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SYSTEMATIC REVIEW

A systematic review on pediatric medication errors by parents or caregivers at home

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ABSTRACT

Introduction: Medication errors (MEs) are frequent and, in some cases, can lead to hospitalization, disability, increased healthcare costs or, even, death. Most of pediatric medications are administered by parents or caregivers at home. It is necessary to explore the MEs at home to improve pediatric patient safety.

Areas covered: This study aimed to review the current literature on the frequency of pediatric MEs by parents or caregivers at home, their associated factors, and pediatric ME reporting systems. Citable original articles of any type of study design or reviews published from 2013 to 2021 were searched in Medline, Scopus, Embase, and ScienceDirect databases.

Expert opinion: The available data about the frequency of pediatric MEs at home varied from 30% to 80%. Current research suggests the risk of making a ME in pediatric patients at home may depend on the characteristics of the caregiver and may increase if a prescription contains ≥3 drugs. Findings conclude that providing dosing tools more closely matched to prescribed dose volumes, recommending the use of syringes as a measurement tool, and educational intervention for caregivers could be useful to reduce MEs. Concerning the reporting systems for pediatric MEs in the outpatient setting, no information was found.

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KEYWORDS
Medication errors; pediatrics; child; parents; caregivers; safety management

1. Introduction

Patient safety is a well-recognized public health issue worldwide [1]. Medication errors (MEs) are frequent and, in some cases, can lead to hospitalization, disability, birth defect, increased healthcare costs or, even, death [2]. Error prevalence rates reported in different countries vary widely according to the population or the data source [3]. A recent systematic review [4] found that the median rate of ME (five studies) was 53% in adult patients after hospital discharge.

The process of medication use is complex and several groups are involved. MEs can occur from the time of prescribing the medication to the time of administration, in different settings of care (hospital, primary care, pharmacy, home), and due to different reasons [5], either the health professional's or the patient's (or caregiver) responsibility. The prevalence rate of prescribing error ranges from 2% to 94% in adult patients [6]. On the other hand, ME rate in the outpatient setting (i.e. patient or caregiver responsibility) ranges from 19 to 59%, and it is higher among pediatric and elderly patients than others [7]. The ME in the outpatient setting (at home) comprises the administration of the drug by the patient or the caregiver.

Due to many factors, including weight-based dosing, high vulnerability, and the inability to self-administer medications, children are at high risk of MEs [8]. The majority of pediatric medications are taken at home and are administered by parents or caregivers and, therefore, the MEs in the outpatient setting are an important health concern for children [9,10].

Most of the errors are preventable [10]. It is necessary to investigate and address pediatric MEs at home in order to improve pediatric patient safety. Pediatric ME reporting systems may be useful to detect and learn from MEs and to manage safety risks in medication use [11]. Digital technologies offer several opportunities to improve drug safety [7]. The present study aimed to review the current literature on the frequency of pediatric MEs by parents or caregivers at home, their associated factors and pediatric ME reporting systems.

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Article highlights

- The risk of making a medication error in pediatric patients at home may increase when the caregiver is a non-native speaker, a man and/or young.
- A prescription containing more than two drugs might affect the comprehension of medication instructions.
- To provide dosing tools more closely matched to prescribed dose volumes, to recommend the use of syringes as a measurement tool, and educational intervention for caregivers could be useful to reduce pediatric medication errors at home.

2. Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard [12].

2.1. Definition of pediatric medication error at home

Pediatric medication error at home was defined as any preventable and unintentional deviation from the appropriate use of prescribed or non-prescribed pediatric medication, committed by parents or caregivers in the outpatient setting.

2.2. Study selection criteria

The inclusion criteria were original articles on MEs, either prescribed or non-prescribed drugs, that parents or other caregivers of children make at home, influencing factors and pediatric ME reporting systems. Any type of study design could be included if they investigated MEs in pediatric population in the outpatient setting (at home). We excluded studies on therapeutic adherence, any type of review, non-citable paper, such as editorials or letters to the editor, or studies for which access to complete information was not available, even after contacting the authors.

2.3. Search strategy and data sources

A literature search was performed using Medline (PubMed), Scopus, Embase, and ScienceDirect electronic databases, covering all papers published from 1 January 2013 to 24 May 2021. We completed the search in May 2021. The terms included in the search were Medical Subject Heading (MeSH) descriptors and keywords (with controlled language and combined with simple or free language): 'medication errors,' 'adverse drug event,' 'dosing error,' 'safety management,' 'adverse drug reaction reporting systems,' 'error reporting systems,' 'child,' 'pediatrics,' 'home,' 'outpatient,' 'parent' and 'caregiver.' Table 1 shows detailed search strategies. We limited results to documents published in English and Spanish language. The reference list of eligible studies was also reviewed. The identified articles were downloaded using the RefWorks® reference manager for the subsequent data extraction process.

2.4. Articles screening

After duplicate publications were excluded, titles and abstracts were screened first by two reviewers to eliminate unrelated studies. Any discrepancy was resolved by discussion with a third reviewer. For all remaining relevant articles, the full text was retrieved, and two reviewers examined them independently according to the eligibility criteria.

2.5. Data extraction

Two reviewers independently extracted data from selected studies, and any differences were resolved by consensus with a third reviewer. The following information was collected from each study: first author, year of publication, the country in which the study was performed, study design, sample size, study objective and main findings. Data were recorded onto a datasheet specifically created for this study.

In order to assess the risk of bias of each study, two reviewers independently gave an overall grading based on the National Institutes of Health (NIH) Quality Assessment Tools for quantitative studies [13], and the Critical Appraisal Skill Programme (CASP) [14] tool for qualitative studies. Any discrepancy was resolved by consensus with a third review. For any quality question where reviewers answered 'no,' we considered some risk of bias. According to the count of 'yes' responses to the questions of quality tools, the studies were categorized as being of poor (0–5), fair (6–9), good (10–13) or excellent (14) quality.

2.6. Data synthesis

We conducted a qualitative analysis of results because it was not possible to carry out a meta-analysis due to the lack of homogeneity of the methodology and the type of analysis carried out in each study. We detailed data of each study in two tables and we performed a descriptive and narrative synthesis about the number of cases of pediatric MEs, pediatric MEs types, risk factors of pediatric MEs, pharmacological groups and medications involved in pediatric MEs and pediatric MEs reporting systems. We used the term of pediatric medication error for any definition of medication error in children by parents or caregivers used in individual studies. We defined a risk factor of MEs as any factor that increased the chance of parents or caregivers made a ME at home. Concerning MEs reporting systems, we focused on systems used to report any pediatric medication errors made by parents or caregivers at home.

3. Results

We identified 467 studies from the database search. Of these, 109 were removed because they were duplicates. We examined the title and abstract of 358 publications and we excluded 308 studies because they did not meet the inclusion criteria. Fifty articles were selected for full-text reading and 19 of them dealt with our research questions. Thus, we included 19 studies in the present review (Figure 1).

Table 1. Search strategies for literature review.

Database	Date	Search	Results
Medline/ Pubmed	May 2021	(('medication errors'[MeSH Terms] OR 'medication errors'[Title/Abstract]) OR 'adverse drug event'[Title/Abstract] OR 'dosing error'[Title/Abstract] AND ((pediatrics[MeSH Terms] OR pediatrics[Title/Abstract]) OR pediatrics [Title/Abstract])) AND (parents [MeSH Terms] OR parents[Title/Abstract])	15
		('medication errors' [Title/Abstract] OR 'adverse drug event' [Title/Abstract] OR"dosing error" [Title/Abstract] AND child [Title/Abstract] AND (home[Title/Abstract] OR parent[Title/Abstract] OR caregiver[Title/Abstract])	26
		('medication errors' [Title/Abstract] OR 'adverse drug event' [Title/Abstract] OR "dosing error" [Title/Abstract]) AND (child [Title/Abstract] OR pediatrics[Title/Abstract]) AND (home[Title/Abstract] OR parent[Title/Abstract] OR caregiver[Title/Abstract])	33
		((('Safety Management'[Mesh]) AND 'Medication Errors'[Mesh]) AND 'Pediatrics'[Mesh]	3
		((('Safety Management'[Mesh]) AND 'Medication Errors'[Mesh]) AND 'Child'[Mesh])	11
		(('medication errors'[MeSH Terms] OR 'medication errors'[Title/Abstract]) OR 'adverse drug event'[Title/Abstract] OR 'dosing error'[Title/Abstract] AND (('adverse drug reaction reporting systems'[MeSH Terms] OR 'adverse drug reaction reporting systems'[Title/Abstract] OR 'error reporting system'[Title/Abstract]) AND ((pediatrics[MeSH Terms] OR pediatrics[Title/Abstract]) OR pediatrics [Title/Abstract] OR child [Title/Abstract]))	20
		('medication errors' [Title/Abstract] OR 'adverse drug event' [Title/Abstract] OR 'dosing error' [Title/Abstract]) AND (child [Title/Abstract] OR pediatrics[Title/Abstract]) AND ('outpatient'[Title/Abstract])	13
Scopus	May 2021	(TITLE-ABS-KEY ('medication error' OR 'dosing error') AND TITLE-ABS-KEY (child OR pediatric OR pediatric) AND TITLE-ABS-KEY (home OR outpatient OR parent OR caregiver)) AND PUBYEAR > 2012 AND (LIMIT-TO (DOCTYPE, 'ar') OR LIMIT-TO (DOCTYPE, 're')) AND (LIMIT-TO (LANGUAGE, 'English') OR LIMIT-TO (LANGUAGE, 'Spanish'))	248
		(TITLE-ABS-KEY ('medication error' OR 'dosing error') AND TITLE-ABS-KEY (home OR parent OR caregiver) AND TITLE-ABS-KEY (child OR pediatrics) AND TITLE-ABS-KEY ('adverse drug reaction reporting systems' OR 'error reporting system')) AND DOCTYPE (ar OR re) AND PUBYEAR > 2012	4
Embase	May 2021	*('medication error':ti,ab,kw OR 'adverse drug event':ti,ab,kw OR 'dosing error':ti,ab,kw) AND [2013–2021]/py AND ('paediatric':ti,ab,kw OR 'children':ti,ab,kw) NOT 'inpatient':ti,ab,kw AND [embase]/lim AND ([article]/lim OR [article in press]/lim)*	121

Table 2 summarizes the characteristics of the 19 studies finally selected. Yin et al. [15,16] published two studies in 2014 from the same database but they were considered as different studies because they answered different questions. Concerning the study quality, Table 2 shows the result of the assessment. Cross-sectional studies allow no time to see if an association between exposure and outcome existed, and this was considered a bias. As the quality assessment tool for longitudinal and cross-sectional studies was the same, the issues that were not applicable for cross-sectional design reduced the quality of these studies. The quality of most of the longitudinal studies was good. However, three of them failed to report something about power or sample sizes [17–19] and most of the cohort studies measured exposure only at baseline. These issues are important elements to obtain results of higher quality. Only three observational studies [20, 22, 28,] analyzed the association of several factors with ME but two of them had a cross-sectional design. Concerning experimental studies, the quality of controlled studies [20–22] was high and the only issue that was considered as a bias was the impossibility of blinding participants and researchers. Table 3 shows the study objective, the study participants and main findings of the included studies.

3.1. Pediatric MEs cases

The proportion of cases of MEs at home were available from some authors in different settings. Glick et al. [23] found that 38% of parents or legal guardians made any pediatric ME within 2 weeks of discharge of pediatric patients from a public hospital of New York (USA). Samuels-Kalow et al. [17] demonstrated that more than 30% of parents made an error in acetaminophen dosing after discharge from a tertiary care pediatric emergency department, despite the provision of a written instruction sheet containing the correct dosing information. Harris et al [24]. analyzed liquid medication dosing errors among Hispanic parents of children <8 years living in the USA, and they reported that over 80% of them made at least one. Sil et al. [25] found that 44.6% of caregivers who were interviewed in an urban hospital in India committed MEs. Solanki et al. [26] determined that the frequency of MEs committed by caregivers at home in neonates (< 3 months of age) discharged from a neonatal intensive care unit of India was 66.3%. Among cancer patients through 20 years old, Walsh et al. [18] calculated that the overall error rate was 70.2 errors per 100 at home. Concerning data from a national database, Smith et al. [27] showed that the Poison Control Center of USA reported an average of 63,358 out-of-hospital ME exposures per year among children < 6 years from 2002 to 2012. On the other hand, Wang et al. [28] determined that 9.3% (n = 443) of the reported out-of-hospital medication adverse event related to cough and cold medication in children < 12 years from 2009 to 2016 were due to medication errors committed by the parents or caregivers.

3.2. Pediatric MEs types

The error types were reported in all the studies. MEs related to dose were assessed in ten studies [15–18, 21, 23–30,]. The qualitative study by Chew et al. [29] showed that mothers admitted that they or their partners had experiences of unintentional overdosing or missed doses of their children's medication, even that they had self-decided to reduce the dose. You et al. [30] reported that 15.1% of participants (88.8% mothers) answered that they were unsure that they had given the correct dosage. Based on participant interviews of Sil et al. [25] study, 9.3% and 31.6% of caregivers (89.7% mothers) made dose and time administration errors, respectively, in the last 12 months. Nine studies [15–18-24,26] measured the medication dosing errors by direct observation among primary caregivers of a child and most of them defined a medication dosing error

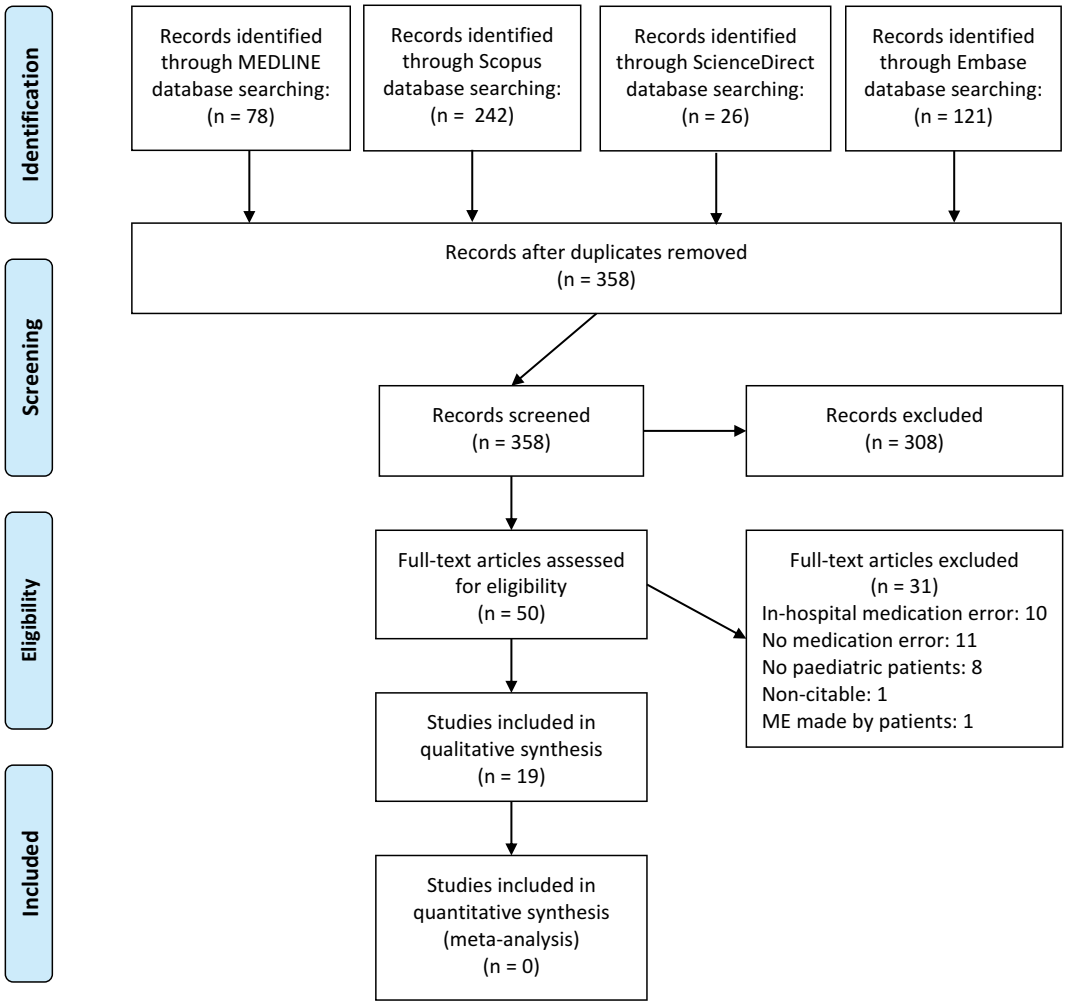

Figure 1. PRISMA 2009 flow diagram.

as ≥ 20% deviation from the appropriate dose. Glick et al. [23] found that 34% and 15% of participants made a dose and frequency error, respectively. Samuels-Kalow et al. [27] showed that 32% of them had an acetaminophen dosing error. Harris et al. [24] found that 83.1% of parents made liquid medication dosing errors (mean [SD] errors/parent = 2.2 [1.9]). And Solanki et al. [26] determined that the rate of errors in dose administration and frequency of dosing was 54.2% and 15.7% among the caregivers (97.6% mothers), respectively. The results of Yin et al. [15,16] showed that 41.1% of parents (90.2% mothers) made a liquid medication dosing error (mean [SD] percentage dose measured 0.9 [0.3]; range 0.08–2.67) in the prescribed dose. Regarding the experimental studies of Yin et al. [20,21], 84.4% and 83.5% of participants made at least one liquid medication dosing error during the assessment in 2016 and 2017, respectively. And 21.0% and 29.3% of study participants, respectively, made at least one large error (>2 times the dose). Among children with cancer, Walsh et al. [18] found that 28% of parents administered the wrong dose and 19% missed scheduled doses of medication.

Concerning the medication preparation method, Chew et al [29]. identified mothers who had been making errors in medication preparation and they had an impact on the control of their children's conditions. Berthe-Aucejo et al. [31] and Sil et al. [25] asked participants to show the reconstitution of oral liquids from dry powders. The first study [31] found that amoxicillin and josacine were incorrectly reconstituted in 46% and 56% of cases, respectively, and the results of the second study [25] showed that 14.1% of participants did not reconstitute the medication correctly.

Self-decided treatment discontinuation was assessed in three studies and the results were 3.6% [26], 50% [25] and 85.5% [30] of caregivers stopped the treatment when the child got better. One participant of Chew et al. [29] study also admitted having decided to discontinue her child's treatment. Other error types were evaluated by authors, such as Sil et al. [25] who estimated that 3.7% of participants administered the wrong medicine. Dayasiri et al. [32] also observed that six caregivers mistakenly gave a wrong medication to their children. Unlike Solanki et al. [26], who found that none of the caregivers had given the wrong medications to their infants. Walsh et al. [15] found that

Table 2. Characteristics of included studies.

First Author	Year of publication	Country	Study design	Sample size	Quality review
Samuels-Kalow ME [17]	2013	USA	Prospective analytical study	145	Good
Walsh KE [18]	2013	USA	Prospective descriptive study	92	Good
Yin HS [15]	2014	USA	Cross-sectional study	287	Fair
Yin HS [16]	2014	USA	Cross-sectional study	287	Fair
Smith ME [27]	2014	USA	Retrospective descriptive study	696,937	Fair
Almazrou S [33]	2015	Saudi Arabia	Cross-sectional study	575	Fair
You M [30]	2015	Korea	Cross-sectional study	179	Fair
Berthe-Aucejo A [31]	2016	France	Prospective analytical study	100	Good
Buddhadev MD [19]	2016	India	Experimental study (pre-post study)	128	Poor
Yin HS [20]	2016	USA	Experimental study (randomized controlled study)	2110	Good
Yin HS [21]	2017	USA	Experimental study (randomized controlled study)	493	Good
Harris LM [24]	2017	USA	Cross-sectional study	1126	Fair
Sil A [25]	2017	India	Cross-sectional study	377	Fair
Solanki R [26]	2017	India	Cross-sectional study	166	Fair
Chew C [29]	2019	Malasia	Qualitative study	15	Good
Glick AF [23]	2019	USA	Prospective cohort study	165	Good
Topal E [22]	2020	Turkey	Experimental study (randomized controlled study)	510	Good
Wang GS [28]	2020	USA	Cross-sectional study	4756	Fair
Dayasiri K [32]	2020	Sri Lanka	Retrospective and prospective descriptive study	11	Poor

12.5% of caregivers had used expired medication. You et al. [30] reported that 26.8% of caregivers admitted having administered the medication to other children, 26.3% of them admitted using the remainder of the prescription medication when the same child developed the same symptoms again, and 13.4% of participants reported administering prescription medications to children not addressed by the prescription.

Only one study [27] analyzed any type of pediatric ME made at home and they are disclosed in Table 4. Regarding cough and cold medications involving an adverse event, Wang et al. [28] found that the dosing error was the most common (86.6%) type of ME, followed by dose frequency error (19.2%) and multiple products administered (11.3%).

3.3. Risk factors of pediatric MEs

Glick et al. [23] suggested that poor comprehension of discharge instructions contributed to ME. They found that complex discharge plans and low health literacy of parents were associated with comprehension errors and, consequently, with

Table 3. Summary of study objective, study participants and main findings of the included studies.

First author	Study objective	Participants	Main finding
Smith ME [27]	To investigate out-of-hospital medication errors among children, using National Poison Database System (2002–2012)	Children < 6 years from USA	There was a significant increase in the number and rate of non–cough and cold medication errors. The medication errors rate increased with decreasing child age.
Samuels-Kalow ME [17]	To study the association between language and discharge comprehension concerning medication dosing.	English- or Spanish-speaking parents of children (2 – 24 months) attending a tertiary care pediatric emergency department.	More than 30% of parents showed to make an error in acetaminophen dosing at the time of discharge, in spite of provision of an instruction sheet about the correct dosing information.
Walsh KE [18]	To describe the types of medication errors at home in children with cancer.	Parents of children with cancer (< 20 years), taking daily home medications and undergoing chemotherapy.	Errors were common. Parent administration errors were often due to communication failures. The most common errors were due to the parent administering the wrong dose or missing scheduled doses of medication.
Yin HS [15]	To examine the association between the recommended provider counseling strategies, including advanced communication techniques and dosing instrument provision, and reductions in parent liquid medication dosing errors.	Parents with children (<9 years) attending pediatric emergency departments.	More than 40% of parents misdosed the liquid medication. Only 1 in 3 parents reported receipt of advanced counseling strategies.
Yin HS [16]	To examine the association between unit used and medication errors in children.	Parents or legal guardians of children (<9 years) attending pediatric emergency departments.	More than 35% of parents made an error in dose measurement. The use of teaspoon or tablespoon units was associated with higher odds of medication error than the use of milliliter units.

(Continued)

Table 3. (Continued).

First author	Study objective	Participants	Main finding
Almazrou S [33]	To assess experiences with measuring cups, syringes, and droppers for oral liquid medications, to compare the accuracy of dosing across these methods, and to determine the effect of education status and pharmacist counseling on dosing accuracy.	Saudi mothers of children < 13 years.	Mothers are at a high risk of making dosing errors when using a dropper. Education status plays an important role in dosing accuracy.
You M [30]	To describe parental reporting of medication usage with their children, their experiences with medication administration to their children at home, and their understanding of adverse drug events related to prescription and to over-the-counter medicines.	Parents of children (< 7 years) from Korea.	Parents widely used dosing cups to measure oral medication. Most parents indicated non-adherence to medication regimens, and some of them confirmed that they lacked knowledge on weight-based dosing. Parent understanding of adverse drug events was associated with parent educational level.
Berthe-Aucejo [31]	To investigate reconstitution and preparation dosing errors of liquid oral medications given by caregivers to children.	French-speaking caregivers of children hospitalized or attending the emergency department.	Nearly 50% of caregivers did not correctly reconstitute the medication, and almost 50% made a dose preparation error with the dosing spoon. Men make more reconstitution errors than women. The risk of making an error with the dosing spoon was higher than with dose-weight graduated pipette.

(*Continued*)

Table 3. (Continued).

First author	Study objective	Participants	Main finding
Buddhadev [19]	To study if an educational intervention can reduce the liquid medication dosing errors in pediatric patients.	Caregivers of pediatric patients.	Dosing medication errors decreased significantly ($p < 0.0001$) after educational intervention. Participants who used a calibrated dosing cup and the cap of the bottle were more likely to measure dose correctly.
Yin HS [20]	To examine if the discordance in unit pairing on the label and tool and dosing tool characteristics affect parent dosing error rates in pediatric patients. And to study the impact of parent health literacy and language on dosing medication error rates.	English or Spanish-speaking parents or legal guardians ≥18 years old with a child ≤8 years old, presenting for nonemergency care.	More than 80% of parents made ≥ 1 dosing error. Parents who received teaspoon-only labels with milliliter and teaspoon dosing tools made significantly more errors than those receiving milliliter-only labels and tools. Use of dosing cups was associated with >4 times the odds of error compared with syringes.
Yin HS [21]	To examine if the use of pictographic diagrams, milliliter-only units, and/or provision of tools more closely matched to prescribed volumes reduce dosing errors made in pediatric patients. And to study the impact of parent health literacy and language on dosing medication error rates.	English or Spanish-speaking parents or legal guardians ≥18 years old with a child ≤8 years old, presenting for nonemergency care.	More than 80% of parents made ≥ 1 dosing error. When the dosing tool provided more closely matched the prescribed dose volume, the risk of dosing error was reduced.
Harris LM [24]	To study the relationship between health literacy and English proficiency and liquid medication dosing errors.	Hispanic parent/ legal guardian of children (≤8 years of age) attending a hospital.	Over 80% of parents made at least one liquid medication dosing error, especially those with limited health literacy and English proficiency.

(*Continued*)

Table 3. (Continued).

First author	Study objective	Participants	Main finding
Sil A [25]	To assess the knowledge, attitude, and practices with medicine administration and literacy in allied matters.	Caregivers of pediatric patients.	Most of caregivers used standardized dosing instruments to measure liquids and reconstitution. 44.5% caregivers made medication errors. A lack of proper knowledge of the quantity implied in one teaspoon and one tablespoon was found. We identified some wrong practices like the addition of medicine to milk.
Solanki R [26]	To determine the medication frequency of medication errors by caregivers of neonates at home and to identify the associated risk factors.	Caregivers of children (<3 months) who were discharged from intensive unit care at home.	Nearly 66% of the infants were subjected to one of the following types of errors: errors in frequency, dose administration and discontinuation. Administration dose was the dominant type of error, (54%).
Chew C [29]	To explore the issues related to medication safety from the caregivers' perspective.	Mothers of children in Malaysia who were < 6 years of age and diagnosed with a chronic disease	No clear instructions and difficulty to remember the time for administration were the reasons of unintentional medication errors. Intentional errors were mainly due to a busy working life and a negative belief about the medications.
Glick AF [23]	To examine the association of parent health literacy, discharge plan complexity, and parent comprehension of with adherence to inpatient discharge instructions.	English- or Spanish-speaking primary caregiver of a child (≤ 12 years) discharged home.	More than 80% of caregivers made comprehension or adherence errors, especially when discharge plans were complex and for parents with low health literacy.
Topal E [22]	To determine if a visual modification to the inhaler spacer instructions could improve the correct usage rate and decrease usage errors.	Caregivers of children (< 6 years) who were prescribed inhalers with spacers for the first time.	Participants who used the modified visual instructions demonstrated a better compression of assessment steps than those who used the unmodified visual guidelines.
Wang GS [28]	To characterize the role of medication errors in out-of-hospital medication-related adverse events from cough and cold medication.	Children < 12 years who were treated with cough and cold medication and reported at least 1 adverse event.	Diphenhydramine and dextromethorphan dosing errors were the most common cause of medication errors. Volume error was the most common error type.
Dayasiri K [32]	To identify patterns of pediatric medication errors.	Children < 12 years attending the emergency department due to pharmaceutical poisoning.	Eleven medications errors made by parents or caregivers were identified. Education interventions and written safety warnings are needed to address the medication errors.

(*Continued*)

ME. Previously, Buddhadev et al. [19] showed that proper education or instructions by the pharmacist could reduce liquid medication dosing errors. According to the study by Harris et al. [24], those parents with both limited English proficiency and limited health literacy are at particular risk. If the primary language of the parent was different from the language of written discharge instructions could be associated with a higher probability of dosing error, even independently of parental health literacy [17]. Yin et al. [21] also found that parents who had low health literacy were at greatest risk for dosing errors, even after the optimization of labels and tools. However, they did not found that the primary language affected the risk of dosing error.

The multivariate analysis of Berthe-Aucejo et al. [31] confirmed that being a non-native speaker caregiver was a risk factor associated with incorrect reconstitution or preparation of medication (OR = 0.2; 95%CI: 0.1 to 0.5; p = 0.001; reference: French is mother tongue). Additionally, they found that male sex (OR = 5.0; 95%CI: 1.5 to 16.7) and younger age of caregiver (OR = 0.9; 95%CI: 0.9 to 1.0; reference: for an age increase of 5 years) were also significantly associated with incorrect reconstitution (p = 0.01 and p = 0.02, respectively). Solanki et al. [26] also analyzed the association of several factors with ME and only a prescription containing more than three drugs was significantly associated with errors (OR = 3.26; 95%CI: 1.34 to 7.93; p = 0.01). Almazrou et al. [33] determined by logistic regression that education status was significantly associated with a high risk of dosing error (p = 0.001), and most errors

Table 4. Number of cases of each pediatric medication error type.

Reference	Type error	Cases, n (%)
Smith et al. [27]	Inadvertently given medication twice	188,399 (27.0)
	Confused units of measure	57,389 (8.2)
	Wrong medication given	54,493 (7.8)
	Medication doses given too close together	47,710 (6.8)
	Inadvertently given someone else's medication	47,534 (6.8)
	Dispensing cup error	35,047 (5.0)
	Incorrect formulation or concentration given	33,856 (4.9)
	Incorrect dosing route	32,745 (4.7)
	Tenfold dosing error	28,138 (4.0)
	Drug interaction	13,622 (2.0)
	Exposure through breast milk	10,354 (1.5)
	Other incorrect dose	7917 (1.1)

were made by using the dropper in comparison with cup and syringe. Moreover, Sil et al. [25] study found a lack of knowledge of the quantity implied in one teaspoon and one tablespoon among the caregivers. The experimental studies of Yin et al. [20,21] revealed that, on the one hand, the risk of making liquid medication errors were higher when participants used a cup than when they used a 0.5-mL-increment syringe (OR = 4.6; 95%CI, 4.2–5.1) and varied by health literacy ($P < 0.001$), especially for smaller doses. Also, they found the use of a teaspoon-only label (with a milliliter and teaspoon tool) was associated with more dosing errors than when milliliter-only labels and tools were used (adjusted OR = 1.2; 95% CI, 1.0–1.4). On the other hand, they found that the risk of liquid medication dosing error was reduced when the dosing tool provided more closely matched the prescribed dose volume, e.g. for the 7.5-mL dose the fewest errors seen with the 10-mL syringe (5- vs 10-mL syringe: OR = 4.0; 95% CI, 3.0–5.4 and cup vs. 10-mL syringe: OR = 2.1; 95%CI, 1.5–2.9). Besides, the risk of large dosing error was higher when participants received text only (versus text and pictogram) instructions or the units used on labels and tools were milliliter/teaspoon (versus milliliter-only): OR = 1.9; 95%CI, 1.1–3.3 and OR = 2.5; 95%CI, 1.4–4.6, respectively. Later, Topal et al. [22] also demonstrated that improving the visual instructions of inhaler spacer increase the compression of usage steps and, therefore, the number of usage errors could be reduced.

Other authors did not analyzed the association but they found trends. Yin et al. [15] reported that the dosing error rate of parents who received at least one advanced counseling strategy in the emergency department was lower than the rate of those who did not report receiving it. Smith et al. [27] observed that the number of MEs increased with decreasing child age. The qualitative study by Chew et al. [29] reported that limited understanding about medications, confusion over instructions, confusion over measurement units, uncertainty about re-administration following vomiting, lack of reassessment by health-care professionals, barriers to communication between caregivers and health-care providers might lead to MEs.

3.4. Pharmacological groups and medications involved in pediatric MEs

Only two studies investigated which types of medication were involved in pediatric MEs by caregivers at home [18,27]. Table 5 shows the ME rate by the therapeutic group of each study.

3.5. Pediatric MEs reporting systems

One of the included studies used databases from national adverse events reporting systems or national poison information centers [27]. However, no studies evaluating error-reporting systems in pediatric patients at home were found.

4. Discussion

We reviewed the current literature on pediatric MEs committed by parents or other caregivers at home, and we identified 19 studies investigating the frequency of pediatric MEs at home, the type of ME and/or their associated factors. No evidence about reporting systems for pediatric MEs at home were found. These studies were carried out in different countries, and included parents or caregivers of children with a different range of ages; therefore, the frequency of pediatric MEs varied over a wide range, according to the type of study and the study population. About the risk of parents and caregivers making errors when they administer medication to children at home may depend on the characteristics of the caregiver and may increase if a prescription contains more than two drugs. In addition, the current evidence shows that providing dosing tools more closely matched to prescribed dose volumes, measuring the dose with a syringe, and providing an educational intervention to caregivers could reduce MEs.

The proportion of cases of pediatric MEs at home ranged from 30% to 80%. This wide range may be due to the differences between study populations, due to some of them analyzed errors related to dose or a specific drug, or due to the differences in methods for error detection (interview or direct observation). A previous review on MEs in adults [6] also reported highly variable prevalence data in community care contexts, which seemed to be higher among older polymedicated patients. Woo et al. [34] concluded that the proportion of children subjected to ME at home were higher than adults.

Regarding the error type, we found that most of the reviewed studies investigated the pediatric ME related to dose. This type of ME was one of the most commented by Neuspiel & Taylor in 2013 [35]. However, according to the results of Smith et al. [27] who provided data about any type of error, the most frequent pediatric ME was accidentally medication administration twice. Moreover, it is remarkable that the proportion of caregivers who reported to discontinue the treatment when the child got better ranged from 3.6% among caregivers of neonates discharged from critical units [26] to 85.5% among Korean parents of children aged < 7 years [30]. On the other hand, two of the reviewed studies proved, through direct observation, some caregivers made errors in medication preparation or reconstitution [25,31].

Table 5. Number of cases of pediatric medication error per pharmacological group.

Reference	Study population	Pharmacological group	Cases, n (%)
Walsh et al. [18]	Children and adolescents (< 20 years) with cancer	Antibiotics, antiviral agents, antifungal	19 (27.5)
		Chemotherapy medications	14 (20.3)
		Behavior/mental health medications	7 (10.1)
		Gastrointestinal medications	6 (8.7)
		Allergy medication	6 (8.7)
		Narcotics	5 (7.2)
		NSAIDS and local anesthetics	4 (5.8)
		Supportive medications	3 (4.3)
		Respiratory medications	3 (4.3)
		Vitamins	1 (1.4)
		Topical agent	1 (1.4)
		Antiepileptic/neurologic medications	0 (0)
Smith et al. [27]	Children < 6 years	Analgesics	175,733 (25.2)
		Cough and cold preparations	171,380 (24.6)
		Antihistamines	104,382 (15.0)
		Antimicrobials	82,401 (11.8)
		Gastrointestinal preparations	28,993 (4.2)
		Asthma therapies	27,076 (3.9)
		Vitamins	20,259 (2.9)
		Hormones and hormone antagonists	12,857 (1.8)
		Eye/Ear/Nose/Throat preparations	11,551 (1.7)
		Cardiovascular drugs	10,256 (1.5)
		Anticonvulsants	8649 (1.2)
		Sedative/Hypnotics/ Antipsychotics	6957 (1.0)
		Electrolytes and minerals	6608 (0.9)
		Topical preparations	5187 (0.7
		Stimulants	4772 (0.7)
		Dietary supplements/ Herbals/Homeopathic	4752 (0.7)
		Antidepressants	3685 (0.5)
		Miscellaneous drugs	2656 (0.4)
		Anesthetics	2631 (0.4)
		Diuretics	1244 (0.2)
		Muscle relaxants	1090 (0.2)
		Serums, toxoids, vaccines	997 (0.1)
		Anticholinergic drugs	565 (0.1)
		Veterinary drugs	212 (0.0)
		Anticoagulants	169 (0.0)
		Antineoplastics	151 (0.0)
		Diagnostic agents	45 (0.0)
		Narcotic antagonists	9 (0.0)
		Radiopharmaceuticals	4 (0.0)

Concerning the risk factors of pediatric MEs, only three studies measured the association between several factors with pediatric ME [15, 22, 30,]. Findings showed that being non-native speaker, the male sex and the younger age of caregiver were associated with incorrect medication reconstitution, a prescription containing ≥ 3 drugs was associated with ME, and education status was associated with dosing error. Additionally, other authors observed that a poor comprehension of instructions or language might lead to MEs at home. In 2009, McD Taylor et al. [36] reported communication factors as causal factors of MEs; however, we did not find information about this in recent years. Regarding the type of medication most implicated in pediatric MEs at home, analgesics were the most frequently reported group in two studies and antibiotics, antiviral agents, antifungal medications among children with cancer. Only three studies [19–21] assessed strategies to reduce the risk of medication dosing errors and they concluded that to provide dosing tools more closely matched to prescribed dose volumes, to recommend the use of syringes as a measurement tool, and educational intervention for caregivers could be useful to decrease the MEs rates in pediatric patients at home.

The caregiver must report any ME that causes harm to the child to the pediatrician or the national adverse events reporting systems. Moreover, if a caregiver detects that he or she could have committed a ME should consult pediatrician. In the present review, we did not find any reporting systems for pediatric MEs in the outpatient setting. In the inpatient setting, Guerrero-Aznar et al. [37] concluded that a system to notify and monitor MEs by healthcare professionals in pediatrics was useful to motivate the report and the search of solutions, to promote safety interventions, to offer necessary training and to make the caregiver aware of this problem.

The present systematic review was carried out using a rigorous methodology and as far as we know, this is the first systematic review about pediatric MEs at home exclusively. However, this study has several limitations. This review included language restrictions and the limitations of the examined studies limit our findings. The most significant bias was those inherent to error detection methods (memory bias for interviews, Hawthorne effect for direct observation, or reliance of self-reporting in those cases where they used a reporting system database). In addition, cross-sectional studies cannot be used to establish causality, and some of the included studies only focused on a specific drug or did not calculate the sample size. We did not consider performing a meta-analysis due to the differences between study populations, data sources and ME definitions.

5. Conclusion

Based on the published data on MEs made by parents or other caregivers at home, pediatricians should be aware that many caregivers commit MEs at home, which can affect importantly the treatment of the child, and should warn parents of this

situation. Thus, it is necessary future research about interventions to detect medication errors and avoid them.

6. Expert opinion

According to current published data, parents or other caregivers make pediatric medication errors at home. The rate of medication error could even be higher in children than in adults in some countries based on data of their reporting systems. There are many types of medication errors but the most frequent pediatric medication error seems to be the dosing error. Moreover, errors in medication preparation or reconstitution have been also identified. Pediatricians should be aware of this fact, which can affect importantly the treatment of the child, and should warn parents of this situation.

Understanding and address pediatric medication errors at home is needed to improve pediatric patient safety. Previous studies have been carried out to identify the factors that most influence when making pediatric medication errors at home. On the one hand, the language, the education status, the male sex and the younger age of the caregiver might be factors associated with pediatric medication errors. On the other hand, a prescription containing ≥ 3 drugs might lead to medication errors at home. Improving communication between caregivers, providing a combination of oral and written information, encouraging that experience can be a plus, definitely, a good comprehension of medication instructions by parents and caregivers may avoid the most frequent medication errors at home. There are few studies assessing strategies to reduce the risk of medication dosing errors but the findings show that providing a dosing tool matched to prescribed dose volume, e.g. a syringe, might also avoid many dosing errors. Further research using multivariate analysis is needed to know the main reasons to commit pediatric medication errors.

The caregiver must report any medication error that causes harm to the child to the pediatrician or the national adverse events reporting systems. Moreover, if a caregiver detects that he or she could have committed a medication error should consult the pediatrician. Pediatric medication error reporting systems may be useful to detect and learn from medication errors and to manage safety risks in medication use. However, no reporting systems for pediatric medication errors in the outpatient setting were found. Thus, it is necessary for future research about interventions to detect medication errors and avoid them.

In the near future, reporting systems for pediatric medication errors in the outpatient setting might be developed and aid in the progress of this research area. The availability of this kind of system for all populations could improve the understanding of this problem, provide possible solutions and raise awareness of medication error risks at home among pediatricians, parents, and caregivers.

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Authors' contributions

MG and JJM contributed to the study conception and design. AL and MG performed the literature search. AL, MG, and JJM examined the papers and assessed study quality. AL, MG, JG, and GM extracted data from the identified articles. AL, MG, and JJM drafted the manuscript. All authors revised the manuscript critically for importance and approved the final to be published.

Declaration of interest

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