland	Haematology/ oncology	Chemotherapy; other treatments used in oncology	Drug chart review	Descriptive statistics							Intravenous drugs, as required drugs
Payne[90]	2007	USA	Anaesthesia	Paediatric anaesthesia	Incident reports	Descriptive statistics		✓					

Continued

Table 2 Continued

Study details			Design				Causes						
First author	Year	Country	Context	Specific focus	Data source	Outcome	CFD	IDC	OLP	MF	CC	EWC	Other
Lesar[38]	1998	USA	Paediatric wards	Dosage equations	Drug chart review	Descriptive statistics		✓					
Manias[53]	2014	Australia	Paediatric wards	–	Incident reports	Descriptive statistics		✓				✓	Inadequate communication within healthcare team, transitions, interruptions, lack of attention to policies
Kozer[91]	2006	Canada	Paediatric wards; ED	Ten-fold dosing errors	Incident reports; drug chart review; simulation	Researcher inference		✓		✓			Human error, systems error
Cousins[2]	2002	UK	All paediatric care settings	–	Press reports	Descriptive statistics		✓		✓			Incomplete information to guide prescribing
Prospective studies in classroom settings													
Rowe[39]	1998	Canada	Paediatric hospital	Resident dose calculation errors	Written test	Hypothesis testing		✓					Workload, fatigue
Potts[41]	1996	USA	Primary care	Resident calculation errors	Written test	Hypothesis testing		✓				✓	Inadequate undergraduate education
Glover[40]	2002	USA	Paediatric hospital	Resident mathematical skills/ calculation errors	Written test	Hypothesis testing		✓				✓	Stress, high workload
Menon[42]	2006	UK	Paediatric hospital	–	Written test	Hypothesis testing		✓				✓	
Prospective studies in simulated settings													
Kozer[92]	2004	Canada	Paediatric hospital	Resuscitation	Simulation	Descriptive statistics		✓					Verbal drug ordering
Porter[93]	2014	USA	ED	Resuscitation	Simulation	Logistic regression		✓					Lack of sleep, absence of pharmacist
Other primary study designs													
Lago[94]	2012	Italy	Paediatric hospital	–	Expert consensus	Descriptive statistics		✓					Not checking, verbal drug ordering, incomplete patient reassessment, inadequate communication within healthcare team
van Tilburg[95]	2006	Netherlands	Oncology	Chemotherapy prescribing, administration and dispensing errors	Expert consensus	Descriptive statistics							Workload, distractions, interruptions, inadequate communication within healthcare team
Kunac[96]	2005	New Zealand	NICU	NICU setting	Expert consensus	Descriptive statistics							Lack of awareness of medication safety
Diav-Citrin[52]	2000	Canada	Immunology	–	Case report	Qualitative analysis		✓			✓	✓	Lack of knowledge, skill or experience, illegible handwriting, similar drug names

Continued

Table 2 Continued

Study details			Design				Causes						
First author	**Year**	**Country**	**Context**	**Specific focus**	**Data source**	**Outcome**	**CFD**	**IDC**	**OLP**	**MF**	**CC**	**EWC**	**Other**
White[97]	2005	USA	PICU	Intravenous potassium prescribing errors in PICU	Direct observation; medical record review; interview (nominative group technique)	Qualitative analysis							Lack of knowledge, late at night, stress, high workload, fatigue, lack of information about the patient, procedural violations, memory lapses, inattention
Coté[98]	2000	USA	Anaesthetic; PICU; ED	Sedation	Incident reports; survey	Descriptive statistics							Lack of knowledge, multiple drugs used
Literature review using systematic search methods													
Kaushal[48]	2004	USA	–	–	–	–		✓	✓	✓	✓	✓	Illegible handwriting, patient condition, unsociable hours, inadequate communication within healthcare team
Conroy[22]	2007	UK	–	Dosing errors	–	–	✓	✓		✓			Patient condition
Review articles													
Paul[23]	2011	UK	–		–	–	✓	✓	✓				
Fox[99]	1996	USA	–	–	–	–		✓					Distractions, workload, sleep deprivation, lack of knowledge, slips, failure to apply knowledge, drug name confusion
Anderson[32]	1999	New Zealand	–	Infants	–	–	✓	✓		✓		✓	Patient complexity, prematurity, organisational issues, poor working conditions, inadequate protocols, illegible handwriting, verbal drug ordering
Lesar[24]	2006	USA	–	Critically ill children	–	–	✓	✓	✓	✓	✓		Human performance deficit
Hughes[30]	2005	USA	–	–	–	–	✓	✓	✓	✓	✓		Drug labelling
Walsh[51]	2005	UK	–	–	–	–		✓		✓			Nights and weekends
Huynh[100]	2017	UK	–	–	–	–							Human factors, inadequate communication within healthcare team
Davis[101]	2013	UK	–	–	–	–	✓	✓	✓				
Wong[37]	2009	UK	–	–	–	–	✓	✓	✓	✓		✓	Inadequate communication within healthcare team, medicines reconciliation
Ruano[33]	2016	Spain	–	Role of new technologies	–	–	✓	✓	✓	✓	✓		Electronic prescribing systems designed for adults
Star[26]	2014	Sweden	–	–	–	–	✓	✓	✓				Work environment

Continued

Table 2 Continued

Study details			Design				Causes						
First author	Year	Country	Context	Specific focus	Data source	Outcome	CFD	IDC	OLP	MF	CC	EWC	Other
Sullivan[27]	2004	USA		–			✓	✓	✓	✓	✓		Lack of information in paediatric populations, inadequate communication within healthcare team, verbal drug ordering
Conroy[34]	2009	UK	–	Education	–	–	✓	✓				✓	Patient condition, inadequate undergraduate teaching
Sammons[35]	2008	UK	–	Education	–	–	✓	✓	✓				
Stebbing[102]	2007	UK	–	Communication	–	–						✓	Workload, time of day, inadequate communication within healthcare team
Gray[36]	2004	UK	–	NICU setting	–	–	✓	✓	✓				Newborns, multiple reference standards
Barata[31]	2007	USA	–	Prehospital/ED setting	–	–	✓	✓					Patient conditions, nights and weekends
Mani[50]	2010	UK	–	Dosage forms	–	–		✓		✓			
Koren[103]	1994	USA	–	Ten-fold errors	–	–		✓				✓	
Policy statements/conference summaries													
[104]Benjamin	2018	USA	–	–	–	–		✓		✓			Complex patients, patients unknown to staff, verbal drug ordering, hectic environment, interruptions, IT systems not paediatric specific, transitions of care, low numbers of children treated
Stucky[28]	2003	USA	–	ED setting	–	–	✓	✓	✓				Inadequate communication within healthcare team, lack of dosing guidelines
Perrin[29]	2004	USA	–	Paediatric inpatient setting	–	–	✓			✓	✓		Inadequate communication within healthcare team

ADHD, attention-deficit/hyperactivity disorder; CC, communication with children; CFD, children's fundamental differences; ED, emergency department; EWC, experience working with children; ICU, intensive care unit; IDC, individualised dosing and calculations; IT, information technology; MF, medication formulations; NICU, neonatal intensive care unit; OLP, off-licence prescribing; PICU, paediatric intensive care unit.

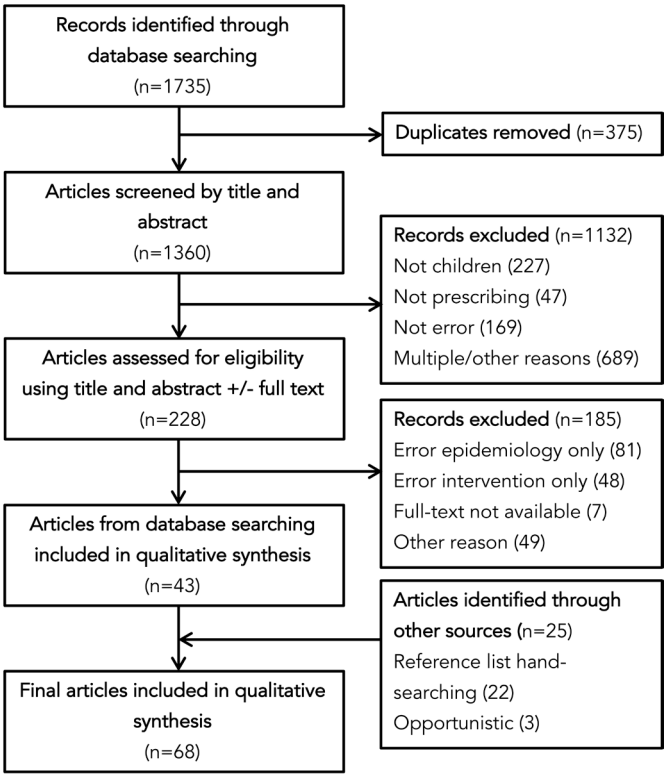

Figure 1 Study selection flow diagram.

references). Development, too, complicates the process of *communication with children* (seven references). Taken together, these paediatric-specific causes of error mean that prescribers need specific *experience working with children* (18 references).

Individualised dosing and calculations

Individualised dosing led to errors by placing a high demand on staff to adjust doses or dosing intervals as children grew (3PP1).[26 27 31 36] Prescribers did not make these changes or made them incorrectly. Children of the same age varying widely in size also contributed to errors.[26–28] Stakeholders recognised this problem and cited examples of small-for-age children receiving excessive doses, even when guidance was correctly followed (1PP1). Obese children were prescribed doses above the maximum recommended for adults (2PP1).

Miscalculation, misplacement of decimal points or confusion around the 'mg/kg/day' dosing equations that are common in paediatrics were a major cause of errors.[38] Four studies assessed doctors' ability to perform calculations in written tests.[39–42] Presented with common prescribing scenarios, junior doctors frequently made errors; in one study, for example, seven of 21 prescribers made tenfold dosing errors.[40] Research showing that computer-calculated doses were significantly more accurate than those calculated manually provided further evidence of this problem.[43] Some authors speculated that a subset of doctors were particularly innumerate[39 41] but tests showed that most doctors made calculation errors. Stakeholders supported this conclusion by noting that cognitive slips occurred in even simple calculations and were made more likely by workplace pressures and distractions (5PT1). Potentially lethal tenfold dosing errors arising from misplaced decimal points were an example of this.[10 44] Checking could not be relied on to prevent errors. In one study, as few as 51% of doctors stated they always double-checked their calculations.[40] Similarly, second checking during administration was not always done (5PT1) and, according to stakeholders, was not always successful when it was.

Weighing children—a prerequisite for many dose calculations—also led to errors. These arose from weights being inaccurately measured, recorded or communicated.[45 46] Errors also occurred when doctors wrote prescriptions for children without a weight measurement being available (6PT2).[32]

Table 3 Summary characteristics of included articles (n=68)

	n (%)
Location*	
USA	29 (43)
UK	18 (26)
Canada	6 (9)
New Zealand	2 (3)
Spain	2 (3)
Taiwan	2 (3)
Other	9 (13)
Year	
2015 to present	8 (12)
2010–2014	15 (22)
2005–2009	23 (34)
2000–2004	13 (19)
1995–1999	7 (10)
Prior to 1995	2 (3)
Article type	
Research article	41 (60)
Review article	19 (28)
Conference abstract	3 (4)
Conference summary	1 (1)
Letter	1 (1)
Case report	1 (1)
Policy statement	2 (3)

*Location where primary study was conducted; for secondary studies, country of corresponding author address.

Off-licence prescribing

There was primary[47] and secondary[48] evidence that using medications without regulatory approval causes prescribing errors. Proposed mechanisms included: a lack of clear dosing information[30 33 49]; multiple or unclear reference standards (8PT2)[25 36]; and 'trial and error'

Table 4 Methodological details of included articles

	n (%)
Study design (n=68)	
Prospective observational	17 (25)
Retrospective observational	21 (31)
Mixed prospective/retrospective observational	1 (1)
Interventional	1 (1)
Case report	1 (1)
Failure Mode and Effects Analysis	3 (4)
Literature review using systematic methods	2 (3)
Literature review without systematic searching	19 (28)
Expert consensus	3 (4)
Mode of data collection in primary studies (n=50*)	
Drug chart/medical record review	21 (42)
Incident reports	13 (26)
Written test	4 (8)
Direct observation	2 (4)
Simulation	3 (6)
Other†	7 (14)
Outcomes contributing causal information in primary studies (n=44)	
Quantitative (n=35*; 80%)	
Descriptive statistics	14 (32)
Hypothesis testing	12 (27)
Multiple logistic regression modelling	7 (16)
Other statistical methods	1 (23)
Researcher inference	2 (5)
Mixed quantitative and qualitative (n=8*; 18%)	
Descriptive statistics	6 (14)
Researcher inference	1 (23)
Qualitative description	2 (5)
Qualitative (n=1; 2%)	

*Total exceeds number of primary studies as some studies used multiple modes of data collection/multiple outcome measures
†Other sources of data: interview 1; survey 1; press reports 1; patients' own drugs, parental report and community pharmacy record 1; case report 1; other database 2.

dosage strategies.[27] In some cases, the lack of a licensed product meant using medicines supplied by specialist manufacturers for specified patients, or prepared extemporaneously (7PP1).[37] Using these preparations caused errors when prescribers lacked information or information was inaccurately conveyed, for example, between paediatricians, general practitioners (GP) and community pharmacies.[37]

Medication formulations

Liquid formulations caused errors because prescribers had to convert doses from millilitres to milligrams, or vice versa (10PN1).[33 50] A lack of paediatric-specific formulations required prescribers to use products designed for adults.[2 22 27 30 33 37] This often led to multiple solution strengths being available,[24 51] causing errors when drugs were inappropriately prescribed in millilitres.[27] Stakeholders confirmed their experiences of relatively small drug volumes leading to massive overdoses, which often did not arouse suspicion in those administering them (9PP1).

Communication with children

Specific difficulties in communicating with children and their parents led to errors. Sometimes parents would give incomplete, misleading or incorrect information about a child's medications (14PT1).[24 30] Often, they stated doses in millilitres, which required prescribers to find out the strength of the solution and convert the volume to a weight for dosing. Doctors' inadequate communication of prescribing decisions and doses also caused errors (15PC1).[29] For example, a GP prescribed a different solution strength from that used in hospital but, due to unclear communication, parents continued to administer the same volume of solution, leading to overdose.[52] Problems could be compounded by children being less able to note and report errors[27 33 48]; equally, however, their parents could act as an important safeguard. One study found that 8% of 2753 reported errors were noticed by parents before administration.[53]

Experience working with children

There was conflicting evidence about how experience of working with children affected prescribing errors. A study showed that emergency department (ED) trainees were more likely to make errors,[54] but in another, most were made by ED attending paediatricians.[55] Two studies of trainees showed no relationship between length of training and the likelihood of error in written tests[39 40]; however, another found that doctors with no paediatric experience were four times less likely to make errors than senior trainees.[42] Errors were most prevalent at the beginning of the academic year[54] or when new doctors joined the clinical team.[44] Paediatric trainees made significantly fewer errors than doctors in other specialties in both clinical and classroom-based studies,[41 43 56 57] perhaps because managing children full-time made prescribers more aware of dosing considerations and paediatric-specific protocols (12PT1).[52 53 58]

DISCUSSION

Main findings

This study used a systematic approach to review and synthesise what is known about the causes of prescribing errors in children. We found that, as in adults, a host of social and contextual factors cause errors, such as busy workplaces, poor communication and individual mistakes.[6 59] Yet, as described previously, the process of prescribing for children differs from practice in adults, and these

Table 5 Summary of stakeholder evidence

Theme	Error mechanism	Ref	Supporting quotation(s)
Individualised dosing and calculations	Wide variation in size within the paediatric age range	1PP1 2PP1	*[With paracetamol] the age band [dosing] has taken a lot of thinking out of it… there's very few months go by that I don't come across an age-banded dose of paracetamol that is essentially a toxic dose… It's 80, 85, 90 milligrams per kilogram per day. It doesn't account for the nutritionally depleted, very small-for-age child.* *On the other side of immaturity, I've seen instances where the bigger kid has got bigger doses than the maximum dose or the adult dose.*
	Need for frequent changes to doses or dosing schedules	3PP1	*Co-amoxiclav has come up in drug errors, and that has been prescribed every eight hours for a child within the first three months of life, whereas it [should be] every 12 hours.*
	Inadequate mathematical skills	4PT2	*I like someone else to check it and say 'yes, that is right', and I like them to know where my calculations are coming from, but I find that some [team] members might need more help with calculations.*
	Calculation errors when distracted	5PT1	*I prescribed an antibiotic on a busy ward round, I made a mistake in my calculation—it was an easy calculation, 10 kilo child, four milligrams per kilogram—I wrote the dose and prescribed 100 mg. It was a mistake, and I was just busy. The nurses mustn't have checked the dose—they gave the dose and then said to me after 'gosh, that child has got quite a big dose, they gave them much more than I gave the child across the bay' and I was like 'oh, what happened?' and then I knew straight away… I mean, I can do four times 10, I did A Level Maths, so distractions happen.*
	Problems with weights and weighing	6PT2	*There are errors when you can't actually get a weight. I've had patients, because of certain problems, arthrogryposis comes to mind, (that weren't) weighed and then received ibuprofen, more than what they should for their weight, and had kidney problems because of it… weights can be difficult and time consuming for the nursing staff.*
Off-licence drug use	'Special' formulations	7PP1	*Off-licence medications are things that (aren't) available with the UK licence… a specialist manufacturer somewhere will start producing a medication, or it'll be licensed in Europe or something like that, and we'll import that. Some of those products need translated so they don't have a UK label on them.*
	Multiple, inconsistent resources	8PT2	*A lot of centres, neonatal units, will have different prescribing manuals, so whereas you're used to [using] a certain medication in such a way, you'll go to a manual, it'll say do it a different way.*
Medication formulations	Formulations intended for adults	9PP1	*They are liquid medications targeted at adult doses, so you can potentially give quite a lot more to a child than you intend to [without administering an] outrageous amount of liquid. If you're going to overdose an adult, you're going to have to give them 25 to 30mls, whereas with a small baby using that preparation you could do a lot of damage with 3 to 4 mils.*
	Problems with liquid formulations	10PN1	*That conversion from milligrams to mils will also be where errors occur.*
Communication with children	Difficulties in accurate medicines reconciliation	14PT1	*They make mistakes like telling you the wrong amount of mils, or they're converting it to milligrams themselves—I was told 10 times the dose of a medication the other day, because the parents said it was 250 when it was actually 25—I think they must have tried to convert it themselves.*
	Inadequate communication of prescribing decisions to parents	15PC1	*I discover they only gave it for three days, and found that they couldn't [administer] it because they didn't know how to do it properly, and it's a very bitter medicine, and then they just gave up, and then this child's had two weeks with no treatment and then they're back to me and they are no better, and I have learnt through that.*
Experience of working with children	Trying to remember doses rather than look them up	11PT1	*Adults were set doses and if it was 'came in with a chest infection from A&E', oh you're going to prescribe them whatever the dose was; you would have known [without looking it up], and you probably just would have looked up their renal function, I wouldn't have looked up everything.*
	Not recognising differences in prescribing for children	12PT1	*I've had both [situations]—being in a District General [Hospital] with ENT surgery, either asking for your help, or fixing a prescription [on their behalf], and again with [intravenous] fluids, both asking for your help and fixing their prescriptions because they just didn't know.*
	Prescribers not checking, despite unfamiliarity	13PN2	*It's about a degree of self-confidence, in the sense that if you are checking and doing your independent calculations and everything else, then you have to be able to say 'look, I don't understand this' and not go with your colleague. So often we see [team members]… not even double checking or anything, just going ahead.*

differences are reflected in rates and types of errors. This study shows how these fundamental differences in children—including growth, development, physiology and drug handling—caused additional errors. While publications generally consider these paediatric-specific factors in isolation from one another, a multidisciplinary group of stakeholders agreed that, like in adults,[6 60] errors occur when multiple factors collide. Within a single prescription, an inexperienced prescriber might have to establish a child's correct weight, reconcile conflicting information

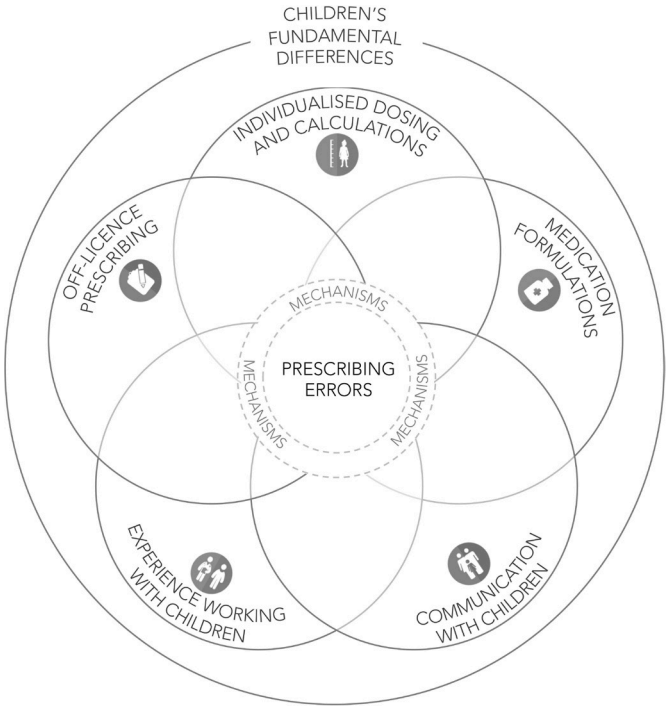

Figure 2 Paediatric-specific causes of prescribing errors. Fundamental differences between children and adults complicate prescribing and lead to errors through the five downstream causes. Factors are interlinked—using a liquid medication necessitates additional calculations and complicates communicating doses to parents, for example. Specific mechanisms—such as a failed conversion from milligrams to millilitres—make underlying causes result in errors in practice.

about an unlicensed product, interpret a complex dosing regimen, calculate an accurate dose and communicate this to parents. Figure 2 shows how these factors inter-relate to increase risk of errors.

Nature of the evidence base

Findings should be interpreted within the limitations of the evidence available. It was not always possible to establish detailed causal relationships from secondary evidence. The primary causal evidence identified was also weak because much of it came from quantitative determinations of error rates, which explored statistical associations between potential causative factors as a secondary objective. The 'causes' identified within these studies were often self-evident (being on multiple medications),[44 61–63] difficult to interpret (junior residents made more errors than more senior ones)[57] or non-modifiable (older prescribers).[64] Moreover, several studies were conducted in simulated and classroom settings which, while informative, may not fully reflect the complexity of prescribing within practice. Research in adults has addressed these limitations by asserting that prescribers themselves know most about the causes of errors[65] and conducting in-depth qualitative interviews with doctors who have been involved in them. This has shown that, rather than just 'lack of knowledge', errors have multiple, complex causes strongly influenced by prescribing contexts.[6] This new understanding is starting to impact education and practice in medication safety.[66]

Most studies were relatively recent, reflecting increasing focus on patient safety. Evidence was constrained, however, because the vast majority of studies were conducted in specialist paediatric settings, even though non-specialists frequently care for children. Almost no evidence referred to general practice settings, despite the fact children make up a significant proportion of GP caseload and have been shown to be at increased risk of error.[67] Evidence, too, predominately originated from developed countries, particularly North America or the UK. It is unclear how differences in health systems affect prescribing safety; for example, in North America, paediatricians provide primary care, whereas in the UK GPs generally represent the first point of contact for children. There is little evidence, too, about prescribing error in low/middle-income countries, even though research suggests that patient safety issues are no less common but may differ in causation.[68]

While the broad themes identified in this review are likely to apply in wide range of settings, these limitations impact the transferability of findings and make its recommendations provisional.

Strengths and limitations

The choice of scoping review methodology enabled us to bring together a heterogeneous body of literature that was not amenable to quantitative forms of synthesis. The fact that we included a stakeholder consultation, often omitted in scoping reviews, helped to triangulate findings and ground them in real-world clinical practice.

Our study also had limitations. Our search was conducted in February 2018; we recognise that other contributory articles may have been published in the intervening period. Moreover, our search may have missed contributory articles in which, for example, the term 'cause' or its synonyms were not present. We decided to include articles in which authors deduced the causes of errors from experience as well as 'fact' because primary evidence for themes other than *individualised dosing and calculations* and *experience in working with children* was insufficient. The heterogeneous nature of this evidence made our selection of articles inescapably subjective. We addressed this by working as a team to refine inclusion and exclusion criteria, and independently screening articles to apply the criteria consistently.

Despite the use of two institutions' libraries, seven potentially contributory articles could not be retrieved. Based on their abstracts, four were review articles that emphasise paediatric-specific factors similar to those described in this study; the other three were primary articles that presented factors including off-licence use of antidepressants, out-of-hours working and specific drug types as associations with error.

Our decision to include secondary evidence introduced a risk of confirmation bias. First, some review articles

made reference to included primary studies, giving them additional weighting. Interestingly, however, primary and secondary articles generally appeared to focus on different causes of errors: primary articles often evaluated specific 'generic' associations with errors, while secondary articles emphasised 'paediatric-specific' causes'. Table 2 enables readers to see the causes of errors found within particular article types.

Second, review articles may have preferentially cited other secondary literature written by influential authors, giving added weight to their opinions. On this point, it is important to note that qualitative evidence syntheses as used in this study are not suited to testing the strength of associations; the numbers of articles offered alongside individual causes give an indication of the attention a factor has received in literature, rather than its importance in causing errors. Moreover, the stakeholder consultation conducted as part of this review compensated for that risk of bias by inviting experienced practitioners to (dis)confirm the provisional results of the review. This supported the relevance of our tentative conclusions to practice, identified mechanisms and provided real-world examples.

Recommendations

The highly inter-related nature of the causes of errors resonates with research in adults which describes prescribing as a complex process.[6] With this in mind, it is clear that solutions on multiple levels will be needed to begin to tackle the problem. Box 2 summarises recommendations to improve paediatric prescribing safety.

Research should respond to the complexity of prescribing error by focusing study on their underlying causes to inform design of interventions. This should reflect both the 'generic' and paediatric-specific causes suggested by this review. As mentioned above, qualitative study designs offer the potential to identify causative factors, and to explain how they lead to errors. Moreover, research should address the wide range of contexts in which paediatric prescribing occurs, including primary care. This review also suggests specific research topics, summarised in box 2.

Beyond further research, there is a need for more immediate action to reduce prescribing error. This review, in demonstrating how use of different formulations leads to error, supports efforts to standardise drug concentrations across practice settings.[69] Governments, too, should work with the pharmaceutical industry to promote development of paediatric-specific products and ensure proper drug licensing. Medication dosing could be simplified by using age-banded instead of weight-based dosing,[70] although further study is needed to confirm the effectiveness of this strategy. Novel formulations, too, show promising results.[71]

That many causes of errors are paediatric specific endorses the role of paediatric pharmacists, whose effectiveness in preventing errors has been shown in previous research.[72] Increasing the availability of non-medical prescribers, with specific paediatric expertise, may also help. Children's high reliance on individualised dosing, calculations and weight/volume conversions means that electronic prescribing, electronic health records and clinical decision support tools all have the potential to reduce errors.[73] It is important to note, however, that computer systems do not prevent all errors[74]—and may generate new ones—and rely on paediatric-specific design and careful implementation.[75] Putting in place rigorous systems to accurately record children's weights could also help reduce errors.

Our findings indicate that education should be targeted at all doctors who have prescribing responsibility for children. Because so many doctors care for children as part of their job, this should begin at undergraduate level and continue in specialty training and as part of induction processes. The content of education should go beyond raising awareness that prescribing for children is different, to targeting the mechanisms by which differences lead to errors. High-risk aspects, in particular, such as calculations and weight-volume conversions, require specific focus. Given the complex, contextual nature of prescribing for children, classroom-based teaching should be supported with opportunities to prescribe in

Box 2 Recommendations to improve paediatric prescribing safety

Research

- Expand existing research to include all areas of practice, including primary care, and wider geographical representation.
- Consider specific unanswered research questions, such as: How can checking processes be improved? How can practitioners with specific mathematical difficulties be supported?
- Explore how parents and children can play an increased role in medication safety.

Policy and drug industry level

- Standardise medicine concentrations across practice settings.
- Promote research to enable paediatric drug licensing.
- Support production of paediatric-specific medicine formulations.
- Consider the use of age-banded, rather than weight-based, dosing regimens.

Practice

- Increase the provision of clinical pharmacists.
- Introduce paediatric-specific electronic prescribing, electronic health records and clinical decision support tools.
- Implement rigorous systems for recording patients' weights.
- Improve mechanisms for practitioners to get support with prescribing, especially for those who do not routinely prescribe for children.

Education

- Ensure that all doctors who care for children receive prescribing education.
- Provide paediatric prescribing education and opportunities at undergraduate level.
- Align educational content with evidence on the specific causes of errors, such as dose calculations and weight-volume conversions.
- Consider up-to-date educational strategies such as providing feedback on practice and encouraging reflection.

context with appropriate supervision. Providing feedback on prescribing practice, too, offers doctors the opportunity to reflect on their own prescribing and become more attuned to areas of risk.[76]

Prescribing decisions, however, are so contextual and nuanced that education alone will be insufficient to prevent errors. Improving support mechanisms, particularly for practitioners with less paediatric experience, will be needed. This might involve shared care arrangements with paediatric teams, or increasing the availability of paediatric pharmacist advice. Increasing error detection, too, has potential benefits. To support this, further research could clarify the effectiveness and most appropriate uses of double-checking processes.[77] Investigating how children and parents can become more involved in medication safety is also a particularly valuable area of study.

CONCLUSION

Prescribing for children was summarised by a stakeholder: '*The term 'children' that we're using, as a single entity, isn't correct. It's a very broad, very complex group, ranging from a premature infant at the limit of viability, right through to teenagers—and that's in the spectrum of normal physiology, and in disease, and in response to medications…making it much more complex to prescribe accurately.*' This study analyses how these unique considerations lead to errors, and demonstrates the need for paediatric-specific education, research and policy.

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