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REVIEW

A systematic review of clinical pharmacist interventions in paediatric hospital patients

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Abstract

Clinical pharmacists provide beneficial services to adult patients, though their benefits for paediatric hospital patients are less defined. Five databases were searched using the MeSH terms 'clinical pharmacist', 'paediatric/paediatric', 'hospital', and 'intervention' for studies with paediatric patients conducted in hospital settings, and described pharmacist-initiated interventions, published between January 2000 and October 2017. The search strategy after full-text review identified 12 articles matching the eligibility criteria. Quality appraisal checklists from the Joanna Briggs Institute were used to appraise the eligible articles. Clinical pharmacist services had a positive impact on paediatric patient care. Medication errors intercepted by pharmacists included over- and under-dosing, missed doses, medication history gaps, allergies, and near-misses. Interventions to address these errors were positively received, and implemented by physicians, with an average acceptance rate of over 95%. Clinical pharmacist-initiated education resulted in improved medication understanding and adherence, improved patient satisfaction, and control of chronic medical conditions.

Conclusion: This review found that clinical pharmacists in paediatric wards may reduce drug-related problems and improve patient outcomes. The benefits of pharmacist involvement appear greatest when directly involved in ward rounds, due to being able to more rapidly identify medication errors during the prescribing phase, and provide real-time advice and recommendations to prescribers.

What is Known:
- *Complex paediatric conditions can require multiple pharmaceutical treatments, utilised in a safe manner to ensure good patient outcomes*
- *The benefits of pharmacist interventions when using these treatments are well-documented in adult patients, though less so in paediatric patients*

What is New:
- *Pharmacists are adept at identifying and managing medication errors for paediatric patients, including incorrect doses, missed doses, and gaps in medication history*
- *Interventions recommended by pharmacists are generally well-accepted by prescribing physicians, especially when recommendations can be made during the prescribing phase of treatment*

Keywords Clinical pharmacist · Prescribing errors · Medication reconciliation · Patient safety · Medication dosing

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Abbreviations

DRP	Drug-related problem
ED	Emergency department
JBI	Joanna Briggs Institute
NICU	Neonatal intensive care unit
PICU	Paediatric intensive care unit
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial

Introduction

Paediatric patients provide a unique set of challenges to their treating health professionals. This is in part due a limited capacity to communicate, particularly when suffering a traumatic illness, and differences in pharmacokinetic profiles compared to adults [4, 11]. Children represent approximately one-quarter of the global population, and although most experience a healthy childhood, a recent survey of children's health estimated nearly half have at least once chronic health condition, and about 60% of children having received a prescription medication during the previous 12 months [6, 9]. The prevalence of complex paediatric conditions is also on the rise, including type 2 diabetes, asthma, hypertension, attention deficit and hyperactivity disorder, and depression [6]. These conditions usually require pharmaceutical interventions, with clinical pharmacists being responsible for providing direct, individualised pharmaceutical care to patients to ensure the optimal use of medications [17].

Clinical pharmacists in a multidisciplinary care team in adult care units play an integral part in ensuring the quality use of medicines, the reduction of medication errors, and enhance patient outcomes that lower costs [6, 32]. Reducing medication errors amongst the vulnerable paediatric population is of even greater significance, with previous research identifying paediatric patients as being at higher risk of errors compared to adults, and three times more likely for these errors to cause harm [16, 20, 39]. These errors, which can include the omission of medications, over-dosing and under-dosing, and administration errors, indicate that involvement of clinical pharmacists in paediatric condition management is essential for patient care [18]. Amongst adult hospital patients, pharmacists have been shown to improve medication adherence, knowledge, appropriateness of prescribed drugs, and reduced hospital stay [19]. However, not all hospitals employ paediatric clinical pharmacists, with fiscal scrutiny and changes in health care financing necessitating that healthcare professionals both outline and justify the medical and economical basis for their involvement in patient care [17].

This systematic review was conducted to evaluate whether paediatric clinical pharmacists afforded similar benefits to paediatric patients as for adult patients, and to what degree their interventions improved health outcomes for paediatric patients, and provided cost-savings to their respective institutions. The underpinning research question for this systematic review was 'How do the professional activities of a clinical pharmacist impact on the treatment of paediatric hospital patients'?

Methods

This systematic review follows the recommendations by the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [27].

Search strategy and study eligibility

Original-research, English-language articles published from 1st January 2000 to 1st October 2017 were eligible for inclusion, and identified through a systematic search of the PubMed, CINAHL, Google Scholar, AustHealth, and EMBASE databases. Searches were performed by a Townsville Hospital and Health Service librarian and the primary author. MeSH terms were clinical pharmacist, paediatric/paediatric, hospital, and intervention. Titles were read to identify potentially relevant articles, and we initially included any article that appeared to involve hospital patients of any age, and any health professional intervention. Abstracts were then read, with articles discussing paediatric patients and pharmacist involvement retained for full-text review. Articles were deemed eligible for inclusion if they recruited paediatric patients in a hospital environment, involved pharmacist-initiated interventions, and reported how these interventions may have influenced patient health. For this review, 'paediatrics' was considered as being between the ages of zero (birth) and 19 years old. Excluded articles were those describing interventions only partially managed by pharmacists, standard pharmacist interventions which were not linked to patient outcomes, only discussed older age groups, or had both paediatric and older patients but did not differentiate their results by age.

Data extraction and quality appraisal

Data extracted from eligible articles included author details, year published, country of participant origin, participant numbers, study design, frequency and methodology of interventions employed, and primary and secondary outcomes reported. The primary outcomes of interest were the types of pharmacist intervention employed, and their resulting health, and other outcomes relating to the care of paediatric patients. Data was grouped into the type of outcome reported, with health outcomes sub-grouped into: reduction in drug-related problems (DRPs), improved control of disease/condition, and reduction in medication-related errors and/or their severity. Study quality was assessed using validated checklists from the Joanna Briggs Institute (JBI). JBI checklists assess for

study clarity, appropriateness of methodological design, analysis, presentation of results, and alignment of results and discussion to research objectives. Three JBI critical appraisal checklists were independently used by two authors for each article to assess study quality for eligible articles: analytical cross-sectional studies, cohort studies, and randomised controlled trials [28, 37]. Differences in scores were discussed until consensus, with articles considered as being of high quality if they scored 'yes' for at least 75% of the criteria, moderate if 50% or higher, and low if less than 50%.

Results

Study characteristics and quality appraisal

The search method initially identified 305 potential articles based on their titles, which was reduced to 28 after an initial abstract screening, with full-text screening leaving 12 articles matching the eligibility criteria. Common reasons for study ineligibility included pharmacist interventions not targeted at paediatric patients, articles not published in a peer-reviewed journal, interventions carried out by a multidisciplinary team, did not differentiate results between paediatric and adult patients, or involved pharmacist interventions in a community setting. Figure 1 illustrates the search strategy and article selection process.

The details of the 12 eligible articles are included in Table 1, all of which were conducted between 2000 and 2015, and evaluated pharmacist-initiated interventions aimed at improving paediatric patient outcomes. These studies were conducted across Africa, Europe, North America, and Asia. Of the 12 eligible articles, eight were prospective cross-sectional or cohort studies [1, 10, 13, 14, 21, 24, 33, 38], one was a retrospective study [25], and three were randomised controlled trials (RCTs) [2, 12, 40]. Common outcomes reported include the frequency, type, and acceptance rate of clinical pharmacist interventions, and their impact on the frequency and severity of DRPs, common medications implicated in DRPs and adverse events, paediatric patient compliance to prescribed medications, total patient health, and economic impact of pharmacist interventions.

Table 2 summarises the results from each of these studies, which cumulatively include over 35,000 paediatric patient admissions and describe 11,209 interventions for prescriptions and medication orders for these patients, with an average acceptance rate of 89.1% for studies reporting on intervention acceptance rates. Three main outcome themes emerged for these studies based on the interventions documented: error interventions, disease/condition improvement, and economic impacts. When excluding the low acceptance rate seen in Maat et al. (2013) [24], the average acceptance rate is 95.3%. Quality assessment of the eligible articles deemed eight articles as being of high quality, and the remaining four as moderate quality, with none as low quality. Common reasons for reductions in quality scores were an insufficient description of participants, a lack of detailed randomisation processes within RCTs, and confounding factors not adequately addressed. None of the articles eligible for inclusion were excluded on the basis of poor quality.

Error detection and interventions by pharmacists

The detection of errors and initiation of interventions by pharmacists were the most commonly reported outcome, though reporting rates per patient varied widely between studies, depending on the size of the facilities involved, and pharmacist

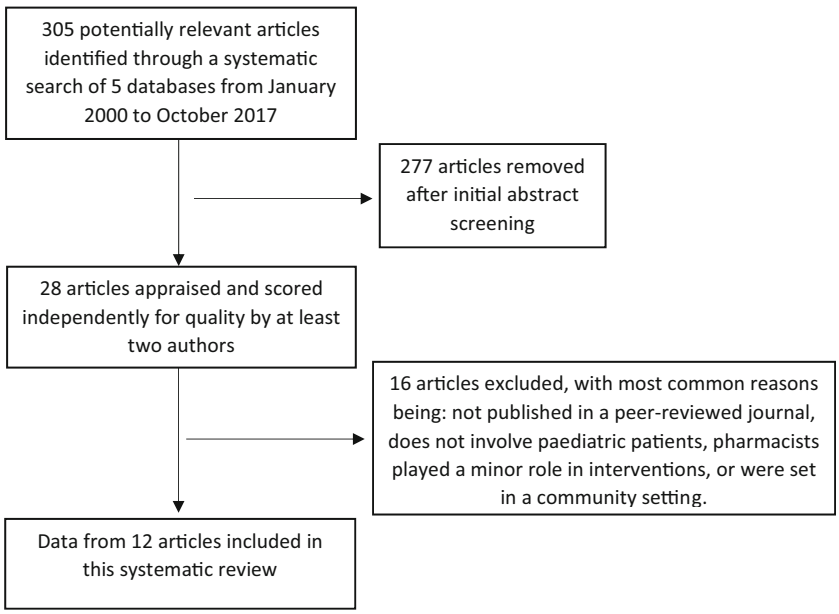

Fig. 1 Flow diagram of database search and article appraisal process outcomes

Table 1 Characteristics of articles eligible for inclusion in this systematic review ($n = 12$)

Main author and year published	Year(s) conducted and study location	Study setting, design and duration, interventions employed, and outcomes reported
Virani (2003) [38]	2001, Canada	A 1-month prospective evaluation of pharmacist interventions within a 17-bed adolescent mental health unit, and a retrospective cost analysis of drug utilisation. Interventions were categorised into actual or potential drug-related problems (DRPs), their effect on patient care (detrimental, no, or positive effect), and effect on costs and hospital stay.
Condren (2004) [10]	2002, USA	A 12-month prospective evaluation of clinical interventions performed by a 53-person paediatric pharmacy team in the general paediatric, NICU^, and PICU^ wards of two hospitals. Interventions were categorised by major type and subtype.
Kaushal (2008) [21]	2000, USA	A 6-month prospective cohort study comparison of serious adverse drug events, pre- and post-clinical pharmacist* intervention in the intensive care, general medical, and general surgical paediatric inpatient units at a single hospital.
Alagha (2011) [1]	2008–2010, Egypt	A 10-month prospective comparison study of medication error and error severity pre- and post- clinical pharmacist interventions in a 12-bed PICU, including the provision of dosing sheets, order and administration charts.
Fernandez-Llamazares (2012) [13]	2007–2009, Spain	A 36-month cross-sectional study of pharmacist interventions in reducing prescribing errors in paediatric patients, in a 180 paediatric-bed maternity and children's hospital. Intervention impact on patient care, clinical significance, intervention acceptance rate, severity of errors identified, and medications involved were recorded outcomes.
Marconi (2012) [25]	2007–2009, USA	A 3 × 1-month retrospective chart comparison of medication omissions and delays in the ED^ of a children's hospital, pre- (April 2007) and post-staffing (April and October 2009) of a full-time ED clinical pharmacist. The number of urgent and non-urgent medications missed, and duration of delays for administration were the reported outcomes.
Zhang (2012) [40]	2010–2011, China	A 4-month RCT in a university hospital comparing paediatric patient outcomes with or without a clinical pharmacists' intervention. Interventions included assessments of diagnosis with drug treatments, pharmacokinetic consultations, identification and management of medication errors, and adverse event prevention. Outcomes reported included the number of ADRs, length of hospital stay, cost of medications used, total cost of hospitalisation, and compliance rate.
Fernandez-Llamazares (2013) [14]	2011, Spain	A 4-month prospective study of clinical pharmacist interventions of prescribing errors in 8 hospitals treating paediatric patients, with a combined total of 1565 paediatric beds. Error rates, common types of errors, error severity, common medications involved, intervention acceptance rate, and effect of interventions on patients were the outcomes reported.
Maat (2013) [24]	2004–2007, Netherlands	A 46-month prospective cohort study (with a case-control) evaluating clinical pharmacy interventions in a single 220-bed children's hospital for medical and surgical paediatric patients. The primary outcome was the frequency of clinical pharmacist interventions, and the determinants for these interventions per 10,000 electronic prescriptions.
Prot-Labarthe (2013) [33]	2009–2010, Europe† and Canada	A 6-month prospective study of four pharmacists and their interventions in PICU and paediatric cardiology units in four countries (total of 3141 beds). Intervention acceptance, patient factors, type of intervention (including medications implicated), intervention economic impact, and estimated impact on patient health were the outcomes reported.
El Borolossy (2014) [12]	2011–2012, Egypt	A 9-month RCT of clinical pharmacist services in end-stage renal disease patients undergoing haemodialysis at a university

Table 1 (continued)

Main author and year published	Year(s) conducted and study location	Study setting, design and duration, interventions employed, and outcomes reported
		children's hospital. The intervention group participants underwent a medication review by a clinical pharmacist, receiving medication recommendations, and counselling three times per week in addition to the control's regular medical care by physicians. Outcomes reported include vitals, multiple serum levels, and health-related quality of life, and DRPs.
Bahnasawy (2017) [2]	2014–2015, Egypt	A 9-month RCT of clinical pharmacist services in iron-overloaded beta-thalassemia major (BTM) children in the haematology clinic of a children's hospital. The control group received standard care (regular transfusions and physical examination), and the intervention group received additional assessment and interventions including: medications, laboratory data, DRPs, and care plan development. Outcomes reported include serum ferritin levels, blood counts, quality of life, and patient satisfaction.

* General medical and surgical wards had part-time pharmacists, whereas the ICU had full-time pharmacists

† France, Belgium, Switzerland

^ NICU: Neonatal Intensive Care Unit; PICU: Paediatric Intensive Care Unit; ED: Emergency Department

numbers and workload. Antibiotics were the most common medications involved in DRPs, as described in six of the eligible articles, followed by drugs used for alimentary tract and metabolic disorders [1, 13, 14, 24, 25, 33]. Drug therapy changes were the most common recommendations by pharmacists in several studies, in response to off-label prescribing, medical conditions not receiving treatment according to accepted guidelines, and the prescribing of drug forms unsuitable for adolescents [10, 33, 38]. Incorrect dosing (under- and over-dose) was also a prominent issue identified in this review, with overdoses of between 1.5 and 10 times the maximum recommended dose being of significant concern for younger patients, increasing the risk of serious adverse events [13, 14, 24, 33, 38].

Studies which tracked pre- and post-pharmacist involvement in prescribing and clinical ward rounds found significant reductions in the frequency of errors made between one-fifth and one-third ($p < .01$) [1, 21]. The clinical significance of these interventions was reported in many studies, with errors made by physicians and intercepted by pharmacists being potentially life-threatening/fatal in 1.0–2.2% of cases, very/extremely significant in 2.9–29.7% of cases, and moderately significant in 38.0–64.7% of cases [1, 10, 13, 14, 33]. One of the studies found that free-text entries by prescribers were nearly five times more likely to have an error ($p < .001$) compared to standardised templates and electronic entries [40]. Other benefits of pharmacist involvement with paediatric patients described in individual studies included a significant reduction in missed doses of urgent and non-urgent medications ($p = .03$ and $p < .001$ respectively) [25], significant reductions in length of hospital stay (from 9.06 to 7.33 days, $p = .02$) and medication compliance rate (from 70.2 to 81.4%, $p < .01$) [40].

Medical condition improvement

Two RCTs discussed the impact of pharmacist interventions on specific disease states in paediatric patients; end-stage renal disease requiring haemodialysis [12], and iron-overloaded beta-thalassemia major [2]. Both studies found that non-compliance to therapy was a significant issue, which was greatly improved after interventions made by clinical pharmacists, particularly patient education. Unlike the other studies discussed, dosing issues in these RCTs (particularly overdosing) were less common, which is theorised to be due to increased prescriber familiarity to a smaller number of medications needed for these specific diseases. There were significant improvements in biomarkers (e.g. serum phosphate, parathyroid hormone, calcium, and serum ferritin) for both conditions in these studies (all $p < .01$), and significant increases in quality of life scores compared to the control groups ($p < .001$) [2, 12].

Economic impacts

For three of the four studies that discussed the financial aspects of clinical pharmacist interventions, all described financial savings from these interventions, as a result of the need for fewer or less expensive medications (reduction in total drug costs), or the prevention of adverse drug events and their associated costs [10, 33, 38]. One study in China found no significant difference in drug costs, or total costs related to patient care with a pharmacists' involvement [40].

Table 2 Quality appraisal outcomes and study results for each of the eligible articles in this systematic review ($n = 12$)

Study details	Study quality	Study results
Virani (2003) [38]	Moderate [28]	During the 4-week study period, 32 DRPs in 6 patients led to 48 recommended interventions. 26 (81%) were actual problems and 6 (19%) as potential problems, with adverse drug reactions, under-dosing, and non-indicated drugs the most common issues identified. 47 of the 48 recommended interventions (98%) were accepted by physicians, with the initiation or discontinuation of a drug comprising the majority (63%) of interventions, and 38 (86%) having a positive impact on patient care. The retrospective cost analysis found a 14% reduction in total drug costs per patient-day 12 months after pharmacist employment, which was statistically significant during the final 8 months ($p < .01$).
Condren (2004) [10]	High [28]	For 3978 patients, a total of 4605 interventions were recorded (approximately 18 interventions per weekday). Drug therapy changes, medication history, patient counselling, drug information, and drug monitoring accounted for the majority (84%) of interventions, with two-thirds (62.9%) involving infectious or respiratory diseases. 91% of interventions were accepted and 4% partially accepted by physicians. 56% of interventions were considered somewhat significant, 38% as significant, 4% as very significant, 1% as an intervention in a life-threatening circumstance. 5% of these interventions prevented an adverse event. Estimated cost savings from preventing medication errors was $US458 516.
Kaushal (2008) [21]	High [28]	Examination of 4863* admissions found 119 serious medication errors, though only the ICU had a significant ($p < .01$) reduction in errors after the introduction of a full-time clinical pharmacist, from 29 to 6 serious errors per 1000 patient days. Concurrent near-miss interceptions in the ICU increased from 32 to 57 per 1000 patients ($p = .08$). Compared to the control ICU, the intervention ICU had a net reduction of 30 fewer serious errors per 1000 patient days ($p = .01$). The majority of errors were detected at the prescribing stage.
Alagha (2011) [1]	High [28]	A total of 1417 pre- and 1096 post-intervention medication orders were evaluated for 240 patients, with a statistically significant ($p < .001$) post-intervention decrease in the rate of prescribing errors (from 1107 to 391), including potentially severe (29.7 to 7.0%), and potentially moderate (39.8 to 24.1%) errors (both $p < .05$). Errors in prescribed intravenous drugs also significantly decreased ($p < .001$) from 86.5 to 31.5% (55.0% reduction), with the wrong rate of administration being the most common error. Antibiotics experienced the greatest relative risk reduction of 72.1% ($p < .001$). The most common error post-intervention was incorrect instructions for nurses (at a rate of 12.1%).
Fernandez-Llamazares (2012) [13]	High [28]	For 14,713 patients, a total of 1391 out of 1475 interventions were accepted (94.3%) from 61,458 medical orders (2.4% of orders). Interventions were considered extremely significant and fairly significant in 40 (2.9%) and 155 (11.1%) of cases respectively, with no recommended interventions deemed harmful. Of 1357 prescribing errors, 833 (61.4%) were dose-related, 30 (2.2%) of which were potentially fatal, 194 (14.3%) were clinically serious, and 874 (64.4%) as significant. Antibiotics, antiemetics and gastroprotective agents were most often implicated.
Marconi (2012) [25]	Moderate [28]	From 1164 admission charts reviewed, there was no statistical difference identified in medication delays ($p = .08$), though there was a significant decrease in omitted doses for both urgent (specifically antibiotics, $p = .03$) and non-urgent medications ($p < .001$) post-staffing of the clinical pharmacist. These improvements were greater over time at 6 months post-staffing ($p < .001$ for missed urgent antibiotics and missed non-urgent medications).
Zhang (2012) [40]	High [37]	Of a total of 160 patients, pharmacists provided 107 interventions for the 76 patients in the intervention group, 31 of which were the prevention of medication errors out of 683 prescriptions checked (4.5%), with 30 (97%) of these accepted. Other interventions were related to providing advice on drug dose, administration, and interactions. There was no significant difference in ADR rate, number of discharge drugs, readmission rate, or costs of drugs used or total costs. There was a statistically significant difference in length of stay between the intervention (7.3 days) and control (9.1 days) groups ($p = .02$), and compliance rate during follow-up at 81.4 and 70.2% respectively ($p < .01$).
Fernandez-Llamazares (2013) [14]	High [28]	A total of 646 interventions were analysed, of which 590 were prescribing errors. 95.4% of recommended interventions were accepted by physicians. Dose errors (overdose and underdose) accounted for 49.3% of interventions, with wrong dosage form, wrong drug, and wrong administration frequency being the next most

Table 2 (continued)

Study details	Study quality	Study results
		common errors at 15.1, 10.7, and 9.3% respectively. Antibiotics were most frequently implicated in errors (30.0%) followed by those for alimentary and metabolic disorders (20.0%). 2.0% of errors were considered potentially fatal, 19.8% asclinically serious, and 51.9% as significant. Pharmacist recommendations were considered to be extremely significant for patient health outcomes in 1.1% of cases, very significant in 16.7% of cases, and significant in 64.7% of cases.
Maat (2013) [24]	Moderate [28]	Of 138,449 electronic prescriptions for 9992 patients during the study period, 1577 (1.1%) received a pharmacists intervention amongst 950 (9.5%) patients, who were prescribed 64,144 (46.3%) prescriptions, indicating these patients were likely more ill, in hospital for a longer period, and prescribed more medications. Prescription corrections often (45.4%) concerned a wrong dose, with 11.4% of these being a dose 10 times higher than the therapeutic dosing range. Only 57.5% of interventions led to a modification of the prescription by the prescriber. Antibiotics and alimentary/metabolic drugs were most often involved (15.6 and 13.9%) respectively. Free-text prescriptions as opposed to standardised templates were nearly five times (4.71) more likely require an intervention ($p < .001$).
Prot-Labarthe (2013) [33]	High [28]	A total of 996 interventions were made by pharmacists for 270* patients over a total of 1450 patient-days, most (71.5%) of which were in the PICU. 97.9% were accepted. Improper administration and untreated indication were the most common errors (29.4 and 25.5% respectively), whereas incorrect dose errors were less common (overdose at 10.6% and underdose at 9.2% of cases). Interventions were considered clinically significant in 17% of cases, and moderately significant in 51% of cases. Antibiotics and alimentary/metabolic drugs were the most frequent specific drug classes implicated (23.4 and 21.9% respectively), as were those with IV administration (53.9%). Most interventions had no or an un-assessable economic impact, 7% saved less than 100 euro, 2% saved between 100 and 1000 euro, and 1% saved over 1000 euro.
El Borolossy (2014) [12]	Moderate [37]	For 50 patients (25 per group), 74 DRPs were reported in the intervention group, most either drug interactions or issues with non-compliance to therapy (40.5 and 20.3% respectively), with only a few patients being prescribed an improper medication, sub-therapeutic dose or improper dosage form (10.8, 10.8, and 4.1% respectively). Ninety-eight percent of interventions were accepted by physicians. The intervention group experienced significant reductions in blood pressure ($p < .001$), serum phosphorus ($p < .01$), serum parathyroid hormone ($p < .001$) and significantly higher serum calcium ($p = .011$) compared to the control group. Quality of life scores were significantly higher in the intervention group ($p < .001$).
Bahnasawy (2017) [2]	High [37]	For 48 patients (24 per group), a total of 64 DRPs were identified in the intervention group, with non-adherence being the primary issue, exhibited by all patients (37.5% of DRPs) followed by adverse drug reactions and under-dosing (both 21.9%), whilst overdosing was much less common at 3.1%. At 6-month follow-up, the number of drug-related problems had reduced to 4 (with only 12.5% of patients exhibiting non-compliance), and 94% of all interventions being accepted by physicians. The intervention group had a significant reduction ($p < .01$) in serum ferritin compared to the control group, and significant increase in healthcare satisfaction and quality of life compared to the control group ($p < .01$ and $p < .001$ respectively).

*A minority of patients (< 3% were over 19 years old)

Discussion

Paediatric clinical pharmacists can provide significant benefits to paediatric patients through identifying a wide range of DRPs and recommending suitable interventions to reduce adverse events and non-compliance issues, improve condition control, and minimise drug expenditure. A previous systematic review (Ghaleb et al. 2006) found that dosing errors were the most common type of medication error, with antibiotics and sedatives most commonly associated with these errors [15].

In this review, we found that pharmacists were adept at identifying and managing these errors, with the acceptance rates of pharmacist-initiated interventions for paediatric patients generally being high, indicating physician confidence

in pharmacists' recommendations. Acceptance rates in studies not included in this review are similarly above 85% for both paediatric and adult patients [3, 8, 22, 26, 34, 35]. Having pharmacists present during clinical ward rounds allows them to provide real-time advice to physicians (rather than recommending changes after prescribing has occurred), which increases the likelihood that errors will be caught, and that interventions to amend these errors will be accepted [5, 20].

It must be noted that medication errors involve not only medications prescribed for inpatient use, but also those required short or long-term after discharge, and medications for chronic conditions unrelated to the presenting compliant [25]. These errors may be more likely when urgent health issues during initial presentation overshadow regular medication recording, particularly in the emergency department [25]. This may have significant adverse effects on patient health, particularly when low therapeutic index or immunosuppressant, anticonvulsant, or other medications requiring strict adherence are not correctly recorded during admission and continued throughout hospital stay [7, 25]. Medication reconciliation services performed by clinical pharmacists are shown to be an effective method for preventing errors during these critical stages of care [23, 29].

The vulnerability of paediatric patients to serious consequences arising from medication errors, combined with the error frequency reported in the studies in this review suggests the need for regular pharmacist involvement in drug treatments, to reduce the incidence and severity of errors, including missed doses [1, 10, 21, 25]. Dosing errors in particular are not only common, but can involve doses as high as 10 times the normal therapeutic range, representing a significant threat to patient safety [13, 14, 33]. One study reported that error rates decreased with an increase in the experience of the physician, suggesting that newly registered prescribers (and their patients) would benefit from a pharmacists' assistance in medication ordering, particularly if free-text (as opposed to electronic) prescribing is relied upon [24, 40]. Two studies also found that younger participants in comparison to adolescents, were at a higher risk of errors, suggesting that pharmacist activities should be focused on younger patients [14, 24]. Pharmacists are trained to provide these interventions for patients, with the vast majority of interventions in the studies included in this review having a positive impact on patient health [13, 33]. In addition to physician experience and pharmacist involvement during prescribing, the use of specialised clinics appears to be an additional protective factor against medication errors for paediatric patients. Two of the RCTs in this review, which enrolled patients with a particular medical condition within a specialised unit, found fewer dosing errors than other studies, potentially due to a smaller number of commonly prescribed medications compared to in general medical or surgical units, and the awareness of staff when prescribing inherently high-risk drugs [2, 12, 13].

However, there are barriers to the involvement of pharmacists in medication prescribing and preventing errors, which may vary considerably between hospitals and health systems between different countries. Medication prescribing which occur at the bedside of the patient in a multidisciplinary setting offers a rapid and effective environment for identifying and resolving errors compared to orders which occur after ward rounds, where a pharmacist may not be involved, and the prescriber more difficult to contact [1, 21]. As many hospitals do not employ pharmacists to participate in ward rounds (including approximately half of those in the USA), delays in correcting medication errors would be more likely in these institutions [1, 31]. However, given the increased utilisation and benefits noted from pharmacist involvement, the number of hospitals including pharmacists in ward rounds has increased from approximately 30% in 2001 [30]. Pharmacist involvement in patient discharge procedures and patient education ensures a continuity of care, through improved patient satisfaction, reduced non-compliance to prescribed medications, and improved laboratory biomarkers [2, 12, 18, 36, 40].

In this review, a contributing factor to medication errors was the unavailability of medications adapted for use in children, with the wrong drug formulation being prescribed a common error in this review [24]. Whilst the availability of commercial formulations in a hospital formulary may be limited, the preparation of 'tailored' pharmaceutical preparations, particularly antibiotics as one of the most commonly prescribed medication classes and prone to errors, is a vital service which can be provided by pharmacists [1, 10, 13, 14, 30]. The availability of commercial medications is subject to market and other forces and is an ongoing issue, and pharmacists can communicate these availability issues to prescribers, nurses, and other relevant health professionals, to prevent errors relating to dosing and dosage forms.

The main strengths of this review are the large total number of admissions included, and the inclusion of health institutions across several countries, making the findings more robust. Limitations to consider when interpreting the results of this systematic review include having some studies with low participant numbers [2, 12, 28], or being conducted at a single site [1, 25, 38, 40], limiting their generalisability to other health institutions. There were also significant differences between studies on what constituted a reportable error, making it difficult to compare individual studies and extrapolating findings elsewhere difficult [1, 13]. This issue also prevented a meta-analytic study, which would have increased the strength of the findings.

Conclusion

Clinical pharmacists can significantly contribute to positive health outcomes for paediatric hospital patients through the identification and management of medication errors. These

errors often involve antibiotics, and occur during prescribing on clinical ward rounds, and would benefit from the involvement of a clinical pharmacist to ensure the prompt and accurate provision of drug-related information to prescribers. Further research using standardised reporting of adverse events is required to allow a clear comparison between studies and a more accurate assessment of the broad range of benefits provided by clinical pharmacists.

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Authors' contributions All authors were responsible for the development of the initial research plan and were involved in quality assessment of eligible articles. AD carried out an independent literature search and was responsible for drafting of the manuscript. KR and MT were responsible for assessing article eligibility and revising of the manuscript drafts. NR and SP assisted in drafting of earlier versions of the manuscript. TK assisted in the literature search, drafting of earlier versions of the manuscript, and review of the final manuscript version.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent is not applicable in this study.

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