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Medicine use and optimisation for paediatric patients – medication administration problems, health literacy and adherence of parents at home

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Medicine use and optimisation for paediatric patients – medication administration problems, health literacy and adherence of parents at home

10 Dania Dahmash, MSc, Aston University, Aston Pharmacy School

11 Zakia Shariff, MPharm, Aston University, Aston Pharmacy School

12 Dr. Daniel Kirby, PhD, Aston Pharmacy School

13 Dr. David Terry, PhD, Aston Pharmacy School

14 Dr. Chi Huynh, PhD, Aston Pharmacy School

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19
20
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Corresponding author;

22 Dr. Chi Huynh, c.huynh3@aston.ac.uk, Work: - 0121 204 3231

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28 Dr. Chi Huynh, PhD, Aston University, Birmingham, United Kingdom, E-mail:
29 c.huynh3@aston.ac.uk.

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33 Aston University, Birmingham, United Kingdom is funding Dania Dahmash PhD project, which as
34 part of her project this review was conducted.

35 The review preliminary results was published on the BMJ (Archives of Disease in childhood) after an
36 abstract was submitted for the NPPG 2018 conference for the purpose of poster presentation.

37 The authors declare no conflicts of interest.
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ABSTRACT

Objective: To review all published evidence related to paediatric medication administration problems by parents who administer the medication to their children aged 0 to 16 years, as well as medication administration related issues by young persons aged 16 and above who take their own medication at home. To identify parental sociodemographic characteristics such as health literacy and its association with medication administration problems.

Study design: Ten electronic databases were systematically searched and supplemented by hand searching through reference lists using the following search terms: i) paediatric ii) medication error including dosing error, medication administration error, medication safety and medication optimisation and iii) health literacy.

Results: Of the (374) records screened, six Randomised Controlled Trials and six qualitative studies were eligible for inclusion all published in the USA. Three analytical themes emerged from the synthesis. The review highlighted that frequencies and magnitudes of dosing errors varies by the measurement tools used, the dose prescribed and by the administration instruction provided. Parent's sociodemographic; such as health literacy and language, is a key factor to be considered when designing an intervention aimed at averting medication administration errors at home. The review summarised some potential strategies that could help in reducing medication administration errors among children at home. Among these recommendations are the use of provisional dose along with verbal instruction, to match the prescribed dose with the measuring tool, to provide an explicit dose intervals and pictographic dosing instructions.

Conclusion: The findings suggest that in order to optimise medication use by parents, problems that parents and children face and administering medication at home, how they understand or interpret administration instructions and tools need to be explored. Sociodemographic characteristics also need to be considered when designing any future potential intervention aimed at reducing medication errors among children and young people at home.

INTRODUCTION

Medication errors occur in a clinical setting, with a study estimating that one child every 8 minutes receives a wrong medication or inaccurate dose of medicine. ⁽¹⁾ When it comes to medication care for children at home, there is a significant burden of responsibility for the parent, caregiver or patient themselves (older children).⁽²⁾ The inability to administer medication correctly may result in adverse drug events and poor patient clinical outcomes. ⁽³⁾ In order to improve medication administration by parents and patients, an initial assessment of the current problems and factors that may contribute to this issue must be identified.

Previous studies have identified potential factors that can contribute to clinician led medication administration errors in children, but there have been no studies recording both the types and risk factors that can contribute towards caregiver's medication administration problems as well as young people. ⁽⁴⁾ ⁽⁵⁾ According to the European health literacy survey (HLS-EU), conducted across eight different countries, the prevalence of low health literacy levels varies from 29% to 62%. ^(6, 7)

In this review, we aimed at reviewing studies that highlighted medication administration problems experienced by parents or children, which also used a validated health literacy test to assess for parent health literacy levels. In this systematic review, we highlighted the common medication administration problems occurring at home as well as the potential causalities and risk factors that further contribute to these medication administration errors.

METHODS

This review was conducted in accordance with the Cochrane Handbook for Systematic Reviews, and followed PRISMA reporting guidelines. ^(8, 9) The review protocol is registered on PROSPERO (ID: CRD42018091590).

Patient and Public Involvement

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3 There is no patient and public involved in the design, or conduct, or reporting, or dissemination
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5 of this review.
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8 **Search Strategy**

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11 The search strategy was designed initially by the research team and verified by an information specialist
12 (D.Y.) using the PICO model. The reviewer (D.D.) systematically searched PubMed, Scopus, Web of
13 Science, Cochrane Library, OpenGrey, NHS Digital Department of Health Office for National
14 Statistics, BBC News, Bielefeld Academic Search Engine (BASE), E-thesis Online Service (EThOS)
15 and Conference proceedings through Web of Science for studies from database inception to May 2019.
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18 Search terms summarised in *(Table S1; supplementary material)* included a comprehensive list of
19 synonyms and multiple Boolean operators relating to: i) paediatric ii) medication error including dosing
20 error, medication administration error, medication safety and medication optimisation and iii) health
21 literacy. (D.D.) further did reference tracking of all included studies to identify any potential studies to
22 be included in the review.
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33 **Study selection**

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35 Two reviewers (D.D., Z.S.) independently evaluated each study for eligibility to reduce bias using the
36 inclusion criteria above. The titles and/or abstracts of all identified studies were reviewed
37 independently, and full manuscripts that appeared to potentially relevant. The reference lists of the final
38 included studies were hand searched by one reviewer (D.D.) for potentially appropriate studies.
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46 **Data extraction process and synthesis**

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48 Two reviewers (D.D. and Z.S.) independently extracted data using a standardised predefined
49 spreadsheet. Inconsistencies in extracted data were resolved through consensus discussion by a third
50 reviewer, if necessary. Results were synthesised and summarised according to analytical themes.
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56 **Quality appraisal**

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3 The quality of the included papers was independently assessed by two reviewers (D.D., Z.S.) using
4 Critical Appraisal Skills Programme (CASP) checklists.⁽¹⁰⁾ Discrepancies were resolved through
5 discussion and consensus.
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10 RESULTS

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13 A total of 374 citations were retrieved from the database and other searches. After screening titles and
14 abstracts, 31 publications were obtained in full text and assessed for suitability. Overall, 12 publications
15 were included in the analysis (*See Figure 1*).⁽¹¹⁻²²⁾
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20 The details of the 12 studies are presented in (*Table S2, Supplementary material*).⁽¹¹⁻²²⁾ The majority
21 of the included studies were published in the last 12 years. All of the studies (n=12) took place in the
22 United States of America.⁽¹¹⁻²²⁾
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27 Overall, nine studies recruited parents or caregivers of children aged between 30 days to less than 9
28 years old, two studies had recruited parents with no age limitations of the child and one study recruited
29 only women of childbearing age. The majority of the studies (n=10) did report the ethnic composition
30 of their recruited sample and they were vastly Hispanic or black African American parents or caregivers.
31 One study had only exclusively recruited women from a white ethnic background.⁽¹⁸⁾ One study did
32 not report ethnicity of the recruited sample.⁽¹⁴⁾
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40 Quality appraisal

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42 The results from the quality appraisal are shown in *Table 1* and *Table 2*. All identified studies were
43 included in the final synthesis with a greater emphasis to the higher quality studies.
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48 Synthesis of results

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50 The data from the 12 studies were analysed and three analytical themes emerged from the synthesis and
51 a summary of the review synthesis are demonstrated in (*Figure 2*).
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Types and causes of medication administration errors among children lead by parents or child outside a clinical setting:

Eight of the included studies indicated that paediatric dosing errors are among the most common medication errors made by parents. ^(11, 14-17, 19, 20, 22) Among these studies, two randomised trials identified that overdosing errors are common in these studies; parents were randomly assigned to measure a certain amount of doses. ^(19, 20) While another cross sectional study tested parents whom have a child on a short course prescribed medication has reported that the majority of the parents measured below the prescribed dose. ⁽¹¹⁾ A study by Morrison *et al.* reported that parents who made under-dosing errors made more dosage errors and frequency errors compared to those who made an overdosing error. ⁽¹⁶⁾

From the included studies, it was noticed that the magnitude and frequency of dosing errors by parents are influenced by various factors. The measurement tool used by parents and the dose amount was one factor. In one study, parents stated that non-standardised kitchen spoon is their primary dosing tool ⁽¹³⁾. Two studies reported that errors were more common with cups than with syringes, particularly with smaller dose amounts. ^(17, 20) Another study reported that cups with printed marking or etched markings were more likely to be associated with overdosing. ⁽¹²⁾ Labels and units of the prescribed medication were contributing factors to dosing errors. Parents made significant dosing errors when the units found on the medication bottle label were not similar to the units used on the dosing tool. ⁽²⁰⁾ Parents who use teaspoon/tablespoon units were likely to use a non-standardised dosing instrument and make errors in measuring the prescribed and intended dose. ⁽¹⁵⁾ Final potential factor was the type of instructions provided. For liquid medication, less error were seen among parents who were provided with text-plus-pictogram instructions 43.9% compared to text-only instructions 59.0% and this group were also less likely to make an overdosing errors. ⁽²²⁾ Parents who received a standard medication counselling were 47.8% more likely to make dosing errors when compared to parents who received pictogram instruction (5.4%). ⁽²¹⁾

Factors related to patients or caregivers and medication errors

Health literacy

1
2
3 Health literacy of caregivers in the studies were assessed, six conducted further analyses of its influence
4 on dose accuracy and other co-factors related to medication errors. Yin *et al.* reported that caregivers
5 with inadequate or marginal health literacy were more likely to use a non-standardised dosing
6 instrument and further lacked knowledge on weight based dosing for over the counter medication when
7 compared to caregivers with adequate health literacy. ⁽¹³⁾ In another study by Yin *et al.*, they found a
8 significant association between health literacy and dosing errors using cups and dosing spoons. ⁽¹²⁾ The
9 use of a teaspoon/tablespoon was associated with errors in the intended dose for those with low Health
10 Literacy but not for those with adequate Health Literacy. ⁽¹⁵⁾ Harris et al. identified that parents with
11 limited health literacy and Limited English Proficiency (LEP) made the most dosing errors. ⁽¹⁷⁾
12 Similarly, Kalow *et al.* revealed that parents with inadequate and marginal health literacy committed
13 dosing errors, but the sample size of this group was small compared to the adequate health literacy
14 group. ⁽¹⁴⁾

31 *Language*

32 Association between health literacy and lack of knowledge of weight-based dosing varied by
33 caregiver's language. For English speaking caregivers 88.6% of inadequate or marginal health literacy
34 caregivers were unaware of weight based dosing in comparison to 54.1% of caregivers with adequate
35 health literacy, but there was no association seen for Spanish speaking caregivers. ⁽¹³⁾ In contrast, Yin
36 found that there is no significant relation between dosing error and (LEP). ⁽²²⁾ However, there were some
37 differences in teaspoon-associated errors in measurement by language. ⁽¹⁵⁾

47 *Comprehension and recall of instructions in relation to parent sociodemographic status*

48 Yin *et al.* reported that parents from a low sociodemographic status who were prescribed daily dose and
49 who received a simple language, pictogram instructions sheets, were less likely to make errors in
50 knowledge of dose frequency and dose accuracy compared to the control group who received standard
51 medication counselling (0% vs 15.1%). ⁽²¹⁾ Participants among the interventional group were less likely
52 to report incorrect medication preparation related to shaking the medication before administration for
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3 both daily doses (10.9% vs 28.3% $P= .04$) and as needed medication (21.5% vs 43.0%). Participants in
4 the interventional group were less likely to use a non-standardised measurement tool compared with
5 the parents in the standard group (daily dose: 93.5% vs 71.7%; as needed: 93.7% vs 74.7%).⁽²¹⁾
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10 **Interventions aimed at reducing medication administration errors occurring among children** 11 **outside a clinical setting**

12 *Parent's sociodemographic factors*

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15 Four studies suggested that parental sociodemographic risk factors should be considered when
16 designing an intervention aimed at averting medication administration errors.^(12, 13, 17, 22) Amongst these
17 factors are parents' health literacy as well as language. Kalow and his colleagues suggested that efforts
18 to streamline interpreter services must be continued as well as, to having a more formalised approach
19 in place to elucidate the patient's preferred language for communication.⁽¹⁴⁾
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29 *Counselling and training*

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31 Three studies suggested that provisional dose counselling in combination with verbal counselling could
32 be associated with less dosing errors.^(11, 13, 19) A by Yin *et al.* indicated that errors occur across different
33 counselling approaches, and they urged for developing new strategies to ensure parent understanding
34 of medicine instructions as well as suggesting the need for further research to identify the best advance
35 counselling strategies and how to incorporate these within clinical practice.⁽¹¹⁾ Yin *et al.* suggested the
36 need for intensive teaching, training and coaching programmes that can accommodate for different
37 parental health literacy levels.⁽²⁰⁾
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47 *Tools, labels and instructions*

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49 Yin *et al.* suggested a promising strategy that can help to reduce paediatric-dosing errors, which is to
50 match the dosing tool with the prescribed dose volume and move towards more simplified numerical
51 markings on the measurement tools as well as to move to millilitre-only units.^(20, 22) Wallace *et al.*
52 indicated in his study that 5.7% of the parents would prefer instructions with explicit dosage intervals
53 with the exact time and dose to be specified on the label.⁽¹⁸⁾ Harris *et al.* suggested improving the
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3 availability of language concordant labels that could accommodate for different health literacy levels.

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5 (17) Three studies from this review strongly suggested the importance of utilising pictographic dosing
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7 instructions and how it could be a positive aid in reducing paediatric dosing errors. (19, 21, 22)
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10 **DISCUSSION**

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13 The results of this study suggest that parents appear to make a range of medication errors, particularly
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15 with liquid medications as documented by prior studies as well as studies from this review. (19, 21, 23,

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17 24) The majority of the included studies indicated that dosing errors are amongst the most common
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19 medication errors made by parents, which is consistent with other studies. (11, 15, 17, 21, 25) This review
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21 identified possible causality reasons behind parents dosing errors; these errors could be linked to the:
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23 dose amount prescribed, measurement tools used, units used on the labels and the instructions provided.
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27 Although standardised measurement tools are usually dispensed with the prescribed liquid medications
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29 in the UK, this review identified that the studies published in the USA indicated that parents still use
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31 non-standardised liquid dosing tools as their primary measuring tool; this has been linked with
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33 medication administration errors. (26, 27) Pairing the medication labels to the closest measurement tool
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35 size, particularly for millilitre-only labels and tools, could be potentially associated with a reduction in
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37 parent dosing and administrating error rates, as well as a decrease in the likelihood of parents using
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39 non-standardised measurement tools. (15, 20)
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43 The review showed that the use of simple pictographic based medication instructions with explicit
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45 dosage intervals could reduce dosing errors by parents. This finding was consistent with previous
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47 existing data regarding the use of pictographic illustrations as a supportive tool to aid parents in
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49 administering medication to their children correctly. (28-36) This further could be helpful for parents or
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51 caregivers with limited or low health literacy levels.
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54 Our findings are consistent with prior studies investigating the link between parent's sociodemographic
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56 factors, particularly health literacy, and child medication administration problems. (37-40) Four studies
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58 explicitly highlighted that sociodemographic factors, such as health literacy and language, must be
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60 incorporated into any future intervention that aims to reduce parental dosing and administration errors.

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3 The results of the review highlighted several interventions to aid parents and patients to potentially
4 reduce medication administration errors at home. This include the use of plain language combined with
5 provision of using the dosing tool provided as well as incorporating pictographic instructions which
6 were consistent in four of the included studies. ^(11, 19, 21, 22) Pictographic-plain instructions significantly
7 improve the accuracy of dosing and administering medication to children especially for those parents
8 with insufficient health literacy. ^(21, 22)

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11 The study emphasised potential areas that could be incorporated into real practice that can help with
12 reducing medication administration errors done by parents/caregivers and patients. Potential strategies
13 include personalised training and coaching that accommodate different health literacy levels and
14 languages as well as the possibility to match the dosing tool with the prescribed volume alongside the
15 use of millilitre units.

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18 This systematic review was designed by interdisciplinary paediatric expertise in the pharmaceuticals and
19 pharmacy practice field. The review was registered on PROSPRO and conducted using PRISMA
20 checklist. However, we found that our review is subject to several limitations. First, our search strategy
21 was designed to be comprehensive, but it is possible that some studies were missed. Second, English
22 and published studies were only included in this review, so publication bias may be exist. Finally, the
23 generalisability of the study results is low due to that the majority of the studies were conducted in the
24 USA and emerged from the same research group Yin *et al.* For this particular research group they have
25 highlighted in their studies several limitations such as the use of hypothetical scenarios that might not
26 be a true reflection on how parents dose at home^(12, 19, 20, 22). For some randomised trial studies, it was
27 difficult to maintain blindness as some of the participants revealed their allocated group, while for the
28 cross sectional studies, no conclusion of the causes could be drawn ^(11, 13, 15, 21).

51 **Conclusions**

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54 The relationship between medication administration errors and problems experienced by and parents
55 outside a clinical setting has not been well described from the literature with no relevant studies
56 examining the issue outside the USA. The studies explored the relation of dosing errors and parent's
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3 understanding, interpretation of administration instructions and tools to help them administer their
4 medication either by the manufacturer or other supplier, health literacy as well as other
5 sociodemographic factors. Due to the gap in the knowledge outside of the USA and the heterogeneity
6 of healthcare provision worldwide, future studies, need to focus on the current medication
7 administration problems among children and young people happening outside a clinical setting, in the
8 UK and worldwide see *(Table S3, Supplementary material)*.

16 **No grant/award information in the Funding information**

17
18
19 This study was not funded. It's done as part of the author (DD) PhD research project.

20 **What is known about this topic?**

- 21 1- Medication administration errors occur frequently among children.
- 22 2- Parent's health literacy could be associated with medication administration problems in
23 children.
- 24 3- Studies examining parent administrator paediatric medicine accuracy were mainly from one
25 particular research group in the USA with participant parents using non-standardised
26 measuring tools

27 **What this study adds:**

- 28 1- The nature of medication administration errors happening at home are not well documented
29 across each age group especially in the UK.
- 30 2- The need to explore parents and patients perspective in regards medication administration
31 challenges happening at home.

Table 1: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Randomised Controlled Trials Research Checklist.⁽¹⁰⁾

CASP Question Number	Authors and date					
	Yin (2017) ⁽¹⁹⁾	Harris et al. (2017) ⁽¹⁷⁾	Shonna Yin et al. (2016) ⁽²⁰⁾	Yin et al. (2008) ⁽²¹⁾	Yin et al. (2011) ⁽²²⁾	Wallace et al. (2012) ⁽¹⁸⁾
1. Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the assignment of patients to treatments randomised?	Yes	Yes	Yes	Yes	Yes	Yes
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes	Yes	Yes	Yes	Yes	Yes
4. Were patients, health workers and study personnel 'blind' to treatment?	No	No	No	No	No	No
5. Were the groups similar at the start of the trial	Yes	Can't Tell	Yes	Yes	Yes	Yes
6. Aside from the experimental intervention, were the groups treated equally?	No	Yes	Yes	Yes	Yes	Yes
7. How large was the treatment effect? ^a	Yes	Uncertain	Yes	Yes	Yes	Uncertain

8.	How precise was the estimate of the treatment effect? ^b	Yes	Yes	Yes	Yes	Yes	Yes
9.	Can the results be applied to the local population, or in your context?	No	No	No	No	No	No
10.	Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes	Yes	Yes
11.	Are the benefits worth the harms and costs?	Yes	Yes	Yes	Yes	Yes	Yes

^a Based on the power calculation of the sample size and the primary outcomes results stated clearly.

^b Based on the extract ρ value and CI value of the primary outcome.

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Table 2: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist. ⁽¹⁰⁾

CASP Question Number	Authors and date					
	Morrison et al. (2017) ⁽¹⁶⁾	Shonna Yin et al. (2014) ⁽¹⁵⁾	Samuels-Kalow et al. (2013) ⁽¹⁴⁾	Yin et al. (2007) ⁽¹³⁾	Yin et al. (2010) ⁽¹²⁾	Yin et al. (2014) ⁽¹¹⁾
1. Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes
2. Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the data collected in a way that addressed the research issues?	Yes	Yes	Yes	Yes	Yes	Yes
6. Has the relationship between researcher and participants been adequately considered?	Can't Tell	Can't Tell	Yes	Yes	Yes	Can't Tell
7. Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes	Yes	Yes

8. Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Yes	Yes	Yes
9. Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes
10. Value of the research?	Yes	Yes	Yes	Yes	Yes	Yes

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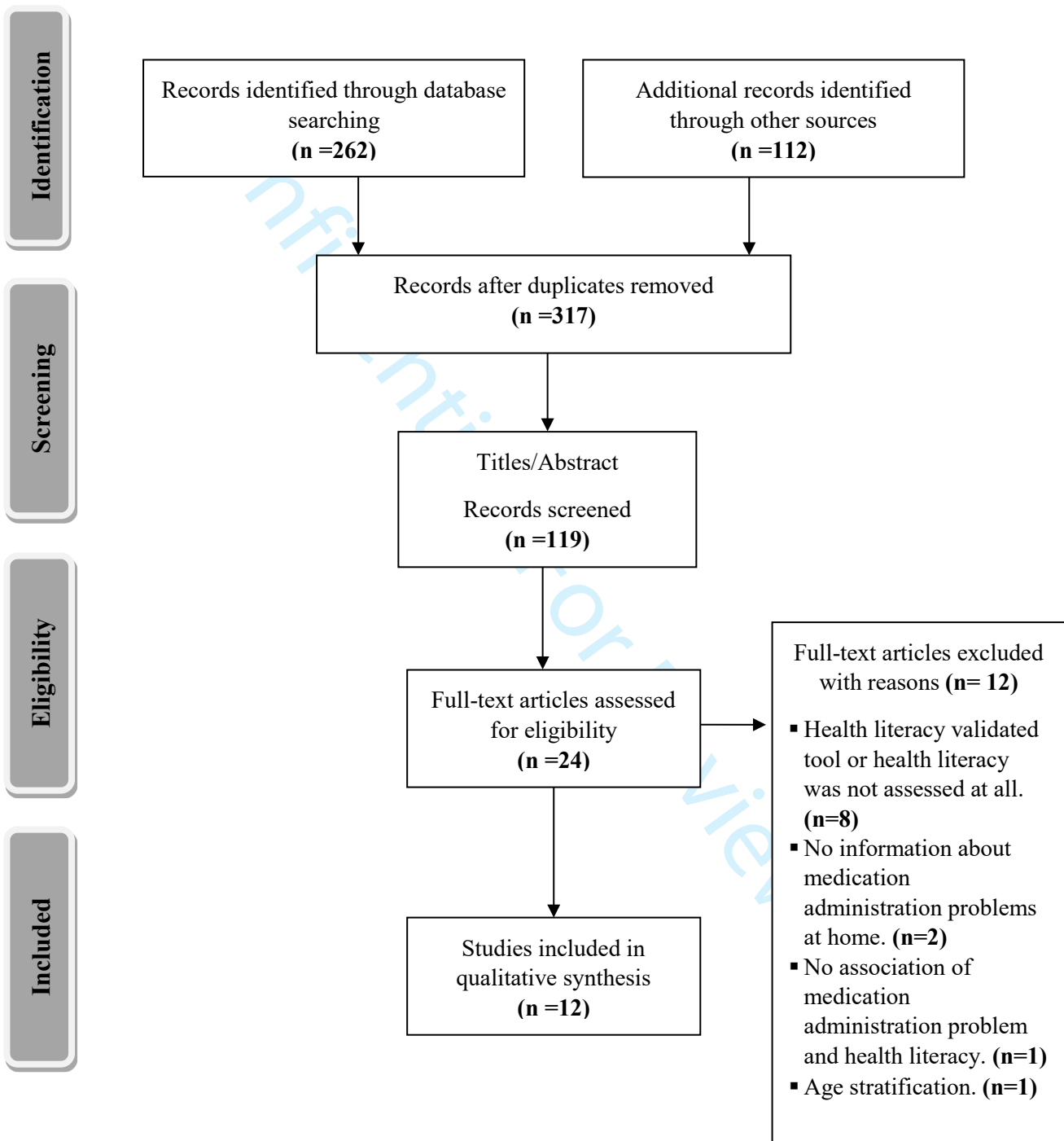
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Figure 1: Flow diagram for the study selection based on PRISMA flow diagram



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Figure 2: list of the review results

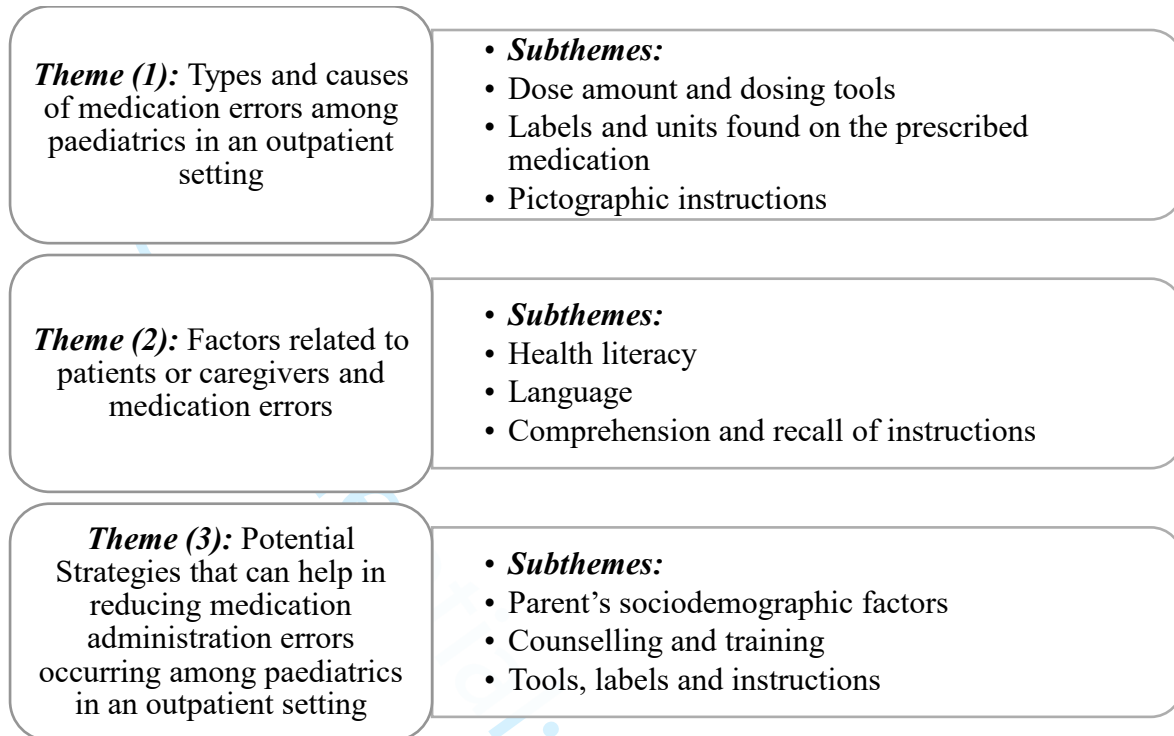


Table S1: Search Strategy for Systematic Review per database

Database	Search strategy
1- PubMed	<p>1- (((child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or teenager* or youth or infant* or newborn* or neonate*))) AND</p> <p>2- (("medical error*" or "medication error*" or "medication administration error*" or "drug administration error*" or "medicine administration error*" or "medication safety" or "optimisation" or "optimization" or "dosing error*")) AND</p> <p>3- (("health literacy" or "literacy" or "literate").</p>
4- Scopus	<p>1- (child OR children OR pediatric* OR paediatric* OR toddler* OR adolescent* OR baby OR babies OR teen* OR teenager* OR youth OR infant* OR newborn* OR neonate*) AND</p> <p>2- (health AND literacy OR literacy OR literate) AND</p> <p>3- (medical AND error* OR medication AND error* OR medication AND administration AND error* OR drug AND administration AND error* OR medicine AND administration AND error* OR medication AND safety OR optimisation OR optimization OR dosing AND error*)</p>
5- Web of Science	<p>1- TOPIC: (child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or youth* or infant* or newborn* or neonate*) <i>AND</i></p> <p>2- TOPIC: ("health literacy" or "literacy" or "literate") <i>AND</i></p> <p>3- TOPIC: ("medical error*" or "medication error*" or "medication safety" or "medication administration error*" or "medicine administration error*" or "drug administration error*" or "dosing error*" or "optimisation" or "optimization")</p>
6- Cochrane Library	<p>1- "health literacy" or "literacy" or "literate" in Title Abstract Keyword AND</p> <p>2- "medication error" or "medical error" or "medication administration error" or "medicine administration error" or "drug administration error" or "dosing error" or "medication safety" or "optimisation" or "optimization" in Title Abstract Keyword AND</p> <p>3- child or children or pediatric or paediatric or toddler or adolescent or baby or babies or teen or teenager or youth or infant or newborn or neonate in Title Abstract Keyword - (Word variations have been searched)</p>

Table S2: Characteristics of included studies (listed alphabetically according to first author).

Citation Characteristics			Study Information		Participants Characteristics			Theme driven from the study	Findings
First Author (Year)	Country of Origin	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps	
Harris et al. (2017) ⁽¹⁷⁾	United States of America	Outpatient	Randomized Controlled Experiment	To examine the association between health literacy and limited English proficiency and liquid medication dosing errors in Hispanic parents	Hispanic parents of children <8 years old.	1126 parents	Newest Vital Sign (NVS)	Dosing errors among the common problems done by parents.	70% of the recruited parents had LEP, 82.7% had limited literacy. Of parents who had LEP 88.8% had limited and 11.2% adequate health literacy. 83.1% of parents made a dosing error at least one out of the nine dosing trials. Parents with limited health literacy and with LEP made the most dosing error and errors varied by dose amount and tool type.
Morrison et al. (2017) ⁽¹⁶⁾	United States	Outpatient clinic and	Interviews and applied assessment	To examine the association between parent	Parents of children 1	100	Newest Vital Sign (NVS)	Dosing errors among the common	Parents with low health literacy made more under

	of America	emergency department		health literacy and pain medication knowledge and applied skills in parents of children with sickle cell disease.	to 12 years old.			problems done by parents.	dose frequency errors on the pain treatment skills. Health literacy was not associated with errors on the applied treatment skills. Parents recalled under-dosing of medication (both dose and frequency). On the applied pain treatment skills, parents made both underdoing and overdosing errors.
Samuels-Kalow et al. (2013) ⁽¹⁴⁾	United States of America	Tertiary	Prospective observational	To examine language-based disparities in discharge communication and parental understanding of discharge instructions.	Parents of children 2 to 24 months.	145	Short Test of Functional Health Literacy (S-TOFHLA)	Dosing errors among the common problems done by parents.	Parents had acetaminophen dosing errors. There is significant association between language and dosing errors. Parents with marginal or inadequate health literacy had dosing errors compared with adequate health literacy.

Shonna Yin et al. (2014) ⁽¹⁵⁾	United States of America	Emergency department	Interviews and observations	To examine the association between unit used and parent medication errors and whether nonstandard instruments mediate the relationship.	Parents of children aged <9 years old.	400	Short Test of Functional Health Literacy in Adults (S-TOFHLA)		Parents made different kind of error in measurement. 1 in 6 parents used kitchen spoon rather than a standard instrument. Parents did not use the unit listed on the prescription or label.
Shonna Yin et al. (2016) ⁽²⁰⁾	United States of America	Pediatric clinic	Randomized controlled experiment	Hypothesized that unit concordance would be associated with fewer errors and that parents would measure most accurately with syringes we also sought to examine differences in impact by parents health literacy and language because low health literacy and limited English	Parents of children aged ≤ 8 years old.	2099 parents	Newest Vital Sign (NVS)		Nearly all parents (99.3%) measured ≥ 1 dose that was not the exact amount. Overdoing (68.0%) was the majority of the errors. Dose amount of 2.5 and 7.5 mL was associated with more errors when compared with 5 mL (2.5 vs 5 mL adjusted odds ratio [aOR]=4.2; 95% CI, 3.8-4.6; 7.5 vs 5 mL [aOR]=1.4; 95% CI, 1.2-1.5).

				proficiency are factors known to place children at risk for errors.				
Wallace et al. (2012) ⁽¹⁸⁾	United States of America	Outpatient clinic	Randomized Controlled Trial	To address the gap by addressing whether instructions wording that implicit versus explicit dosage intervals was associated with participant's ability to describe and correctly measure a dose of a commonly prescribed liquid pediatric prescription medication.	Women of childbearing age.	193	<p>Estimated using three established items:</p> <ul style="list-style-type: none"> -How often do you have problems learning about your medical condition because of difficulty understanding written information? - How often do you have someone help you read hospital materials? - How confident are you filling out medical 	One third of the participants (32.1%) were able to describe and measure the dose accurately. Participants with inadequate health literacy skills were one third as likely to measure a dose of the medication correctly.

							forms by yourself?		
Yin et al. (2007) ⁽¹³⁾	United States of America	Pediatric emergency department.	Interviews	To assess whether low caregiver health literacy was related to risk factors for liquid medication dosing errors, including reported use of non-standardised dosing tools and lack of knowledge about weight based dosing.	Parents and caregivers of children aged between 30 days to 8 years old.	292	Test of Functional Health Literacy in Adults (TOFHLA)	Dosing errors among the common problems done by parents.	Low health literacy, particularly reading comprehension, was associated with reported use of non-standardised dosing instruments and lack of knowledge regarding weight based dosing. In addition, this has been found previously to be associated with decreased dosing accuracy.
Yin et al. (2014) ⁽¹¹⁾	United States of America	Paediatric emergency department	Interviews and observations	To examine the degree to which recommended provider-counselling strategies, including advanced communication techniques and dosing instruments	Parents of children aged < 8 years old.	287	Short Test of Functional Health Literacy (S-TOFHLA)	Dosing errors among the common problems done by parents.	Majority of the patents made underdoing errors as well as few made overdosing errors. Recipient of at least one advanced counselling were less likely to make a dosing error compared to those who did not report

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				provision, are associated with reductions in parents liquid medication dosing errors.					received advanced counselling. Parent who received dosing instrument from the emergency department made fewer errors. For adequate health literacy levels was significantly associated with fewer errors when they have received advanced counselling in combination with instrument provision but not the low literacy.
Yin et al. (2008) ⁽²¹⁾	United States of America	Pediatric emergency department	Randomized Controlled Trial	To evaluate the efficacy of a pictogram based health literacy intervention to decrease liquid medication administration errors by caregivers of young children.	Parents and caregivers of children aged 30 days to 8 years.	245	Test of Functional Health Literacy in Adults (TOFHLA)		Caregiver's dose accuracy was higher among the intervention group prescribed daily and as needed medications regardless of the cut-off point was 20% or 40%. 5.4% of the intervention caregivers whose children had been

									prescribed daily doses gave inaccurate dose at the 20% cut-off point, compared with 47.8% of control caregivers. The study suggested that there is no health literacy association with the dosing errors.
Yin et al. (2011) ⁽²²⁾	United States of America	Outpatient pediatric clinic	Randomized Controlled Trial	To sought whether a pictographic dosing diagram included as part of written instructions can decrease parent errors in dosing infant acetaminophen as well as whether pictogram benefit varies by parent health literacy level.	Parents or caregiver of a child with no specific age limitation.	299 parents were assessed	Newest Vital Sign (NVS)		Both groups were associated with poor dosing with the tendency for the parents who have received text plus pictogram significantly less likely to make dosing error (0.6%) compared to parents who received text only instructions (5.6%). Parents with low literacy who received the text plus pictogram instructions were significantly less likely to make

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									errors in dosing compared who received text only instructions(50.4% vs 66.4%; $P=.02$).
Yin et al. (2010) ⁽¹²⁾	United States of America	Pediatric clinic	Observational	To assess parents' liquid medication administration errors by dosing instrument type and to examine the degree to which parents' health literacy influences dosing accuracy.	Parents of children with no specific age limitation.	302(287 mothers, 8 fathers, 7 legal guardians)	Newest Vital Sign (NVS)	Dosing errors among the common problems done by parents.	Health literacy was significantly related to doing errors with the cups as well as the dosing spoon, while non-significant trend was seen for the dropper and the oral syringes with the bottle adaptor.
Yin et al. (2017) ⁽¹⁹⁾	United States of America	Pediatric outpatient clinic	Randomized controlled experiment	To examine the degree to which errors could be reduced with pictographic diagrams, millilitre-only units, and provision of tools more closely matched to prescribed volumes	Parents of children aged ≤ 8 years old.	2099 for all arms	Newest Vital Sign (NVS)	Dosing errors among the common problems done by parents.	Majority of the parents (99.3%) made dosing errors. More errors with the 2 and 7.5 mL dosing amount when compared with the 10 mL (2mL vs 10 mL aOR =3.7; 7.5 mL vs 10 mL aOR= 1.4). Parents who received text and pictogram dosing

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									instructions with mL only labels and tools had decreased odds of making a dosing error compared to received mL/tsp labels and tools with or without pictographic dosing instructions.
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Table S3: Key findings per study in relation to the aims of the study

First Author (Year)	Key Findings derived from the included studies
Harris et al. (2017) ⁽¹⁷⁾	<ul style="list-style-type: none"> - The magnitude and frequency of dosing errors varied by measurement tool and dose amount. - The link of health literacy levels as well as language and dosing errors. - Parent's sociodemographic need to be considered when designing an intervention aiming at reducing medication administration errors. - Suggested to have language concordant labels that could accommodate for different health literacy levels.
Morrison et al. (2017) ⁽¹⁶⁾	<ul style="list-style-type: none"> - Under-dosing errors made more dosage errors and frequency errors compared to those who made an overdosing error.
Samuels-Kalow et al. (2013) ⁽¹⁴⁾	<ul style="list-style-type: none"> - The link of health literacy levels and dosing errors. - Parent's sociodemographic need to be considered when designing an intervention aiming at reducing medication administration errors such as asking the parents what would be the preferred language for communication.
Shonna Yin et al. (2014) ⁽¹⁵⁾	<ul style="list-style-type: none"> - The magnitude and frequency of dosing errors varied by measurement tool. - The link between dosing errors and health literacy with the measurement tools. - The link between teaspoon measurement associated error by language
Shonna Yin et al. (2016) ⁽²⁰⁾	<ul style="list-style-type: none"> - The magnitude and frequency of the dosing errors varies by dose amount. - Labels and units found on the prescribed medication - There is a need for an Intensive teaching programme that can accommodate for different parental health literacy levels. - Suggested some potential solution to reduce paediatric-dosing errors.
Wallace et al. (2012) ⁽¹⁸⁾	<ul style="list-style-type: none"> - Provided potential suggestions to reduce dosing errors done parents, such as providing explicit dosing intervals with the exact time and dose on the label.

Yin et al. (2007) ⁽¹³⁾	<ul style="list-style-type: none"> - The magnitude and frequency of the dosing errors varies by measurement tool. - Association between health literacy and lack of knowledge of weight-based dosing varied by caregiver's language. - Parent's sociodemographic need to be considered when designing an intervention aiming at reducing medication administration errors. - Provisional dose counselling in combination with verbal counselling could be associated with less dosing errors.
Yin et al. (2014) ⁽¹¹⁾	<ul style="list-style-type: none"> - Provisional dose counselling in combination with verbal counselling could be associated with less dosing errors.
Yin et al. (2008) ⁽²¹⁾	<ul style="list-style-type: none"> - The type of instructions provided and dosing errors. - For parents from a low sociodemographic background less errors were seen when simple language along with pictures of how to administer was provide. - Suggested that using a pictographic instruction could be a solution to reduce paediatric-dosing errors.
Yin et al. (2011) ⁽²²⁾	<ul style="list-style-type: none"> - The type of instructions provided and dosing errors. - Parent's sociodemographic need to be considered when designing an intervention aiming at reducing medication administration errors. - Suggested some potential solution to reduce paediatric-dosing errors. - Suggested that using a pictographic instruction could be a solution to reduce paediatric-dosing errors.
Yin et al. (2010) ⁽¹²⁾	<ul style="list-style-type: none"> - The magnitude and frequency of the dosing errors varies by measurement tool. - The link between dosing errors and health literacy with the measurement tools. - Parent's sociodemographic need to be considered when designing an intervention aiming at reducing medication administration errors.
Yin et al. (2017) ⁽¹⁹⁾	<ul style="list-style-type: none"> - Provisional dose counselling in combination with verbal counselling could be associated with less dosing errors. - Suggested that using a pictographic instruction could be a solution to reduce paediatric-dosing errors.

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A Literature review of medication administration problems in paediatrics by parent/caregiver and the role of health literacy

Dania Dahmash, MSc, Aston University, Aston Pharmacy School

Zakia Shariff, MPharm, Aston University, Aston Pharmacy School

Dr. Daniel Kirby, PhD, Aston Pharmacy School

Dr. David Terry, PhD, Aston Pharmacy School

Dr. Chi Huynh, PhD, Aston Pharmacy School

Corresponding author;

Dr. Chi Huynh, c.huynh3@aston.ac.uk, Work: - 0121 204 3231

List of key words not in the title;

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Dr. Chi Huynh, PhD, Aston University, Birmingham, United Kingdom, E-mail: c.huynh3@aston.ac.uk.

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ABSTRACT

Objective: To review all published evidence related to paediatric medication administration problems by parents who administer the medication to their children aged 0 to 16 years, as well as medication administration related issues by young persons aged 16 and above who take their own medication at home. To identify parental sociodemographic characteristics such as health literacy and its association with medication administration problems.

Study design: Ten electronic databases were systematically searched and supplemented by hand searching through reference lists using the following search terms: i) paediatric ii) medication error including dosing error, medication administration error, medication safety and medication optimisation and iii) health literacy.

Results: Of the (1,230) records screened, fourteen studies were eligible for inclusion. Three analytical themes emerged from the synthesis. The review highlighted that frequencies and magnitudes of dosing errors varies by the measurement tools used, the dose prescribed and by the administration instruction provided. Parent's sociodemographic; such as health literacy and language, is a key factor to be considered when designing an intervention aimed at averting medication administration errors at home. The review summarised some potential strategies that could help in reducing medication administration errors among children at home. Among these recommendations is to show the prescribed dose to the parents or young people along with the verbal instructions, as well as to match the prescribed dose with the measuring tool dispensed, to provide an explicit dose intervals and pictographic dosing instructions.

Conclusion: The findings suggest that in order to optimise medication use by parents, further work is needed to address the nature these issues at home. Counselling, medication administration instructions and measurement tools are some of the areas in addition to the sociodemographic characteristics of parents and young people need to be considered when designing any future potential intervention aimed at reducing medication errors among children and young people at home.

1 INTRODUCTION

2 When it comes to medication care for children at home, there is a significant burden of responsibility
3 for the parent, caregiver or patient themselves (older children).⁽¹⁾ It's been documented that medication
4 administration among children are well known to occur⁽²⁾. In previous studies it have recognised that
5 more than 40% of parents and caregivers make dosing errors in an outpatient setting. ^(3, 4) The inability
6 to administer medication correctly may result in adverse drug events and poor patient clinical
7 outcomes.⁽⁵⁾ Causes of medication administration problems at home are multifactorial and potentially
8 depends on various factors. ⁽²⁾ So in order to improve medication administration by parents and patients,
9 an initial assessment of the current problems and factors that may contribute to this issue must be
10 identified first.

11 Previous studies have identified potential factors that can contribute to clinician led medication
12 administration errors in children, but there have been no studies recording both the types and risk factors
13 that can contribute towards caregiver's medication administration problems as well as young people. ⁽⁶⁾
14 ⁷⁾ According to the European Health Literacy Survey (HLS-EU), conducted across eight different
15 countries, the prevalence of low health literacy levels varies from 29% to 62%.^(8, 9)

16 In this study, we aimed at reviewing studies that highlighted medication administration problems
17 experienced by parents or children, which also used a validated health literacy test to assess for parent
18 health literacy levels. In this systematic review, the common medication administration problems
19 occurring at home as well as the potential causalities and risk factors that further contribute to these
20 medication administration errors have been highlighted.

21 METHODS

22 This review was conducted in accordance with the Cochrane Handbook for Systematic Reviews, and
23 followed PRISMA reporting guidelines ^(10, 11) The review protocol is registered on PROSPERO (ID:
24 CRD42018091590).

25 Patient and Public Involvement

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2
3 26 There is no patient and public involved in the design, or conduct, or reporting, or dissemination of this
4
5 27 review.
6
7

8 28 **Eligibility Criteria**

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11 29 Studies were eligible for inclusion if they are related to medication errors among children and adolescent
12
13 30 between the ages of 0 to 18 years old as per the World Health Organisation definition of population age
14
15 31 group. This includes studies reporting medication related problems outside clinical setting; where the
16
17 32 parent or the child is responsible in administering or taking the medication. Studies must have assessed
18
19 33 the health literacy levels of the participants using a validated health literacy assessment tool. There were
20
21 34 no restrictions on the date of publication, only English language articles studies where included.
22
23

24 35 **Search Strategy**

25

26
27 36 The search strategy was designed initially by the research team and verified by an information specialist
28
29 37 using the Population, Intervention, Comparison and Outcomes (PICO) model. The reviewer (D.D.)
30
31 38 systematically searched PubMed, Scopus, Web of Science, Cochrane Library, OpenGrey, NHS Digital
32
33 39 Department of Health Office for National Statistics, BBC News, Bielefeld Academic Search Engine
34
35 40 (BASE), E-thesis Online Service (EThOS) and Conference proceedings through Web of Science for
36
37 41 studies from database inception to September 2020.
38
39

40
41 42 Search terms summarised in *(Table S1; supplementary material)* included a comprehensive list of
42
43 43 synonyms and multiple Boolean operators relating to: i) paediatric ii) medication error including dosing
44
45 44 error, medication administration error, medication safety and medication optimisation and iii) health
46
47 45 literacy. (D.D.) further performed reference tracking of all included studies to identify any potential
48
49 46 studies to be included in the review.
50

51 47 **Study selection**

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54
55 48 Two reviewers (D.D., Z.S.) independently evaluated each study for eligibility to reduce bias using the
56
57 49 inclusion criteria above. The titles and/or abstracts of all identified studies were reviewed
58
59 50 independently, and full manuscripts that appeared to potentially relevant.
60

51 **Data extraction process and synthesis**

52 Two reviewers (D.D. and Z.S.) independently extracted data using a standardised predefined
53 spreadsheet. Inconsistencies in extracted data were resolved through consensus discussion by a third
54 reviewer (C.H.), if necessary. Results were synthesised and summarised according to analytical themes.
55 Thematic analysis was opted by the research team as it's known for its flexibility and ability of
56 identifying patterns of meaningful information within the data. ⁽¹²⁾

57 **Quality appraisal**

58 The quality of the included papers was independently assessed by two reviewers (D.D., Z.S.) using
59 Critical Appraisal Skills Programme (CASP) checklists.^(13, 14) Discrepancies were resolved through
60 discussion and consensus.

27 **RESULTS**

61 A total of 672 citations were retrieved from the database and other searches. After screening titles and
62 abstracts, 38 publications were obtained in full text and assessed for suitability. Overall, 14 publications
63 were included in the analysis (*See Figure 1 for PRISMA flow chart*).⁽¹⁵⁻²⁸⁾ all reasons for excluded
64 studies at the full text stage are summarised in (*Table S2*).

65 The details of the 14 studies are presented in (*Table S3 and S4*).⁽¹⁵⁻²⁸⁾ The majority of the included
66 studies were published in the last 12 years. All of the studies (n=14) took place in the United States of
67 America.

68 Overall, eleven studies recruited parents or caregivers of children aged between 30 days to less than 9
69 years old, two studies had recruited parents with no age limitations of the child and one study recruited
70 only women of childbearing age. The majority of the studies (n=13) did report the ethnic composition
71 of their recruited sample and they were vastly Hispanic or black African American parents or caregivers.
72 One study had only exclusively recruited women from a white ethnic background. ⁽²²⁾

58 **Quality appraisal**

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2
3 74 The results from the quality appraisal are shown in (*Table 1 and Table 2*). All identified studies were
4
5 75 included in the final synthesis with a greater emphasis to the higher quality studies.
6
7

8 76 **Synthesis of results**

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10
11 77 The data from the 14 studies were analysed and three analytical themes emerged from the analysis and
12
13 78 a summary of the review results are demonstrated in (*Figure 2*).
14

15 79 **Types and causes of medication administration errors among children led by parents or child** 16 17 18 80 **outside a clinical setting:**

19
20
21 81 Eight of the included studies indicated that paediatric dosing errors are among the most common
22
23 82 medication errors made by parents.^(15, 18, 20, 21, 23, 24, 26, 29) Among these studies, two randomised trials
24
25 83 identified that overdosing errors are more common among parents.^(23, 24) While another cross sectional
26
27 84 study looking at parents with child on a short course prescribed medication has reported that the
28
29 85 majority of the parents measured below the prescribed dose.⁽¹⁵⁾ A study by Morrison *et al.* reported that
30
31 86 parents who made under-dosing errors made more dosage errors and frequency errors compared with
32
33 87 those who made an overdosing error.⁽²⁰⁾
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35

36 88 From the included studies, it was noticed that the magnitude and frequency of dosing errors by parents
37
38 89 were influenced by two factors: measurement tool used by parents and the dose volume (amount) . In
39
40 90 one study, parents stated that non-standardised kitchen spoon is their primary dosing tool.⁽¹⁷⁾ Two studies
41
42 91 reported that errors were more common with measuring cups than with syringes, in particularly with
43
44 92 small dose volumes (amounts).^(21, 24) In a cross sectional study conducted in the USA, 23.5% of the
45
46 93 recruited parents reported that cups are the best tool for dose accuracy⁽²⁷⁾. Another study reported that
47
48 94 cups with printed marking or etched markings were more likely to be associated with overdosing.⁽¹⁶⁾
49
50 95 Labels and units of the prescribed medication were contributing factors to dosing errors.⁽²⁴⁾ Parents
51
52 96 made significant dosing errors when the units found on the medication bottle label were not similar to
53
54 97 the units used on the dosing tool.⁽²⁴⁾ Parents who use teaspoon/tablespoon units were likely to use a non-
55
56 98 standardised dosing instrument and make errors in measuring the prescribed and intended dose.⁽²⁹⁾ Final
57
58 99 potential factor was the type of instructions provided. For liquid medication, less error were seen among
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3 100 parents who were provided with text-plus-pictogram instructions 43.9% compared with text-only
4
5 101 instructions 59.0% and this group were also less likely to make overdosing errors. ⁽²⁶⁾ Parents who
6
7 102 received a standard medication counselling were 47.8% more likely to make dosing errors when
8
9 103 compared with parents who received pictogram instruction (5.4%).⁽²⁵⁾

104 **Factors related to patients or caregivers and medication errors**

105 *Health Literacy*

106 Health literacy of caregivers in the studies were assessed, six conducted further analyses of its influence
107 on dose accuracy and other co-factors related to medication errors. Yin *et al.* reported that caregivers
108 with inadequate or marginal health literacy were more likely to use a non-standardised dosing
109 instrument and further lacked knowledge on weight based dosing for over the counter medication when
110 compared with caregivers with adequate health literacy. ⁽¹⁷⁾ In another study by Yin *et al.*, they found
111 a significant association between health literacy and dosing errors using cups and dosing spoons. ⁽¹⁶⁾In
112 adjusted analysis conducted by Williams *et al.*, they found that there is a strong association between
113 health literacy levels and measurement tool preference in particular cups, parents with limited literacy
114 reported that dosing cups were the tool of choice most of the time (aOR=2.4).⁽²⁷⁾ The use of a
115 teaspoon/tablespoon was associated with errors in the intended dose for those with low health literacy
116 but not for those with adequate health literacy.⁽¹⁹⁾ Harris *et al.* identified that parents with limited health
117 literacy and Limited English Proficiency (LEP) made the most dosing errors. ⁽²¹⁾ Similarly, Kalow *et*
118 *al.* revealed that parents with inadequate and marginal health literacy committed dosing errors, but the
119 sample size of this group was small compared with the adequate health literacy group. ⁽¹⁸⁾

120 *Language*

121 Association between health literacy and lack of knowledge of weight-based dosing varied by English
122 speaking caregiver's. For English speaking caregivers 88.6% of inadequate or marginal health literacy
123 caregivers were unaware of weight based dosing in comparison to 54.1% of caregivers with adequate
124 health literacy. ⁽¹⁷⁾ In contrast, Yin found that there is no significant relation between dosing error and

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3 125 (LEP).⁽²⁶⁾ However, there were some differences in teaspoon-associated errors in measurement by
4
5 126 language.⁽²⁹⁾
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8 127 *Comprehension and recall of instructions in relation to parent sociodemographic status*

9

10 128 Yin *et al.* reported that parents from a low sociodemographic status who were prescribed daily dose and
11
12 who received a simple language, pictogram instructions sheets, were less likely to make errors in
13 129 knowledge of dose frequency and dose accuracy compared with the control group who received
14
15 130 standard medication counselling (0% vs 15.1%).⁽²⁵⁾ Participants among the interventional group were
16
17 131 less likely to report incorrect medication preparation related to shaking the medication before
18
19 132 administration for both daily doses (10.9% vs 28.3% $P= 0.04$) and as needed medication (21.5% vs
20
21 133 43.0%).⁽²⁵⁾ Participants in the interventional group were less likely to use a non-standardised
22
23 134 measurement tool compared with the parents in the standard group (daily dose: 93.5% vs 71.7%; as
24
25 135 needed: 93.7% vs 74.7%).⁽²⁵⁾ Torres *et al.* a cross-sectional study that analysed data from a randomised
26
27 136 control study, looked at parents preference and perceptions in regards to units of measurements. It was
28
29 137 found that over 80% of the parents perceived a change to millilitre only instructions would be easy in
30
31 138 comparison to 14% will find it some how hard and 4.1% very hard.⁽²⁸⁾
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36 140 **Interventions aimed at reducing medication administration errors occurring among children**

37 141 **outside a clinical setting**

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39 142 *Parent's sociodemographic factors*

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41 143 Four studies suggested that parental sociodemographic risk factors should be considered when
42
43 144 designing an intervention aimed at averting medication administration errors.^(16, 17, 21, 26) Amongst these
44
45 145 factors are parents' health literacy as well as language. Kalow and his colleagues suggested that efforts
46
47 146 to streamline interpreter services must be continued as well as, to having a more formalised approach
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49 147 in place to elucidate the patient's preferred language for communication.⁽¹⁸⁾
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53 148 *Counselling and training*

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3 149 Three studies suggested that provisional dose counselling in combination with verbal counselling could
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5 150 be associated with less dosing errors. ^(15, 17, 23) A study by Yin *et al.* indicated that errors occur across
6
7 151 different counselling approaches, and they have recommended developing new strategies to ensure that
8
9 152 parents understand medication instructions as well as they have suggested the need for further research
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11 153 to identify the best advance counselling strategies and how to incorporate these within clinical practice.
12
13
14 154 ⁽¹⁵⁾ Yin *et al.* suggested the need for intensive teaching, training and coaching programmes that can
15
16 155 accommodate for different parental health literacy levels. ⁽²⁴⁾

156 *Tools, labels and instructions*

157 Yin *et al.* suggested a promising strategy that could potentially help to reduce paediatric-dosing errors,
158 which is to match the dosing tool with the prescribed dose volume and move towards more simplified
159 numerical markings on the measurement tools as well as to move to millilitre-only units. ^(24, 26, 28) Wallace
160 *et al.* indicated in his study that some parents would prefer instructions with explicit dosage intervals
161 with the exact time and dose to be specified on the label. ⁽²²⁾ Harris *et al.* suggested improving the
162 availability of language concordant labels that could accommodate for different health literacy levels. ⁽²¹⁾
163 Three studies from this review strongly suggested the importance of utilising pictographic dosing
164 instructions and how it could be a positive aid in reducing paediatric dosing errors. ^(23, 25, 26) Majority of
165 parents would be comfortable with millilitre dosing instructions only.

166 **DISCUSSION**

167 The results of this study suggest that parents appear to make a range of medication errors, particularly
168 with liquid medications as documented by prior studies as well as studies from this review. ^(2, 4, 23, 25) The
169 majority of the included studies indicated that dosing errors are amongst the most common medication
170 errors made by parents, which is consistent with other studies. ^(15, 21, 25, 29, 30) This review identified
171 possible causality reasons behind parents dosing errors; these errors could be linked to the: dose volume
172 prescribed, measurement tools used, units used on the labels and the instructions provided.

173 Although standardised measurement tools are usually dispensed with the prescribed liquid medications
174 in the UK, this review identified that the studies published in the USA indicated that parents still use

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3 175 non-standardised liquid dosing tools as their primary measuring tool; this has been linked with
4
5 176 medication administration errors. ^(31, 32) Pairing the medication labels to the closest measurement tool
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7 177 size, particularly for millilitre-only labels and tools, could be potentially associated with a reduction in
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9 178 parent dosing and administrating error rates, as well as a decrease in the likelihood of parents using
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11 179 non-standardised measurement tools. ^(29, 33)

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13
14 180 The review showed that the use of simple pictographic based medication instructions with explicit
15
16 181 dosage intervals could reduce dosing errors by parents. This finding was consistent with previous
17
18 182 existing data regarding the use of pictographic illustrations as a supportive tool to aid parents in
19
20 183 administering medication to their children correctly. ⁽³⁴⁻⁴²⁾ Potentially this could benefit both parents
21
22 184 and caregivers with limited or low health literacy levels.

23
24
25 185 Our findings are consistent with prior studies investigating the link between parent's sociodemographic
26
27 186 factors, particularly health literacy, and child medication administration problems. ⁽⁴³⁻⁴⁶⁾ Four studies
28
29 187 explicitly highlighted that sociodemographic factors, such as health literacy and language, must be
30
31 188 incorporated into any future intervention that aims to reduce parental dosing and administration errors.

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33
34 189 The results of the review highlighted several interventions to aid parents and patients to potentially
35
36 190 reduce medication administration errors at home. This include the use of plain language combined with
37
38 191 provision of using the dosing tool provided as well as incorporating pictographic instructions which
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40 192 were consistent in four of the included studies. ^(15, 23, 25, 26) Pictographic-plain instructions significantly
41
42 193 improve the accuracy of dosing and administering medication to children especially for those parents
43
44 194 with insufficient health literacy. ^(25, 26)

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47
48 195 The study emphasised potential areas that could be incorporated into real practice that can help with
49
50 196 reducing medication administration errors done by parents/caregivers and patients. Potential strategies
51
52 197 include personalised training and coaching that accommodate different health literacy levels and
53
54 198 languages as well as the possibility to match the dosing tool with the prescribed volume alongside the
55
56 199 use of millilitre units.

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2
3 200 This systematic review was designed by interdisciplinary paediatric expertise in the pharmaceuticals and
4
5 201 pharmacy practice field. The review was registered on PROSPRO and conducted using PRISMA
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7 202 checklist. However, we found that our review is subject to several limitations. Firstly, our search
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9 203 strategy was designed to be comprehensive, but it is possible that some studies were missed. Secondly,
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11 204 English and published article were only included in this review, so publication bias may exist. Third,
12
13 205 although the study aimed at including medication administration challenges for younger people aged
14
15 206 between 16 and 18 years old, however non were included as they did not pass the eligibility criteria for
16
17 207 this review. future studies are needed where young people aged 16 to 18 years old are included as a
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19 208 participants. Thirdly the generalisability of the study results is low, this is due to the fact that the
20
21 209 majority of the studies were conducted in the USA and emerged from the same research group Yin *et*
22
23 210 *al.* This research group, have highlighted in their studies several limitations, such as the use of
24
25 211 hypothetical scenarios that might not be a true reflection on how parents measure the dose at home.^{(16,}
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27 212 ^{23, 24, 26)} For some randomised trial studies, it was difficult to maintain blindness as some of the
28
29 213 participants revealed their allocated group, while for the cross sectional studies, no conclusion of the
30
31 214 causes could be drawn.^(15, 17, 25, 29) Finally the date of publication for one of the studies was 13 years
32
33 215 old⁽¹⁷⁾, which would not take into account the changes that have occurred in terms of interventions that
34
35 216 would vary locally, nationally and internationally. However, this review highlights that non-standard
36
37 217 dosing still occurs to date due to parent preference based on recent evidence in 2018 ⁽²⁸⁾.

218 **Conclusions**

219 The relationship between medication administration errors and problems experienced by and parents
220 outside a clinical setting has not been well described from the literature with no relevant studies
221 examining the issue outside the USA. The studies explored the relation of dosing errors and parent's
222 understanding, interpretation of administration instructions and tools to help them administer their
223 medication either by the manufacturer or other supplier, health literacy as well as other
224 sociodemographic factors. Due to the gap in the knowledge outside of the USA and the heterogeneity
225 of healthcare provision worldwide, future studies, need to focus on the current medication
226 administration challenges among children and young people happening outside a clinical setting from

227 a patient and a parent perspective, in the UK and worldwide see (*Table S3 and S4, Supplementary*
228 *material*).

229 **No grant/award information in the Funding information**

230 This study was not funded. It's done as part of the author (DD) PhD research project.

231 **What is known about this topic?**

- 232 1- Medication administration errors occur frequently among children.
- 233 2- Parent's health literacy could be associated with medication administration problems in
234 children.
- 235 3- Studies examining parent administrator paediatric medicine accuracy were mainly from one
236 particular research group in the USA with participant parents using non-standardised
237 measuring tools

238 **What this study adds:**

- 239 1- The nature of medication administration error's happening at home are not well documented
240 across each age group..
- 241 2- The need to explore parents and patients perspective in regards to medication administration
242 challenges happening at home.

Table 1: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Randomised Controlled Trials Research Checklist.⁽¹³⁾

CASP Question Number	Authors and date					
	Yin (2017) ⁽²³⁾	Harris et al. (2017) ⁽²¹⁾	Shonna Yin et al. (2016) ⁽²⁴⁾	Yin et al. (2008) ⁽²⁵⁾	Yin et al. (2011) ⁽²⁶⁾	Wallace et al. (2012) ⁽²²⁾
1. Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the assignment of patients to treatments randomised?	Yes	Yes	Yes	Yes	Yes	Yes
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes	Yes	Yes	Yes	Yes	Yes
4. Were patients, health workers and study personnel 'blind' to treatment?	No	No	No	No	No	No
5. Were the groups similar at the start of the trial	Yes	Can't Tell	Yes	Yes	Yes	Yes
6. Aside from the experimental intervention, were the groups treated equally?	No	Yes	Yes	Yes	Yes	Yes
7. How large was the treatment effect? ^a	Yes	Uncertain	Yes	Yes	Yes	Uncertain
8. How precise was the estimate of the treatment effect? ^b	Yes	Yes	Yes	Yes	Yes	Yes
9. Can the results be applied to the local population, or in your context?	No	No	No	No	No	No
10. Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes	Yes	Yes
11. Are the benefits worth the harms and costs?	Yes	Yes	Yes	Yes	Yes	Yes

^a Based on the power calculation of the sample size and the primary outcomes results stated clearly.

^b Based on the extract ρ value and CI value of the primary outcome.

Table 2: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist.(14)

CASP Question Number	Authors and date							
	Williams et al. (2019) ⁽²⁷⁾	Torres et al. (2018) ⁽²⁸⁾	Morrison et al. (2017) ⁽²⁰⁾	Shonna Yin et al. (2014) ⁽²⁹⁾	Samuels- Kalow et al. (2013) ⁽¹⁸⁾	Yin et al. (2007) ⁽¹⁷⁾	Yin et al. (2010) ⁽¹⁶⁾	Yin et al. (2014) ⁽¹⁵⁾
1. Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the data collected in a way that addressed the research issues?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Has the relationship between researcher and participants been adequately considered?	Yes	Yes	Can't Tell	Can't Tell	Yes	Yes	Yes	Can't Tell
7. Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Is there a Value of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

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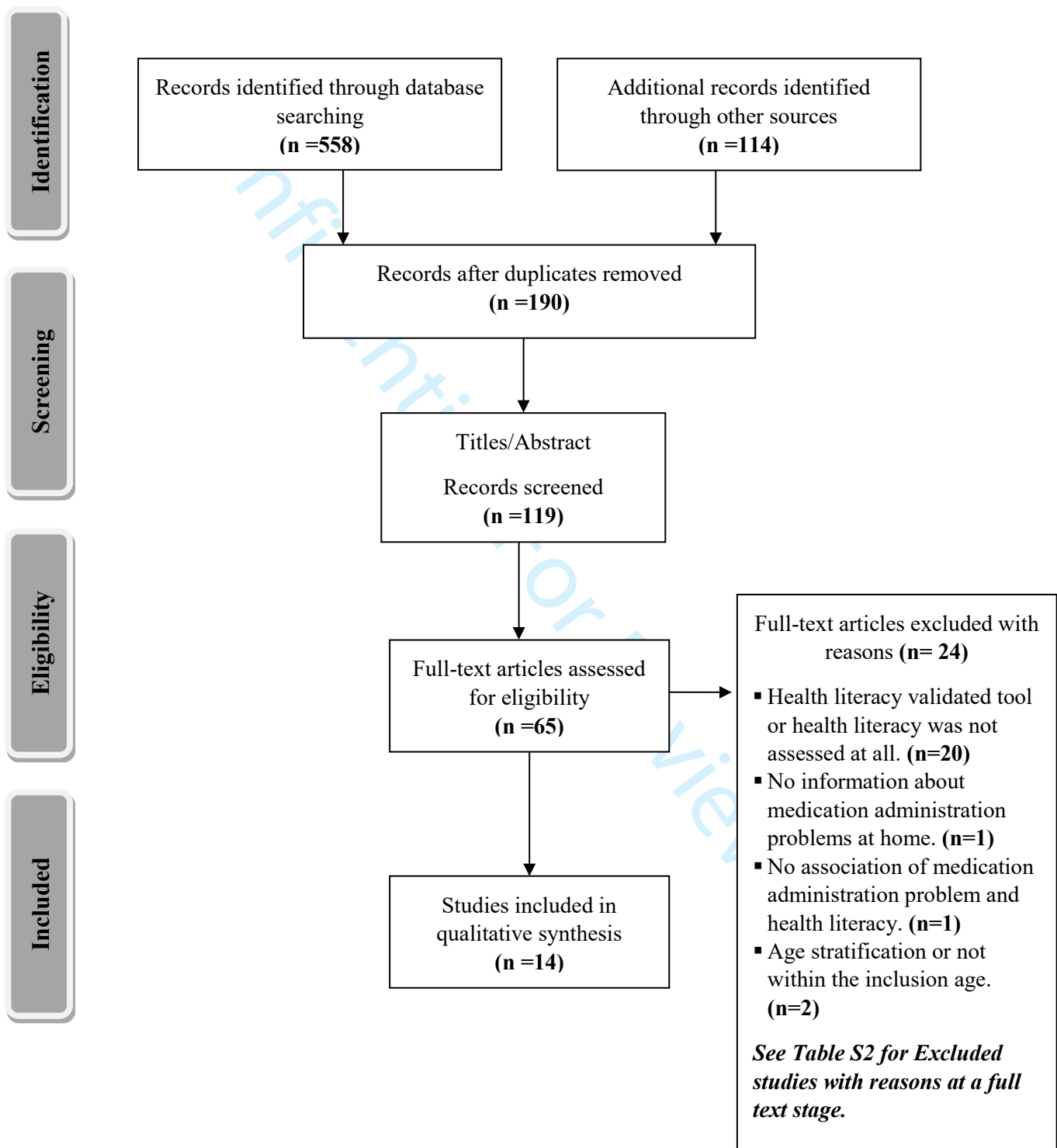
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Figure 1: Flow diagram for the study selection based on PRISMA flow diagram



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Figure 2: list of the review results

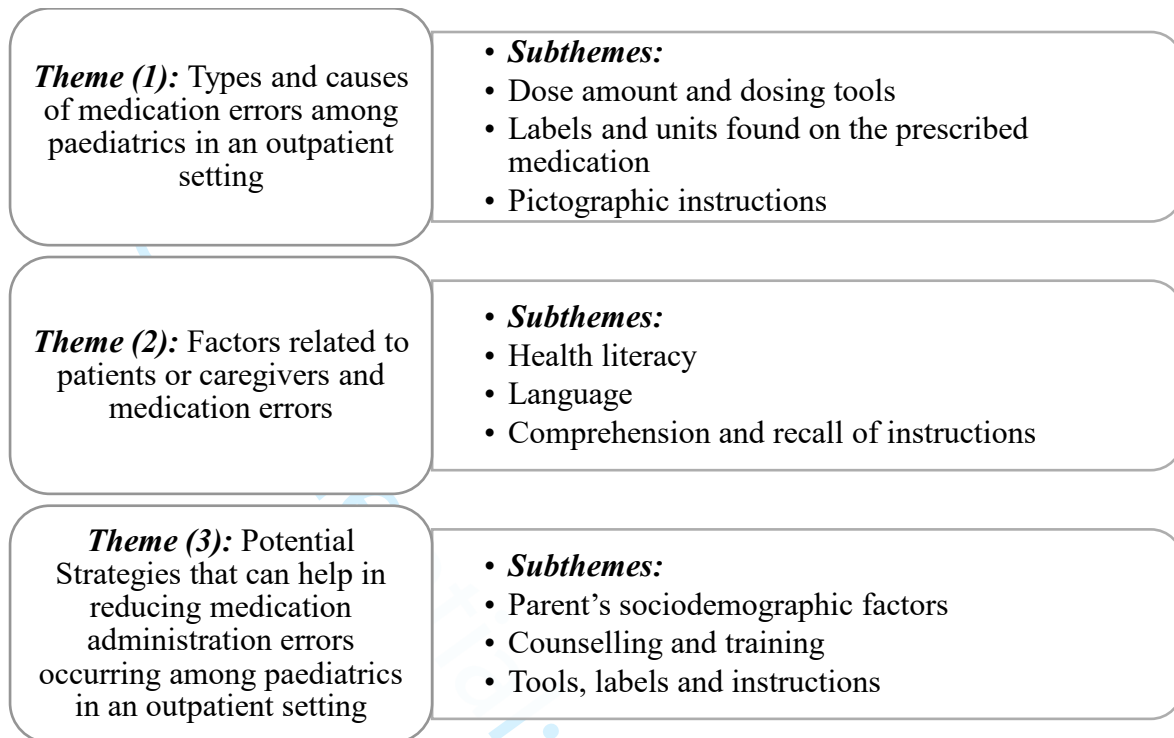


Table S1: Search Strategy for Systematic Review per database

Database	Search strategy
1- PubMed	<p>1- (((child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or teenager* or youth or infant* or newborn* or neonate*))) AND</p> <p>2- (("medical error*" or "medication error*" or "medication administration error*" or "drug administration error*" or "medicine administration error*" or "medication safety" or "optimisation" or "optimization" or "dosing error*")) AND</p> <p>3- (("health literacy" or "literacy" or "literate")).</p>
4- Scopus	<p>1- (child OR children OR pediatric* OR paediatric* OR toddler* OR adolescent* OR baby OR babies OR teen* OR teenager* OR youth OR infant* OR newborn* OR neonate*) AND</p> <p>2- (health AND literacy OR literacy OR literate) AND</p> <p>3- (medical AND error* OR medication AND error* OR medication AND administration AND error* OR drug AND administration AND error* OR medicine AND administration AND error* OR medication AND safety OR optimisation OR optimization OR dosing AND error*)</p>
5- Web of Science	<p>1- TOPIC: (child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or youth* or infant* or newborn* or neonate*) <i>AND</i></p> <p>2- TOPIC: ("health literacy" or "literacy" or "literate") <i>AND</i></p> <p>3- TOPIC: ("medical error*" or "medication error*" or "medication safety" or "medication administration error*" or "medicine administration error*" or "drug administration error*" or "dosing error*" or "optimisation" or "optimization")</p>
6- Cochrane Library	<p>1- "health literacy" or "literacy" or "literate" in Title Abstract Keyword AND</p> <p>2- "medication error" or "medical error" or "medication administration error" or "medicine administration error" or "drug administration error" or "dosing error" or "medication safety" or "optimisation" or "optimization" in Title Abstract Keyword AND</p> <p>3- child or children or pediatric or paediatric or toddler or adolescent or baby or babies or teen or teenager or youth or infant or newborn or neonate in Title Abstract Keyword - (Word variations have been searched)</p>

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Table S2: Excluded studies at full text stage with reasons for exclusion:

Author	Study Title	Reason For Exclusion
Tanner, S.(2014)	Parents' understanding of and accuracy in using measuring devices to administer liquid oral pain medication	No validated health literacy assessment used
Sil, A.(2017)	A study of knowledge, attitude and practice regarding administration of pediatric dosage forms and allied health literacy of caregivers for children	No validated health literacy assessment used
You, M. A. (2015)	Parental experiences of medication administration to children at home and understanding of adverse drug events	No validated health literacy assessment used
Walsh, K. E. (2013)	Medication errors in the home: A multisite study of children with cancer	No validated health literacy assessment used
Walsh, K. E. (2011)	Medication errors in the homes of children with chronic conditions	No validated health literacy assessment used
Tobaiqy, M. (2020)	Parental Experience of Potential Adverse Drug Reactions Related to Their Oral Administration of Antipyretic Analgesic Medicines in Children in Saudi Arabia	No validated health literacy assessment used
Taybeh, E. (2020)	The awareness of the Jordanian population about OTC medications: A cross-sectional study	No validated health literacy assessment used
Solanki, R. (2017)	Medication errors by caregivers at home in neonates discharged from the neonatal intensive care unit	No validated health literacy assessment used
Ryu, G. S. (2012)	Analysis of liquid medication dose errors made by patients and caregivers using alternative measuring devices	No validated health literacy assessment used
Manchanayake, M. G. C. A. (2018)	Patients' ability to read and understand dosing instructions of their own medicines - A cross sectional study in a hospital and community pharmacy setting	No validated health literacy assessment used
Lubrano, R. (2016)	Acetaminophen administration in pediatric age: An observational prospective cross-sectional study	Used education level not validated health literacy assessment tool.
Joshi, P. (2019)	Liquid Drug Dosage Measurement Errors with Different Dosing Devices	No validated health literacy assessment used

Huang, W. T. (2015)	Immigrant mothers' knowledge of medication safety and administration for young children	No validated health literacy assessment used
Chew, C. C. (2019)	Medication Safety at Home: A Qualitative Study on Caregivers of Chronically Ill Children in Malaysia	No validated health literacy assessment used
Almazrou, S. (2014)	Ability of Saudi mothers to appropriately and accurately use dosing devices to administer oral liquid medications to their children	No validated health literacy assessment used
Erickson, S. R.	Health literacy and medication administration performance by caregivers of adults with developmental disabilities	The study looked at medication administration at adults with disabilities not within the age range of this review.
Shone, L. P. (2011)	Misunderstanding and potential unintended misuse of acetaminophen among adolescents and young adults	Although young people were recruited but data for young people was not stratified from the adults.
Emmerton, L. (2014)	Management of children's fever by parents and caregivers: Practical measurement of functional health literacy	The study did not state the health literacy tool used . and used the educational level as a guide of literacy levels.
Lee, C. H. (2017)	Inappropriate self-medication among adolescents and its association with lower medication literacy and substance use	No validated health literacy assessment used
Boztepe, H. (2016)	Administration of oral medication by parents at home	No validated health literacy assessment used
Freedman, R. B. (2012)	Influence of Parental Health Literacy and Dosing Responsibility on Pediatric Glaucoma Medication Adherence	Looked at medication adherence not administration.
Glick, A. F. (2020)	Accuracy of Parent Perception of Comprehension of Discharge Instructions: Role of Plan Complexity and Health Literacy	No medication administration related information more about parent's perception of comprehension of discharge instructions.

1 2 3 4 5 6 7 8 9	Chan, H. K. (2017)	Influences of pictogram-based instructions in paediatric drug labelling on dosing accuracy among caregivers: a pilot study from Malaysia	No validated health literacy assessment used
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Brass, E. P. (2018)	Medication Errors With Pediatric Liquid Acetaminophen After Standardization of Concentration and Packaging Improvements	No validated health literacy assessment used

Table S3: Characteristics of the observational included studies in the review (listed alphabetically according to first author).

Citation Characteristics			Study Information		Participants Characteristics			Findings
First Author (Year)	Country of Origin	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Morrison et al. (2017) ⁽²⁰⁾	United States of America	Outpatient clinic and emergency department	Interviews and applied assessment	To examine the association between parent health literacy and pain medication knowledge and applied skills in parents of children with sickle cell disease.	Parents of children 1 to 12 years old.	100	Newest Vital Sign (NVS)	Parents with low health literacy made more under dose frequency errors on the pain treatment skills. Health literacy was not associated with errors on the applied treatment skills. Parents recalled under-dosing of medication (both dose and frequency). On the applied pain treatment skills, parents made both underdoing and overdosing errors.
Samuels-Kalow et al. (2013) ⁽¹⁸⁾	United States of America	Tertiary	Prospective observational	To examine language-based disparities in discharge communication and parental understanding of discharge instructions.	Parents of children 2 to 24 months.	145	Short Test of Functional Health Literacy (S-TOFHLA)	Parents had acetaminophen dosing errors. There was significant association between language and dosing errors. Parents with marginal or inadequate health literacy had dosing errors compared with adequate health literacy.
Shonna Yin et al. (2014) ⁽²⁹⁾	United States of America	Emergency department	Interviews and observations	To examine the association between unit used and parent medication errors and whether nonstandard instruments mediate the relationship.	Parents of children aged <9 years old.	400	Short Test of Functional Health Literacy in Adults (S-TOFHLA)	Parents made different kind of error in measurement. 1 in 6 parents used kitchen spoon rather than a standard instrument. Parents did not use the unit listed on the prescription or label.
Torres et al. (2018) ⁽²⁸⁾	United States of America	Paediatric outpatient clinics	Cross sectional analysis	Sought to examine the interrelationships between parents' preferences and perceptions regarding units of measurement, parents millilitre dosing experiences, and parent health literacy.	Parents or legal guardian of children ≤ 8 years old.	493	Newest Vital Sign (NVS)	Parents preferred the millilitre dosing to be easy; few 11.5% prefer teaspoon units. Parents with low health literacy levels had a higher odd of having a teaspoon preference and greater odds of perceiving difficulty with the millilitre only dosing.

Williams et al. (2019) ⁽²⁷⁾	United States of America	Outpatient clinics	Cross sectional analysis	To assess parent decision-making regarding dosing tools, a known contributor to medication dosing errors, by evaluating parent dosing tool use, beliefs, and access, and the role of health literacy, with a focus on dosing cups, which are associated with an increased risk of multi-fold overdose.	Parents or legal guardians of children aged ≤ 8 years old.	473	Newest Vital Sign (NVS)	Health literacy is one of the factors that could be associated with the dosing tool choice. Parents with limited health literacy reported that dosing cups were the tool used most of the time.
Yin et al. (2007) ⁽¹⁷⁾	United States of America	Pediatric emergency department.	Interviews	To assess whether low caregiver health literacy was related to risk factors for liquid medication dosing errors, including reported use of non-standardised dosing tools and lack of knowledge about weight based dosing.	Parents and caregivers of children aged between 30 days to 8 years old.	292	Test of Functional Health Literacy in Adults (TOFHLA)	Low health literacy, particularly reading comprehension, was associated with reported use of non-standardised dosing instruments and lack of knowledge regarding weight based dosing. In addition, this has been found previously to be associated with decreased dosing accuracy.
Yin et al. (2014) ⁽¹⁵⁾	United States of America	Paediatric emergency department	Interviews and observations	To examine the degree to which recommended provider-counselling strategies, including advanced communication techniques and dosing instrument provision, are associated with reductions in parents liquid medication dosing errors.	Parents of children aged < 8 years old.	287	Short Test of Functional Health Literacy (S-TOFHLA)	Majority of the parents made underdosing errors as well as a few made overdosing errors. Recipient of at least one advanced counselling were less likely to make a dosing error compared with those who did not report received advanced counselling. Parents who received dosing instrument from the emergency department made fewer errors. For adequate health literacy levels was significantly associated with fewer errors when they have received advanced counselling in combination with instrument provision but not the low literacy.

Yin et al. (2010) ⁽¹⁶⁾	United States of America	Pediatric clinic	Observational	To assess parents' liquid medication administration errors by dosing instrument type and to examine the degree to which parents' health literacy influences dosing accuracy.	Parents of children with no specific age limitation.	302(287 mothers, 8 fathers, 7 legal guardians)	Newest Vital Sign (NVS)	Health literacy was significantly related to doing errors with the cups as well as the dosing spoon, while non-significant trend was seen for the dropper and the oral syringes with the bottle adaptor.
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Table S4: Characteristics of the randomised controlled experiment included in the review (listed alphabetically according to first author).

Citation Characteristics			Study Information		Participants Characteristics			Findings
First Author (Year)	Country of Origin	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Harris et al. (2017) ⁽²¹⁾	United States of America	Outpatient	Randomized Controlled Experiment	To examine the association between health literacy and limited English proficiency and liquid medication dosing errors in Hispanic parents	Hispanic parents of children <8 years old.	1126 parents	Newest Vital Sign (NVS)	70% of the recruited parents had Limited English Proficiency (LEP), 82.7% had limited literacy. Of parents who had Limited English Proficiency (LEP) 88.8% had limited and 11.2% adequate health literacy. 83.1% of parents made a dosing error at least one out of the nine dosing trials. Parents with limited health literacy and with Limited English proficiency (LEP) made the most dosing error and errors varied by dose amount and tool type.
Shonna Yin et al. (2016) ⁽²⁴⁾	United States of America	Pediatric clinic	Randomized controlled experiment	Hypothesized that unit concordance would be associated with fewer errors and that parents would measure most accurately with syringes we also sought to examine differences in impact by parents health literacy and language because low health literacy and limited English proficiency are factors known to place children at risk for errors.	Parents of children aged ≤ 8 years old.	2099 parents	Newest Vital Sign (NVS)	Nearly all parents (99.3%) measured ≥ 1 dose that was not the exact amount. Overdoing (68.0%) was the majority of the errors. Dose amount of 2.5 and 7.5 mL was associated with more errors when compared with 5 mL (2.5 vs 5 mL adjusted odds ratio [aOR]=4.2; 95% CI,3.8-4.6; 7.5 vs 5 mL [aOR]= 1.4;95%CI, 1.2-1.5).
Wallace et al. (2012) ⁽²²⁾	United States of America	Outpatient clinic	Randomized Controlled Trial	To address the gap by addressing whether instructions wording that implicit versus explicit dosage intervals was associated with participant's ability to describe and correctly measure a dose of a	Women of childbearing age.	193	Estimated using three established items: -How often do you have problems learning about	One third of the participants (32.1%) were able to describe and measure the dose accurately. Participants with inadequate health literacy skills were one third as likely to measure a dose of the medication correctly.

				commonly prescribed liquid pediatric prescription medication.			your medical condition because of difficulty understanding written information? - How often do you have someone help you read hospital materials? - How confident are you filling out medical forms by yourself?	
Yin et al. (2008) ⁽²⁵⁾	United States of America	Pediatric emergency department	Randomized Controlled Trial	To evaluate the efficacy of a pictogram based health literacy intervention to decrease liquid medication administration errors by caregivers of young children.	Parents and caregivers of children aged 30 days to 8 years.	245	Test of Functional Health Literacy in Adults (TOFHLA)	Caregivers' dose accuracy was higher among the intervention group prescribed daily and as needed medications regardless of the cut-off point was 20% or 40%. 5.4% of the intervention caregivers whose children had been prescribed daily doses gave inaccurate dose at the 20% cut off point, compared with 47.8% of control caregivers. The study suggested that there is no health literacy association with the dosing errors.
Yin et al. (2011) ⁽²⁶⁾	United States of America	Outpatient pediatric clinic	Randomized Controlled Trail	To sought whether a pictographic dosing diagram included as part of written instructions can decrease parent errors in dosing infant acetaminophen as well as whether pictogram benefit varies by parent health literacy level.	Parents or caregiver of a child with no specific age limitation.	299 parents were assessed	Newest Vital Sign (NVS)	Both groups were associated with poor dosing with the tendency for the parents who have received text plus pictogram significantly less likely to make dosing error (0.6%) compared with parents who received text only instructions (5.6%). Parents with low literacy who received the text plus pictogram instructions were significantly less likely to make errors in dosing compared with who received text only instructions(50.4% vs 66.4%; $P=.02$).

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Yin et al. (2017) ⁽²³⁾	United States of America	Pediatric outpatient clinic	Randomized controlled experiment	To examine the degree to which errors could be reduced with pictographic diagrams, millilitre-only units, and provision of tools more closely matched to prescribed volumes	Parents of children aged ≤ 8 years old.	2099 for all arms	Newest Vital Sign (NVS)	Majority of the parents (99.3%) made dosing errors. More errors with the 2 and 7.5 mL dosing amount when compared with the 10 mL (2mL vs 10 mL aOR =3.7; 7.5 mL vs 10 mL aOR= 1.4). Parents who received text and pictogram dosing instructions with mL only labels and tools had decreased odds of making a dosing error compared with received mL/tsp labels and tools with or without pictographic dosing instructions.
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Author's response to the Associate Editor and the reviewer's comments

The authors want to thank the associate editor and the reviewers for their comments. The authors have addressed the reviewer's comments and highlighted it with the yellow on the manuscript.

Kindly, this review has been now updated up till September 2020. And for that two more studies have been added to the analysis.

Associate Editor Comments

Comment Number	Details of the comment	Author Response
1	You must update your search which is over 12 months old.	Thank you for your valuable comment, we have now updated the search and two new articles have been added to the review analysis.
2	Your title needs to reflect your study - a scoping review of medication errors in paediatrics by parents.	Thank you for your important comment. The title has been change and now reads as: "A Literature review of medication administration problems in paediatrics by parent/caregiver and the role of health literacy" – We have opted for the term problem rather than error, just to reflect on the systematic review initial aims which was to identify administration problems, but what was found in the results were mainly reported errors.
3	Abstract needs to include more details in Methods, eg no mention of parent in search.	Thank you for your comment, it was advised by our information specialist to exclude parents from the search terms and instead hand search the studies that are relevant to the inclusion criteria. In addition to that, as young children were part of the population in this review, which they may or may not be self-administering their own medication so we did not want to exclude these type of studies. Hence, a broader search terms used.

4	Results Table S2 needs to be in the main paper. divide table into two separating RCTs from observational studies.	Thank you for your comment. This has been done initially however, it was advised by the journal to have it as a supplementary tables as its too long to be embedded within the manuscript and it would be so difficult to reduce it into two pages. We have separated the table into two tables one for RCT and another for qualitative data.
5	You appear to have missed studies, eg Solanki R, Mondal N, Mahalakshmy T, et al Medication errors by caregivers at home in neonates discharged from the neonatal intensive care unit Archives of Disease in Childhood 2017;102:651-654.	Thank you for your comment. This study has been identified from our search, however, was excluded at full text stage as no validated health literacy tool was used in the study. We have added a supplementary table that list all excluded studies at the full text review (Table S3) We have added in the methodology section (inclusion criteria heading) to explain the criteria of inclusion and exclusion.
6	Clarify whether you only included studies that evaluated literacy. If so, you will miss a lot of studies	Thank you for your comment. We only included medication administration issues among children and young people aged between 0 to 18 years that are occurring at home outside of a clinical setting. The included studies must have a validated health literacy tool. Inclusion criteria section has been added in the methods.

Reviewer 1

Comment number	Details of comment	Author response
1	Introduction – P4 L7 – First sentence quotes an error every 8 minutes I cannot find reference to this statistic in the cited reference, which is a review article. Review.	Thank you for your comment. The authors opted to remove this and add more relevant statistics data about parents and dosing errors at home.

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	L18 European health literacy consider upper case letters for this.	Thank you for your comment. This has been amended and now reads as: European Health Literacy Survey (HLS-EU).
	L18 – Whole sentence is a statement but the context is not clear and reason for stating this is not clear – re-word	Thank you for your comment. This has been re-worded now. The paragraph reads as the following: “Causes of medication administration problems at home are multifactorial and potentially depends on various factors (1). So In in order to improve medication administration by parents and patients an initial assessment of the current problems and factors that may contribute to this issue must be identified first.”
	L23 Para 3 re-word first sentence two uses of “review”	Thank you for your comment. We have amended this and now ready as the following: “In this study, we aimed at reviewing studies that highlighted medication administration problems experienced by parents or children, which also used a validated health literacy test to assess for parent health literacy levels.”
	L27 review tense “we highlighted”	Thank you for your comment. This has been amended and now reads as the following: “In this systematic review, we highlighted the common medication administration problems occurring at home as well as the potential causalities and risk factors that further contribute to these medication administration errors have been highlighted.”

	Methods P5 L29 Query need for initials to be in parenthesis	Thank you for your comment. This is now been removed as per the third reviewer suggestion (it's a repeated sentence).
	L29 reword – “did” performed?	Thank you for your comment. This now has been changed and reads as the following: “(D.D.) further performed reference tracking of all included studies to identify any potential studies to be included in the review.”
	L39 – mention of inclusion criteria above I can't see them.	Thank you for your comment. Inclusion criteria of the review has been add as a separate heading in the method section.
2	Results P6 L36 “only exclusively” use just one word Synthesis of results P7	Thank you for your comment. This has now been amended and the sentence reads like: “The data from the 14 studies were analysed and three analytical themes emerged from the analysis and a summary of the review results are demonstrated in (Figure 2).”
	L3 – Do you mean “Lead” or Led in the subtitle, lead seems wrong.	Thank you for your comment. This has been amended and changed to led. The subtitle reads as the following. “Types and causes of medication administration errors among children led by parents or child outside a clinical setting”
3	L 10 second sentence does not make complete sense – re-word in the context of the study being referred to	Thank you for your comment. This has been reworded and now reads as the following: “Among these studies, two randomised trials identified that overdosing errors are more common among parents”

	L15 third sentence re-word "whom have a child on a short course prescribed medication has...."	Thank you for your comment, this now has been amended and the sentence reads as the following. "While another cross sectional study looking at parents with child on a short course prescribed medication has reported that the majority of the parents measured below the prescribed dose."
	L26 – tense – are or were influenced – check with journal style.	Thank you for your comment. This has been checked and amended to were.
	L26 "the measurement tool...." This cites 2 factors not one – re-word.	Thank you for your comment. This has been re-worded and now reads as the following: "From the included studies, it was noticed that the magnitude and frequency of dosing errors by parents were influenced by two factors"
	L28 sentence needs reviewing	Thank you for your comment. This has been reviewed and now reads as the following: "In one study, parents stated that non-standardised kitchen spoon is their primary dosing tool. Two studies reported that errors were more common with measuring cups than with syringes, in particularly with small dose volumes (amounts)."
	L35-36 Sentence needs a reference	Thank you for your comment. The sentence: "Labels and units of the prescribed medication were contributing factors to dosing errors." ⁽²⁴⁾ has been referenced.
	L49 – reword - likely to make an overdosing errors.	Thank you, this has been reworded to "...likely to make overdosing errors"
	P8	Thank you for your comment. This has been changed. All were made low case except

	First paragraph – health literacy appears several times but with a variety of upper and lower case initials – review for consistency please	headings and the name of the health literacy test.)
	Paragraph relating to language – interesting result but not explained very well what do you mean by no association for Spanish speakers, just needs a little more clarification I think. You only cite a couple of papers from the review here (and only one in the next section about comprehension) – how many of the papers looked at this issue?	Thank you for your comment. This has been amended now. In regards to the comprehension only the ones cited in the section had discussed it.
4	P9 L9 – this is the kind of paragraph I would expect for the previous ones much better wording.	Thank you for your feedback.
5	L34 second sentence missing the word “study”	Thank you for your comment. This has now been added to the sentence.
6	L36 tense not quite right “urged for developing” review.	Thank you for your comment, this has been changes and now reads as the following: “A study by Yin et al. indicated that errors occur across different counselling approaches, and they have recommended developing new strategies to ensure that parents understand medication instructions as well as they have suggested the”
	L50 you cite a strategy that can help – where is the proof that is can help or do you mean could/may help?	Thank you for your comment. This has been modified and now reads as the following: “Yin et al. suggested a promising strategy that could potentially help to reduce paediatric-dosing errors”
	P10 L24 “dose amount prescribed” cumbersome phrase – dose volume?	Thank you for your comment. This has now been changed to volume.
	L49 “this further....” Re-word this sentence.	Thank you for your comment. This has been re-worded and now reads as the following:

		“Potentially, this could benefit both parents and caregivers with limited or low health literacy levels.”
	P11 L5 – Replace this with these	Thank you for your comment. This sentence has been modified and now reads as the following: “Finally, the generalisability of the study results is low, this is due to the fact that the majority of the studies were conducted in the USA and emerged from the same research group Yin et al. This research group, have highlighted in their studies several limitations, such as the use of hypothetical scenarios that might not be a true reflection of how parents measure the dose at home”
	L40 “for this particular...” reword this sentence	Thank you for your comment. This sentence has been modified and now reads as the following: “Finally, the generalisability of the study results is low, this is due to the fact that the majority of the studies were conducted in the USA and emerged from the same research group Yin et al. This research group, have highlighted in their studies several limitations, such as the use of hypothetical scenarios that might not be a true reflection of how parents measure the dose at home”
	L49 – “drown” should be drawn	Thank you for your comment, this now has changed to drawn.
7	Conclusions P11	Thank you for your comment. This now has been clarified and reads as the following:

	<p>L55 what do you mean here when you describe problems experienced by parents? You might be referring to health literacy for example – I would not describe these generally as “problems”</p>	<p>“Due to the gap in the knowledge outside of the USA and the heterogeneity of healthcare provision worldwide, future studies, need to focus on the current medication administration challenges among children and young people happening outside a clinical setting from a patient and parent perspective, in the UK and worldwide (Table S3, Supplementary material).”</p>
<p>8</p>	<p>What is know what this adds – good stuff here.</p>	<p>Thank your feedback. We appreciate it.</p>

Reviewer 2

comment number	Details of comment	Author response
<p>1</p>	<p>Should the title say that this is a literature review?</p>	<p>Thank you for your important comment. The title has been change and now reads as: Medication administration errors among paediatric at home- A systematic review</p>
<p>2</p>	<p>Abstract Line 42 mentions "provisional dose" - what is this - it is not clear.</p>	<p>Thank you for your valuable comment. We have amended this and the paragraph now reads as the following: “Among these recommendations is to provision (show) the prescribed dose to the parents or young people along with the verbal instructions as part of medication counselling, as well as to match the prescribed dose with the measuring tool dispensed, to provide an explicit dose intervals and pictographic dosing instructions.”</p>
<p>3</p>	<p>Sentence from line 49-52 is not clear</p>	<p>Thank you for your comment. We have amended the conclusion and now reads as the following:</p>

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		<p>“The findings suggest that in order to optimise medication use by parents, further work is needed to address the nature of medication administration issues and challenges at home. Counselling, medication administration instructions and measurement tools are some of the areas that need to be explored in order to reduce medication errors at home. Sociodemographic characteristics including health literacy and language need to be considered when designing any future potential intervention aimed at reducing medication errors among children and young people at home.”</p>
4	There is no mention of health literature in the abstract and yet it is a fundamental part of the study	Thank you for your comment, this has been added in the abstract.
5	Introduction Firts line makes a fundamental about an error every 8 minutes - might help if this states if it is in hospital, community or everywhere - assume this is in the US?	Thank you for your comment. This has been amended now, and the authors opted to provide more relevant statistics for an out patient setting.
6	Results In teh 4th line under language it states that there is "no association for Spanish speaking caregivers" - this needs to be expressed differently as it is not clear what that means or the relevance.	Thank you for your comment. We opted to remove the part of Spanish language.
7	page 9 (line 56) - "5.7% of parents would prefer instructions" - this stat has been used to say that instructions may be useful. However as a statistic i could argue that 94.3% didn't want instructions... - thus this needs to be stated differently.....that some parents have suggested that instructions may be useful?	<p>Thank you for your comment. We have amended this as per your recommendation. The sentence reads now as the following:</p> <p>“Wallace <i>et al.</i> indicated in his study that some parents would prefer instructions with explicit dosage intervals with the exact time and dose to be specified on the label.”</p>

8	Within the limitations there should be a statement about the age of some of the data eg the main paper associating poor dosing with kitchen spoons was 13 years ago. Since then many interventions have changed. What is critical is that we know that these practices do still happen today even if less, that is because of silo'd and localised interventions. What we are missing is a systematic definition of interventions that should be carried out so that there is standardisation of improvement	Thank you for your comments. The date of publication of the paper by Yin and colleagues in 2007 has been commented on as well as the variation of interventions.
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Reviewer3:

Comment number	Details of comment	Author response
1	Methods: Line 14: 'D.Y' is not among the authors. Seems there is a typo error here.	Thank you for your comment. This has been amended.
2	Also, the abbreviation PICO needs to be written in full in the first	Thank you for your comment. This has been amended.
3	Line 20: The search was done more than a year ago – did the author update the literature search before submitting and they didn't find any new eligible studies? This needs to be clarified in the manuscript.	Thank you for your comment. We have now updated our search to (September 2020) this yielding two new studies, which has been integrated in the analysis.
4	Line 43: the sentence is a repetition of what is included in the previous section (lines: 30-31).	Thank you for your comments. This has been deleted now.
5	Line 53: add the initials for the third reviewer.	Thank you for your comment. The third reviewer initials has been added.
6	Why the approach of using 'analytical themes' for the data analysis. Could benefit from a justification for this approach.	Thank you for your comment. This has been added and now reads as the following: "Thematic analysis was opted by the research team as it's known for its flexibility and ability of identifying patterns of meaningful information within the data"
7	Results:	Thank you for your feedback. we have opted to remove the part of Spanish speaking.

	Line 18-20: it is worth commenting on the studies' findings related to LEP association with dosing errors. The studies were conducted in the US (an English-speaking country) only, therefore, whether this contributing factor might exist in other countries is not clear.	
8	Line 37: typo error; missing comma.	Thank you for your comment. We could not find the missing comma but the author have proofread the results section for typos and made the relevant edits, e.g. no conclusion of the causes could be drawn (was misspelt as drown in the manuscript accidentally)
9	Line 34-41: check the sentence. Comparing English language vs health literacy or vs another language?	Thank you for your comment. It has been amended not to English speaking caregivers.
10	Discussion: Line 49: study 21 was an RCT not a cross-sectional study – is the reference correct for this sentence?	Thank you for your comment. Study 21 is a randomised control trail and the citation is correct here as I am trying to elaborate on both RCT and cross sectional studies.
11	Table S3 was suddenly introduced in the conclusion only – not sure why not referred to in the results section.	Thank you for your comment. This has been introduced earlier in the manuscript.
12	The review aimed to include studies that reported on administration errors made by parents as well young people aged >16 years. The included studies only recruited parents/caregivers. It is worth highlighting this point in the discussion and the need for future studies where young people are included as participants.	Thank you for your comment. This has been addressed now in the discussion section. The following has been added: "Third, although the study aimed at including medication administration challenges for younger people aged between 16 and 18 years old, however, none were included as they did not pass the eligibility criteria for this review. future studies are needed where young people aged 16 to 18 years old are included as a participants."
13	What the study adds:	Thank you for your comment. This has been amended and the points reads as the following:

	<p>first point: There were no studies identified from the UK as per your results, therefore the statement can't be stipulated about the UK – it is not supported by the review findings. Second point: typo error; preposition is missing.</p>	<p>1-The nature of medication administration error's happening at home are not well documented across each age group .especially in the UK. 2-The need to explore parents and patients perspective in regards to medication administration challenges happening at home.</p>
14	<p>Sometimes it is written 'compare to' and sometimes 'compared with' – need to check that throughout the manuscript.</p>	<p>Thank you for your comment. We have amended this across the manuscript to "Compared with"</p>
15	<p>Table S2: add a footnote for the abbreviations included in the table., e.g. LEP</p>	<p>Thank you for your comment. Any abbreviation within the table has been checked and added within the text of the table,.</p>

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A Literature review of medication administration problems in paediatrics by parent/caregiver and the role of health literacy

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4 1 **A Literature review of medication administration problems in**
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6 2 **paediatrics by parent/caregiver and the role of health literacy**
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8 3 Dania Dahmash, MSc, Aston University, Aston Pharmacy School

9 4 Zakia Shariff, MPharm, Aston University, Aston Pharmacy School

10 5 Dr. Daniel Kirby, PhD, Aston Pharmacy School

11 6 Dr. David Terry, PhD, Aston Pharmacy School

12 7 Dr. Chi Huynh, PhD, Aston Pharmacy School

13
14
15
16
17
18 9 **Corresponding author;**

19
20 10 Dr. Chi Huynh, c.huynh3@aston.ac.uk, Work: - 0121 204 3231

21
22 11 **List of key words not in the title;**

23 12 Systematic Review; Children; Medication Error

24
25 13 **Reprint request;**

26
27 14 Dr. Chi Huynh, PhD, Aston University, Birmingham, United Kingdom, E-mail:
28 15 c.huynh3@aston.ac.uk.

29
30 16 **Source of funding and conflict of interest statement, if applicable;**

31 17 Aston University, Birmingham, United Kingdom is funding Dania Dahmash PhD project, which as
32 18 part of her project this review was conducted.

33
34 19 The review preliminary results was published on the BMJ (Archives of Disease in childhood) after an
35 20 abstract was submitted for the NPPG 2018 conference for the purpose of poster presentation.

36
37 21 The authors declare no conflicts of interest.
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23 ABSTRACT

24 **Objective:** To review all published evidence related to paediatric medication administration problems
25 parents who administer the medication to their children aged 0 to 16 years, as well as medication
26 administration related issues by young persons aged 16 and above who take their own medication at
27 home with the association of health literacy levels.

28 **Study design:** Ten electronic databases were systematically searched and supplemented by hand
29 searching through reference lists using the following search terms: i) paediatric ii) medication error
30 including dosing error, medication administration error, medication safety and medication optimisation
31 and iii) health literacy.

32 **Results:** Of the (1,230) records screened, fourteen studies were eligible for inclusion. Three analytical
33 themes emerged from the synthesis. The review highlighted that frequencies and magnitudes of dosing
34 errors varies by the measurement tools used, the dose prescribed and by the administration instruction
35 provided. Parent's sociodemographic; such as health literacy and language, is a key factor to be
36 considered when designing an intervention aimed at averting medication administration errors at home.
37 The review summarised some potential strategies that could help in reducing medication administration
38 errors among children at home. Among these recommendations is to show the prescribed dose to the
39 parents or young people along with the verbal instructions, as well as to match the prescribed dose with
40 the measuring tool dispensed, to provide an explicit dose intervals and pictographic dosing instructions.

41 **Conclusion:** The findings suggest that in order to optimise medication use by parents, further work is
42 needed to address the nature these issues at home. Counselling, medication administration instructions
43 and measurement tools are some of the areas in addition to the sociodemographic characteristics of
44 parents and young people that need to be considered when designing any future potential intervention
45 aimed at reducing medication errors among children and young people at home.

46

47

48 INTRODUCTION

49 When it comes to medication administration for children at home, a significant burden of responsibility
50 relays on the on parents or on the patients themselves.⁽¹⁾ It's been documented that medication
51 administration among children are well known to occur⁽²⁾. Previous studies recognised that more than
52 40% of parents and caregivers make dosing errors in an outpatient setting.^(3,4)The inability to administer
53 medication correctly may result in adverse drug events and poor patient clinical outcomes.⁽⁵⁾ Causes of
54 medication administration problems at home are multifactorial and potentially depend on various
55 factors. ⁽²⁾ So in order to improve medication administration by parents and patients, an initial
56 assessment of the current problems and factors that may contribute to this issue must be identified first.
57 Previous studies have recognised potential factors that can contribute to clinician led medication
58 administration errors in children, but there have been no studies recording both the types and risk factors
59 that can contribute towards caregiver's medication administration problems as well as young people. ⁽⁶⁾
60 ⁷⁾ According to the European Health Literacy Survey (HLS-EU), conducted across eight different
61 countries, the prevalence of low health literacy levels varies from 29% to 62%.^(8,9)

62 Owing to this high prevalence of low health literacy levels and its potential association with medication
63 administration issues among children. This review aimed at identifying studies that highlighted
64 medication administration problems experienced by parents and children, which also looked at health
65 literacy aspect using a validated tool to assess for literacy. In this systematic review, the common
66 medication administration problems occurring at home as well as the potential causalities and risk
67 factors other than health literacy that further could contribute to medication administration errors have
68 been highlighted.

69 METHODS

70 This review was conducted in accordance with the Cochrane Handbook for Systematic Reviews, and
71 followed PRISMA reporting guidelines^(10, 11) The review protocol is registered on PROSPERO (ID:
72 CRD42018091590).

73 **Patient and Public Involvement**

74 There was no patient and public involved in the design, or conduct, or reporting, or dissemination of
75 this review.

76 **Eligibility Criteria**

77 Studies were eligible for inclusion if they were related to medication administration errors among
78 children and adolescent between the ages of 0 to 18 years old as per the World Health Organisation
79 definition of population age group. This includes studies reporting medication related problems outside
80 the clinical setting; where the parent or the child is responsible for administering or taking the
81 medication. Studies must have assessed the health literacy levels of the participants using a validated
82 health literacy assessment tool. Any study that looked only at education levels of the participants
83 without assessing the literacy levels was excluded. There were no restrictions on the date of publication,
84 only English language articles studies where included.

85 **Search Strategy**

86 The search strategy was designed initially by the research team and verified by an information specialist
87 using the Population, Intervention, Comparison and Outcomes (PICO) model. The reviewer (D.D.)
88 systematically searched PubMed, Scopus, Web of Science, Cochrane Library, OpenGrey, NHS Digital
89 Department of Health Office for National Statistics, BBC News, Bielefeld Academic Search Engine
90 (BASE), E-thesis Online Service (EThOS) and Conference proceedings through Web of Science for
91 studies from database inception to September 2020.

92 Search terms summarised in *(Table S1; supplementary material)* included a comprehensive list of
93 synonyms and multiple Boolean operators relating to: i) paediatric ii) medication error including dosing
94 error, medication administration error, medication safety and medication optimisation and iii) health
95 literacy. (D.D.) further performed reference tracking of all included studies to identify any potential
96 studies to be included in the review.

97 **Study selection**

98 Two reviewers (D.D., Z.S.) independently evaluated each study for eligibility to reduce bias using the
99 inclusion criteria above. The titles and/or abstracts of all identified studies were reviewed
100 independently, and full manuscripts that appeared to potentially relevant.

101 **Data extraction process and synthesis**

102 Two reviewers (D.D. and Z.S.) independently extracted data using a standardised predefined
103 spreadsheet. Inconsistencies in extracted data were resolved through consensus discussion by a third
104 reviewer (C.H.), if necessary. Results were synthesised and summarised according to analytical themes.
105 Thematic analysis was opted by the research team as it's known for its flexibility and ability of
106 identifying patterns of meaningful information within the data. ⁽¹²⁾

107 **Quality appraisal**

108 The quality of the included papers was independently assessed by two reviewers (D.D., Z.S.) using
109 Critical Appraisal Skills Programme (CASP) checklists.^(13, 14) Discrepancies were resolved through
110 discussion and consensus.

34 **RESULTS**

111 A total of 672 citations were retrieved from the database and other searches. After screening titles and
112 abstracts, 38 publications were obtained in full text and assessed for suitability. Of which, 14 met the
113 inclusion criteria and were included in the analysis (*See Figure 1 for PRISMA flow chart*).⁽¹⁵⁻²⁸⁾ See
114 (*Table S2; supplementary material*) for reasons of exclusion.

115 The details of the 14 studies are presented in (*Table 1 and 2*).⁽¹⁵⁻²⁸⁾ The majority of the included studies
116 were published in the last 12 years. All of the studies (n=14) took place in the United States of America.

117 Overall, eleven studies recruited parents or caregivers of children aged between 30 days to less than 9
118 years old, two studies had recruited parents with no age limitations of the child and one study recruited
119 only women of childbearing age. The majority of the studies (n=13) did report the ethnic composition
120 of their recruited sample and they were vastly Hispanic or black African American parents or caregivers.
121 One study had only exclusively recruited women from a white ethnic background. ⁽²²⁾

122 **Quality appraisal**

123 The results from the quality appraisal are shown in (*Table S3 and Table S4; supplementary material*).

124 All identified studies were included in the final synthesis with a greater emphasis on the higher quality
125 studies.

126 **Synthesis of results**

127 The data from the 14 studies were analysed and three analytical themes emerged from the analysis and
128 a summary of the review results are demonstrated in (*Figure 2*).

129 **Types and causes of medication administration errors among children led by parents or child** 130 **outside a clinical setting:**

131 Eight of the included studies indicated that paediatric dosing errors are among the most common
132 medication errors made by parents. ^(15, 18-21, 23, 24, 26) Among these studies, two randomised trials identified
133 that overdosing errors are more common among parents. ^(23, 24) While another cross sectional study
134 looking at parents with child on a short course prescribed medication reported that the majority of the
135 parents measured below the prescribed dose. ⁽¹⁵⁾ A study by Morrison *et al.* reported that parents who
136 made under-dosing errors made more dosage errors and frequency errors compared with those who
137 made an overdosing error. ⁽²⁰⁾

138 From the included studies, it was noticed that the magnitude and frequency of dosing errors by parents
139 were influenced by two factors: measurement tool used by parents and the dose volume (amount) . In
140 one study, parents stated that non-standardised kitchen spoon was their primary dosing tool. ⁽¹⁷⁾ Two
141 studies reported that errors were more common with measuring cups than with syringes, in particularly
142 with small dose volumes (amounts). ^(21, 24) In a cross sectional study conducted in the USA, the majority
143 66% of the parents considered oral syringes are the best tool for dosing accuracy, while 23.5% believed
144 that cups were the best, however, few 10.1% believed that dosing spoon, measuring spoon, kitchen
145 teaspoon and droppers were the best. ⁽²⁷⁾ Another study reported that larger dosing errors; (>40%
146 deviation of the recommended dose) were made by parents using cups with printed marking and etched
147 markings, this was thought to be due to confusion about teaspoon vs tablespoon instructions,

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3 148 assumptions that the cup is the unit of measure and the full cup is the dose. ⁽¹⁶⁾ Labels and units of the
4
5 149 prescribed medication were contributing factors to dosing errors.⁽²⁴⁾ Parents made significant dosing
6
7 150 errors when the units found on the medication bottle label were not similar to the units used on the
8
9 151 dosing tool.⁽²⁴⁾ Parents who used teaspoon/tablespoon units were likely to use a non-standardised dosing
10
11 152 instrument and make errors in measuring the prescribed and intended dose. ⁽¹⁹⁾The final potential factor
12
13 153 was the type of instructions provided. For liquid medication, less errors were seen among parents who
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15 154 were provided with text-plus-pictogram instructions 43.9% compared with text-only instructions 59.0%
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17 155 and this group were also less likely to make overdosing errors. ⁽²⁶⁾ Parents who received standard
18
19 156 medication counselling were 47.8% more likely to make dosing errors when compared with parents
20
21 157 who received pictogram instruction (5.4%).⁽²⁵⁾

25 158 **Factors related to patients or caregivers and medication errors**

27 159 *Health Literacy*

29
30 160 Health literacy of caregivers in the studies were assessed, six conducted further analyses of its influence
31
32 161 on dose accuracy and other co-factors related to medication errors. Yin *et al.* reported that caregivers
33
34 162 with inadequate or marginal health literacy were more likely to use a non-standardised dosing
35
36 163 instrument and further lacked knowledge on weight based dosing for over the counter medication when
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38 164 compared with caregivers with adequate health literacy. ⁽¹⁷⁾ Another study by Yin *et al.*, found a
39
40 165 significant association between health literacy and dosing errors using cups and dosing spoons. ⁽¹⁶⁾In
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42 166 adjusted analysis conducted by Williams *et al.*, they found that there was a strong association between
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44 167 health literacy levels and measurement tool preference in particular cups, parents with limited literacy
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46 168 reported that dosing cups were the tool of choice most of the time (aOR=2.4).⁽²⁷⁾ The use of a
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48 169 teaspoon/tablespoon was associated with errors in the intended dose for those with low health literacy
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50 170 but not for those with adequate health literacy.⁽¹⁹⁾ Harris *et al.* identified that parents with limited health
51
52 171 literacy and Limited English Proficiency (LEP) made the most dosing errors. ⁽²¹⁾ Similarly, Kalow *et*
53
54 172 *al.* revealed that parents with inadequate and marginal health literacy committed dosing errors, but the
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56 173 sample size of this group was small compared with the adequate health literacy group. ⁽¹⁸⁾

174 *Language*

175 Association between health literacy and lack of knowledge of weight-based dosing varied by English
176 speaking caregiver's. For English speaking caregivers 88.6% of inadequate or marginal health literacy
177 caregivers were unaware of weight based dosing in comparison to 54.1% of caregivers with adequate
178 health literacy.⁽¹⁷⁾ In contrast, Yin *et al.* found that there was no significant relation between dosing
179 error and (LEP).⁽²⁶⁾ However, there were some differences in teaspoon-associated errors in measurement
180 by language.⁽¹⁹⁾

181 *Comprehension and recall of instructions in relation to parent sociodemographic status*

182 Yin *et al.* reported that parents from a low sociodemographic status who were prescribed a daily dose
183 and who received a simple language, pictogram instructions sheets, were less likely to make errors in
184 knowledge of dose frequency and dose accuracy compared with the control group who received
185 standard medication counselling (0% vs 15.1%).⁽²⁵⁾ Participants among the interventional group were
186 less likely to report incorrect medication preparation related to shaking the medication before
187 administration for both daily doses (10.9% vs 28.3% $P= 0.04$) and as needed medication (21.5% vs
188 43.0%).⁽²⁵⁾ Participants in the interventional group were less likely to use a non-standardised
189 measurement tool compared with the parents in the standard group (daily dose: 93.5% vs 71.7%; as
190 needed: 93.7% vs 74.7%).⁽²⁵⁾ Torres *et al.* a cross-sectional study that analysed data from a randomised
191 control study, looked at parents preference and perceptions in regards to units of measurements. It was
192 found that over 80% of the parents perceived a change to millilitre only instructions would be easy in
193 comparison to 14% found it some how hard and 4.1% very hard.⁽²⁸⁾

194 **Interventions aimed at reducing medication administration errors occurring among children** 195 **outside a clinical setting**

196 *Parent's sociodemographic factors*

197 Four studies suggested that parental sociodemographic risk factors should be considered when
198 designing an intervention aimed at averting medication administration errors.^(16, 17, 21, 26) Amongst these
199 factors were parents' health literacy as well as language. Kalow and his colleagues suggested that efforts

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3 200 to streamline interpreter services must be continued as well, to having a more formalised approach in
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5 201 place to elucidate the patient's preferred language for communication. ⁽¹⁸⁾
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8 202 *Counselling and training*

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11 203 Three studies suggested that provisional dose counselling (showing the patient how to prepare the dose)
12
13 204 in combination with verbal counselling could be associated with less dosing errors. ^(15, 17, 23) A study by
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15 205 Yin *et al.* indicated that errors occur across different counselling approaches, and they have
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17 206 recommended developing new strategies to ensure that parents understand medication instructions as
18
19 207 well as the need for further research to identify the best counselling strategies and how to incorporate
20
21 208 these within clinical practice. ⁽¹⁵⁾ Yin *et al.* suggested the need for intensive teaching, training and
22
23 209 coaching programmes that can accommodate for different parental health literacy levels. ⁽²⁴⁾
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26 210 *Tools, labels and instructions*

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29 211 Yin *et al.* suggested a promising strategy that could potentially help to reduce paediatric-dosing errors,
30
31 212 which was to match the dosing tool with the prescribed dose volume and move towards more simplified
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33 213 numerical markings on the measurement tools as well as to move to millilitre-only units. ^(24, 26, 28) Wallace
34
35 214 *et al.* indicated in his study that some parents would prefer instructions with explicit dosage intervals
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37 215 with the exact time and dose to be specified on the label. ⁽²²⁾ Harris *et al.* suggested improving the
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39 216 availability of language concordant labels that could accommodate for different health literacy levels. ⁽²¹⁾
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41 217 Three studies from this review strongly suggested the importance of utilising pictographic dosing
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43 218 instructions and how it could be a positive aid in reducing paediatric dosing errors. ^(23, 25, 26) Majority of
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45 219 parents would be comfortable with millilitre dosing instructions only.
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48 220 **DISCUSSION**

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52 221 The results of this study suggest that parents appear to make a range of medication errors, particularly
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54 222 with liquid medications as documented by prior studies that were conducted also in the USA as well as
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56 223 studies from this review. ^(2, 4, 23, 25) The majority of the included studies indicated that dosing errors were
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58 224 amongst the most common medication errors made by parents, which is consistent with another study,
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3 225 which was conducted on Spanish –speaking Latino parents.^(15, 19, 21, 25, 29)This review identified possible
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5 226 causality behind parents dosing errors other than just the effect of health literacy; these errors could be
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7 227 linked to the: dose volume prescribed, measurement tools used, units used on the labels and the
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9 228 instructions provided.

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12 229 Although standardised measurement tools are usually dispensed with the prescribed liquid medications
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14 230 in the UK, this review identified that the studies published in the USA indicated that parents still use
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16 231 non-standardised liquid dosing tools as their primary measuring tool; this has been previously linked
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18 232 with medication administration errors by both Yaffe *et al.* and McMahon *et al.*.^(30, 31) The review found
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20 233 that pairing the medication labels to the closest measurement tool size, particularly for millilitre-only
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22 234 labels and tools, could be associated with a reduction in parent dosing and administrating error rates, as
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24 235 well as a decrease in the likelihood of parents using non-standardised measurement tools as suggested
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26 236 by another research.^(19, 32)

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30 237 The review showed that the use of simple pictographic based medication instructions with explicit
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32 238 dosage intervals could reduce dosing errors by parents. This finding was consistent with previous
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34 239 existing data from both South and West Africa as well as the USA regarding the use of pictographic
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36 240 illustrations as a supportive tool to aid parents in administering medication to their children correctly.
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38 241⁽³³⁻⁴¹⁾ Potentially this could benefit both parents and caregivers with limited or low health literacy levels.

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41 242 Our findings are consistent with prior USA studies investigating the link between adult's
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43 243 sociodemographic factors, particularly health literacy, and medication administration problems.⁽⁴²⁻⁴⁵⁾
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45 244 Four studies explicitly highlighted that sociodemographic factors, such as health literacy and language,
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47 245 must be incorporated into any future intervention that aims to reduce parental dosing and administration
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49 246 errors.

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52 247 The results of the review highlighted several interventions to aid parents and patients to potentially
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54 248 reduce medication administration errors at home. This include the use of plain language combined with
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56 249 provision of using the dosing tool provided as well as incorporating pictographic instructions which
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58 250 were consistent in four of the included studies.^(15, 23, 25, 26) Pictographic-plain instructions significantly
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251 improve the accuracy of dosing and administering medication to children especially for those parents
252 with insufficient health literacy. ^(25, 26)

253 This study emphasised potential areas that could be incorporated into real practice that could help with
254 reducing medication administration errors done by parents/caregivers and patients. Potential strategies
255 include personalised training and coaching that accommodate different health literacy levels and
256 languages as well as the possibility to match the dosing tool with the prescribed volume alongside the
257 use of millilitre units.

258 Our review is subject to several limitations. Firstly, our search strategy was designed to be
259 comprehensive, but it is possible that some studies were missed. Secondly, English and published article
260 were only included in this review, so publication bias may exist. Third, although the study aimed at
261 including medication administration challenges for younger people aged between 16 and 18 years old,
262 however non were included as they did not pass the eligibility criteria for this review. Future studies
263 are needed where young people aged 16 to 18 years old are included as a participants. Thirdly the
264 generalisability of the study results maybe low, this is due to the fact that the majority of the studies
265 were conducted in the USA and emerged from the same research group Yin *et al.* This research group,
266 have highlighted in their studies several limitations, such as the use of hypothetical scenarios that might
267 not be a true reflection on how parents measure the dose at home. ^(16, 23, 24, 26) For some randomised trial
268 studies, it was difficult to maintain blindness as some of the participants revealed their allocated group,
269 while for the cross sectional studies, no conclusion of the causes could be drawn. ^(17, 19, 25) Finally the
270 date of publication for one of the studies was 13 years old⁽¹⁷⁾, which would not take into account the
271 changes that have occurred in terms of interventions that would vary locally, nationally and
272 internationally. However, this review highlights that non-standard dosing still occurs to date due to
273 parent preference based on recent evidence in 2018 ⁽²⁸⁾.

274 **Conclusions**

275 The relationship between medication administration errors and problems experienced by and parents
276 outside a clinical setting has not been well described from the literature with no relevant studies

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3 277 examining the issue outside the USA. The studies explored the relation of dosing errors and parent's
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5 278 understanding, interpretation of administration instructions and tools to help them administer their
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7 279 medication either by the manufacturer or other supplier, health literacy as well as other
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9 280 sociodemographic factors. Due to the gap in the knowledge outside of the USA and the heterogeneity
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11 281 of healthcare provision worldwide, future studies, need to focus on the current medication
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13 282 administration challenges among children and young people happening outside a clinical setting from
14
15 283 a patient and a parent perspective, in the UK and worldwide..

18 284 **No grant/award information in the Funding information**

21 285 This study was not funded. It's done as part of the author (DD) PhD research project.

24 286 **What is known about this topic?**

- 26 287 1- Medication administration errors occur frequently among children.
- 28 288 2- Parent's health literacy could be associated with medication administration problems in
30 289 children.
- 32 290 3- Studies examining parent administrator paediatric medicine accuracy were mainly from one
34 291 particular research group in the USA with participant parents using non-standardised
36 292 measuring tools

40 293 **What this study adds:**

- 42 294 1- The nature of medication administration error's happening at home are not well documented
44 295 across each age group.
- 46 296 2- The need to explore parents and patients perspective in regards to medication administration
48 297 challenges happening at home.

Table 1 : Characteristics of the observational included studies in the review (listed by health literacy test).

Study Information		Participants Characteristics			Findings		
First Author (Year)	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Morrison et al. (2017) ⁽²⁰⁾	Outpatient clinic and emergency department	Interviews and applied assessment	To examine the association between parent health literacy and pain medication knowledge and applied skills in parents of children with sickle cell disease.	Parents of children 1 to 12 years old.	100	Newest Vital Sign (NVS)	Parents with low health literacy made more under dose frequent errors on the pain treatment skills. Health literacy was not associated with errors on the applied treatment skills. Parents recalled under-dosing of medication (both dose and frequency). On the applied pain treatment skills, parents made both underdosing and overdosing errors.
Torres et al. (2018) ⁽²⁸⁾	Paediatric outpatient clinics	Cross sectional analysis	Sought to examine the interrelationships between parents' preferences and perceptions regarding unites of measurement, parents millilitre dosing experiences, and parent health literacy.	Parents or legal guardian of children ≤ 8 years old.	493	Newest Vital Sign (NVS)	Parents preferred the millilitre dosing to be easy; few 11.5% prefers teaspoon units. Parents with low health literacy levels had a higher odd of having a teaspoon preference and greater odds of perceiving difficulty with the millilitre only dosing.
Williams et al. (2019) ⁽²⁷⁾	Outpatient clinics	Cross sectional analysis	To assess parent decision-making regarding dosing tools, a known contributor to medication dosing errors, by evaluating parent dosing tool use, beliefs, and access, and the role of health literacy, with a focus on dosing cups, which are associated with an increased risk of multi-fold overdose.	Parents or legal guardians of children aged ≤ 8 years old.	473	Newest Vital Sign (NVS)	Health literacy is one of the factors that could be associated with the dosing tool choice. Parents with limited health literacy reported that dosing cups were the tool used most of the time.
Yin et al. (2010) ⁽¹⁶⁾	Pediatric clinic	Observational	To assess parents' liquid medication administration errors by dosing instrument	Parents of children with no specific age limitation.	302(287 mothers, 8 fathers, 7	Newest Vital Sign (NVS)	Health literacy was significantly related to doing errors with the cups as well as the dosing spoon, while non-significant trend was seen for the dropper and the oral syringes with the bottle adaptor.

			type and to examine the degree to which parents' health literacy influences dosing accuracy.		legal guardians)		
Samuels-Kalow et al. (2013) ⁽¹⁸⁾	Tertiary	Prospective observational	To examine language-based disparities in discharge communication and parental understanding of discharge instructions.	Parents of children 2 to 24 months.	145	Short Test of Functional Health Literacy (S-TOFHLA)	Parents had acetaminophen dosing errors. There is significant association between language and dosing errors. Parents with marginal or inadequate health literacy had dosing errors compared with adequate health literacy.
Yin et al. (2014) ⁽¹⁵⁾	Paediatric emergency department	Interviews and observations	To examine the degree to which recommended provider-counselling strategies, including advanced communication techniques and dosing instruments provision, are associated with reductions in parents liquid medication dosing errors.	Parents of children aged < 8 years old.	287	Short Test of Functional Health Literacy (S-TOFHLA)	Majority of the patents made underdoing errors as well as few made overdosing errors. Recipients of at least one advanced counselling were less likely to make a dosing error compared with those who did not report received advanced counselling. Parent who received dosing instrument from the emergency department made fewer errors. For adequate health literacy levels was significantly associated with fewer errors when they have received advanced counselling in combination with instrument provision but not the low literacy.
Shonna Yin et al. (2014) ⁽¹⁹⁾	Emergency department	Interviews and observations	To examine the association between unit used and parent medication errors and whether nonstandard instruments mediate the relationship.	Parents of children aged <9 years old.	400	Short Test of Functional Health Literacy in Adults (S-TOFHLA)	Parents made different kind of error in measurement. 1 in 6 parents used kitchen spoon rather than a standard instrument. Parents did not used the unit listed on the prescription or label.
Yin et al. (2007) ⁽¹⁷⁾	Pediatric emergency department.	Interviews	To assess whether low caregiver health literacy was related to risk factors for liquid medication dosing errors, including reported use of non-standardised dosing tools and lack of knowledge about weight based dosing.	Parents and caregivers of children aged between 30 days to 8 years old.	292	Test of Functional Health Literacy in Adults (TOFHLA)	Low health literacy, particularly reading comprehension, was associated with reported use of non-standardised dosing instruments and lack of knowledge regarding weight based dosing. In addition, this has been found previously to be associated with decreased dosing accuracy.

Table 2: Characteristics of the randomised controlled experiment included in the review (listed alphabetically according to first author).

Study Information		Participants Characteristics			Findings		
First Author (Year)	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Wallace et al. (2012) ⁽²²⁾	Outpatient clinic	Randomized Controlled Trial	To address the gap by addressing whether instructions wording that implicit versus explicit dosage intervals was associated with participant's ability to describe and correctly measure a dose of a commonly prescribed liquid pediatric prescription medication.	Women of childbearing age.	193	Estimated using three established items: -How often do you have problems learning about your medical condition because of difficulty understanding written information? - How often do you have someone help you read hospital martials? - How confident are you filling out medical forms by yourself?	One third of the participants (32.1%) were able to describe and measure the dose accurately. Participants with inadequate health literacy skills were one third as likely to measure a dose of the medication correctly.
Shonna Yin et al. (2016) ⁽²⁴⁾	Pediatric clinic	Randomized controlled experiment	Hypothesized that unit concordance would be associated with fewer errors and that parents would measure most accurately with syringes we also sought to examine differences in impact by parents health literacy and language because low health literacy and limited English proficiency are factors known to place children at risk for errors.	Parents of children aged ≤ 8 years old.	2099 parents	Newest Vital Sign (NVS)	Nearly all parents (99.3%) measured ≥ 1 dose that was not the exact amount. Overdoing (8.0%) was the majority of the errors. Dose amount of 2.5 and 7.5 mL was associated with more errors when compared with 5 mL (2.5 vs 5 mL adjusted odds ratio [aOR]=4.2; 95% CI,3.8-4.6; 7.5 vs 5 mL [aOR]=2.4;95%CI, 1.2-1.5).
Harris et al. (2017) ⁽²¹⁾	Outpatient	Randomized Controlled Experiment	To examine the association between health literacy and limited English proficiency and	Hispanic parents of children <8 years old.	1126 parents	Newest Vital Sign (NVS)	80% of the recruited parents had Limited English Proficiency (LEP), 82.7% had limited literacy. Of parents who had Limited English

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			liquid medication dosing errors in Hispanic parents				Proficiency (LEP) 88.8% had limited and 1.2% adequate health literacy. 3.1% of parents made a dosing error at least one out of the nine dosing trials. Parents with limited health literacy and with limited English Proficiency (LEP) made the most dosing error and errors varied by dose amount and tool type.
Yin et al. (2011) ⁽²⁶⁾	Outpatient pediatric clinic	Randomized Controlled Trial	To sought whether a pictographic dosing diagram included as part of written instructions can decrease parent errors in dosing infant acetaminophen as well as whether pictogram benefit varies by parent health literacy level.	Parents or caregiver of a child with no specific age limitation.	299 parents were assessed	Newest Vital Sign (NVS)	Both groups were associated with poor dosing with the tendency for the parents who have received text plus pictogram significantly less likely to make dosing error (0.6%) compared with parents who received text only instructions (5.6%). Parents with low literacy who received the text plus pictogram instructions were significantly less likely to make errors in dosing compared with who received text only instructions (50.4% vs 66.4%; $P=.02$).
Yin et al. (2017) ⁽²³⁾	Pediatric outpatient clinic	Randomized controlled experiment	To examine the degree to which errors could be reduced with pictographic diagrams, millilitre-only units, and provision of tools more closely matched to prescribed volumes	Parents of children aged \leq 8 years old.	2099 for all arms	Newest Vital Sign (NVS)	Majority of the parents (99.3%) made dosing errors. More errors with the 2 and 7.5 mL dosing amount when compared with the 10 mL (2 mL vs 10 mL aOR =3.7; 7.5 mL vs 10 mL aOR= 1.4). Parents who received text and pictogram dosing instructions with mL only labels and tools had decreased odds of making a dosing error compared with received mL/tsp labels and tools with or without pictographic dosing instructions.
Yin et al. (2008) ⁽²⁵⁾	Pediatric emergency department	Randomized Controlled Trial	To evaluate the efficacy of a pictogram based health literacy intervention to decrease liquid medication administration errors by caregivers of young children.	Parents and caregivers of children aged 30 days to 8 years.	245	Test of Functional Health Literacy in Adults (TOFHLA)	Caregiver's dose accuracy was higher among the intervention group prescribed daily and as needed medications regardless of the cut-off point was 20% or 40%. 4% of the intervention caregivers whose children had been prescribed daily doses gave inaccurate dose at the 20% cut-off point, compared with 47.8% of control caregivers. The study suggested that there is no health literacy association with the dosing errors.

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Author's response to the Associate Editor and the reviewer's comments

The authors want to thank the associate editor and the reviewers for their comments. The authors have addressed the reviewer's comments in track changes (marked copy) in the main manuscript.

Associate Editor Comments

Comment Number	Details of the comment	Author Response
1	Several of the papers you have excluded have looked at effect of health literacy on med errors. It suggests that your exclusion criteria are too strict. You ideally should include these studies. These studies are from countries where illiteracy is a greater problem. This will significantly improve your paper. If you need more time ask for it. you will need to create another table listing these studies	<p>Thank you for your comment. The authors have re-evaluated the excluded studies carefully again upon your recommendation and based on that, further explanation behind the excluded studies were added beyond health literacy assessment if appropriate. The issue with the excluded studies is that they did not directly address health literacy or/ nor used a validated tool, which is important as its one of the eligibility criteria of this review. We appreciate that there were many studies in the excluded studies from countries where illiteracy is a greater problem, however, for example the paper by Almazrou, S (2014) assessed the mothers experience with using devices and compared that with their accuracy in dosing the devices, but they did not assess the health literacy but used educational level as a proxy measure.</p> <p>At this stage, if we elect to change our inclusion and exclusion criteria, the authors would need to rewrite the entire review which at this stage of the peer-review. We would be grateful if BMJ Open Paediatrics would accept this systematic review with this current inclusion and exclusion criteria and methodology, which has been registered with NIHR PROSPERO and on the basis that this manuscript has been reviewed twice by the peer-reviewers and their comments addressed.</p>
2	Apologies for the advice given by the editorial assistant re tables. Tables S3 and S4 NEED to be in the main paper. Delete country of origin from the tables as they are all from the USA and this can be stated in the text.	Thank you for your comment. Included studies table S3 and S4 now have been moved to the main manuscript (Table 1 and table 2). The origin of country has been removed.
3	List the studies by the health literacy test NOT alphabetically.	Thank you for your comment. This has been amended.

4	Tables 1 and 2 should become supplementary tables	Thank you for your comment. This has been moved as a supplementary tables S2 and S3.
5	Your study has become clearer in that you only included studies that evaluated health literacy. You therefore need to word your paper appropriately.	Thank you for your comment. Amendments were made across the manuscript to address your feedback in regards to health literacy. As the research team aimed to look at medication administration issues in relation to health literacy, more causalities were obtained in the literature and were addressed in the manuscript but all were looking at health literacy of their targeted population.
6	Abstract Objective - combine the two sentences or include health literacy within the 1st sentence.	Thank you for your comment. This has been amended.
7	Discussion - you need to compare your findings in relation to the general literature re med errors where health literacy is not studied.	Thank you for your comment. Amended were done on the discussion to further highlight our results with previous data as well as adding a global perspective to it. it was noted during this process that limited data were found outside the US however most information reported in the manuscript could be applied elsewhere as advised by one of the reviewers to amend the generalisability of this review.
8	Discussion page 12 delete the first 2 sentences and " However, we found that "in the 3rd sentence.	Thank you for your comment. The discussion has been amended We have removed the sentences, "This systematic review was designed by interdisciplinary paediatric expertise in the pharmaceuticals and pharmacy practice field. The review was registered on PROSPRO and conducted using PRISMA checklist. However, we found that" and start the paragraph off with: - "Our review....."
9	The restriction of your review to English papers only is a MAJOR limitation and this needs to be clearly stated.	Thank you for your comment. We have stated within the discussion section the main limitations of the study. In addition, we have emphasised that one of the limitations is including English only studies.
10	Literacy is a greater problem in Low and lower middle income countries and thus your search strategy excludes any studies	Thank you for your feedback. we have not initially excluded studies from low and lower middle income initially, but we had to be systematic and follow the stated eligibility to ensure accuracy across included studies as this was not conducted by one reviewer. The

	from these countries by only including validated health literacy tests.	research question as well as the protocol was designed by the research authors named in this paper, however, further guidance and assistance to ensure the designed protocol was accurate information specialist as well as other academics reviewed the strategy and amendment was done accordingly.
11	You need to expand your discussion to give a global perspective	Thank you for your comment. The authors have where possible attributed the discussed studies to the country where the study was conducted, e.g. USA, South and West Africa.

Reviewer number 1

Comment Number	Details of the comment	Author Response
1	line 53: people THAT need	Thank you for your comment. The amendment has been made and the sentence referred to by reviewer 1 reads:- - “Counselling, medication administration instructions and measurement tools are some of the areas in addition to the sociodemographic characteristics of parents and young people that need to be considered when designing any future potential intervention aimed at reducing medication errors among children and young people at home. “
2	Introduction line 3: medication ERRORS?	Thank you for your comment. Errors has been added.
3	line 4: Previous studies have recognised... Results	Thank you for your comment. We have amended this sentence and now reads as the following:

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		“Previous studies have recognised potential factors that can contribute to clinician led medication administration errors in children”
4	line 92: you say that 23% of parents thought cups were best, but it is not clear if 76% thought they were worst!?	Thank you for your comment. This sentence has been amended and now reads as the following: “In a cross sectional study conducted in the USA, the majority 66% of the parents considered oral syringes are the best tool for dosing accuracy, while 23.5% believed that cups were the best, however, few 10.1% believed that dosing spoon, measuring spoon, kitchen teaspoon and droppers were the best.”
5	line 94: is there any clarification as to why markings should lead to an overdose. It is quite a statement to make without any clarity.	Thank you for your comment. The following sentence has been amended and further clarification was added. Now reads as the following: “Another study reported that larger dosing errors; (>40% deviation of the recommended dose) were made by parents using cups with printed marking and etched markings, this was thought to be due to confusion about teaspoon vs table spoon instructions, assumptions that the cup is the unit of measure and the full cup is the dose.”
6	line 149: what is "provisional dose counselling"?? Discussion	Thank you for your comment. The following explanation is added : “(showing the patient how to prepare the dose)”
7	line 208: I would say the generalisability of the study "may be" low - most aspects can be considered everywhere.	Thank you for your comment. This has been changed now.

Reviewer number 2:

Comment Number	Details of the comment	Author Response
1	L3 – Second sentence needs rewording it does not make sense	Thank you for your comment. This has been changed and now reads as the following: “When it comes to medication administration for children at home, a significant burden of responsibility relies on the parent or on the patients themselves”

2	L4 - third sentence – change tense – remove “In”	Thank you for your comment. This has been amended.
3	L8 - depends should be depend	Thank you for your comment. We have changed it to depend.
4	L26 – is should be was	Thank you for your comment. We have changed it to was.
5	L29 – are should be were	Thank you for your comment. This has now changed to were.
6	L61 – gap between 672 and citations	Thank you for your input. A gap has been added.
7	L63 – sentence does not make sense excluded should be exclusion possibly	Thank you for your comment. The sentence has been amended. Now reads as the following: “Of which, 14 met the inclusion criteria and were included in the analysis (See Figure 1 for PRISMA flow chart). (15-28) See (Table S2) for reasons of exclusion.”
8	L75 – to should be on	Thank you for your comment. This has been amended to on instead of to.
9	L84 – remove has	Thank you for your comment. It has now removed.
10	L90 - is should be was	Thank you for your comment. This has now been changed.
11	L93 – are should be were	Thank you for your comment. This now has been changed to were.
12	L97 – use should be used	Thank you for your comment. This now has been changed to used.
13	L98 – Add The to the beginning of the sentence	Thank you for your comment. This has been added now.
14	L 99 - error should be errors	Thank you for your comment. This has been changed to errors.
15	L102 – remove a	Thank you for your comments. This has been removed now.
16	L110 – Remove In and they	Thank you for your comment. Both have been removed now.

17	L112 – is should be was	Thank you for your comment. This has been changed to was now.
18	L116 – et al should be in italics	Thank you for your comment. This has been changed now.
19	L124 - add et al	Thank you for your comment. This has been added now.
20	L128 – add a between prescribed and daily	Thank you for your comment. This has now been added.
21	L136 - et al in italics	Thank you for your comment. This has been changed now.
22	L139 – will find should be found	Thank you for your comment. Will find has been removed and found added instead.
23	L145 – are should be were	Thank you for your comment. This has been amended.
24	L146 remove as, to	Thank you for your comment. As has been removed.
25	L152 – remove they have suggested	Thank you for your comment. This has been removed now.
26	L153 remove advance	Thank you for your comment. Advance has been removed now.
27	L158 which is should be was	Thank you for your comment. This has been changed now to was.
28	L160 - a gender specific pronoun has been used – check this	Thank you. The authors have checked through the papers to look for gender specific pronouns such as, “him”, “her”, “He”, “she”, but could not locate this pronoun. The only time gender specific pronouns the authors may have used were in the articles that may have mentioned mother and father specifically.
29	L169 are should be were	Thank you for your comment. This has been changed now.
30	L171 remove reasons	Thank you for your comment. This has been removed now.

31	L177 use either could be or potentially not both	Thank you for your comment. Potentially has been removed.
32	L195 The should be this	Thank you for your comment. The has been removed and this has been added instead.
33	195 can should be could	Thank you for your comment. This has been changed now.

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Figure 1: Flow diagram for the study selection based on PRISMA flow diagram

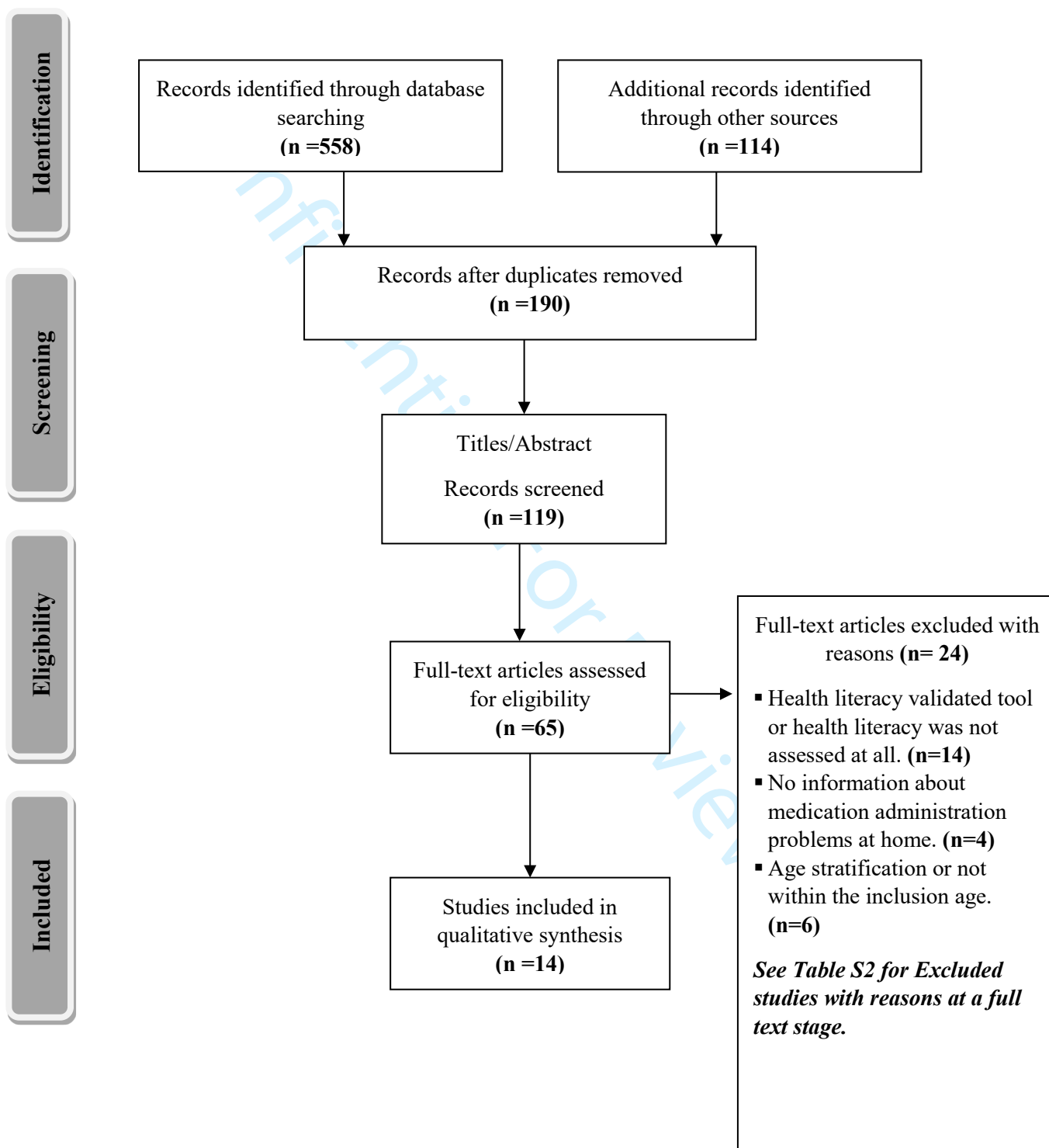


Figure 2: list of the review results

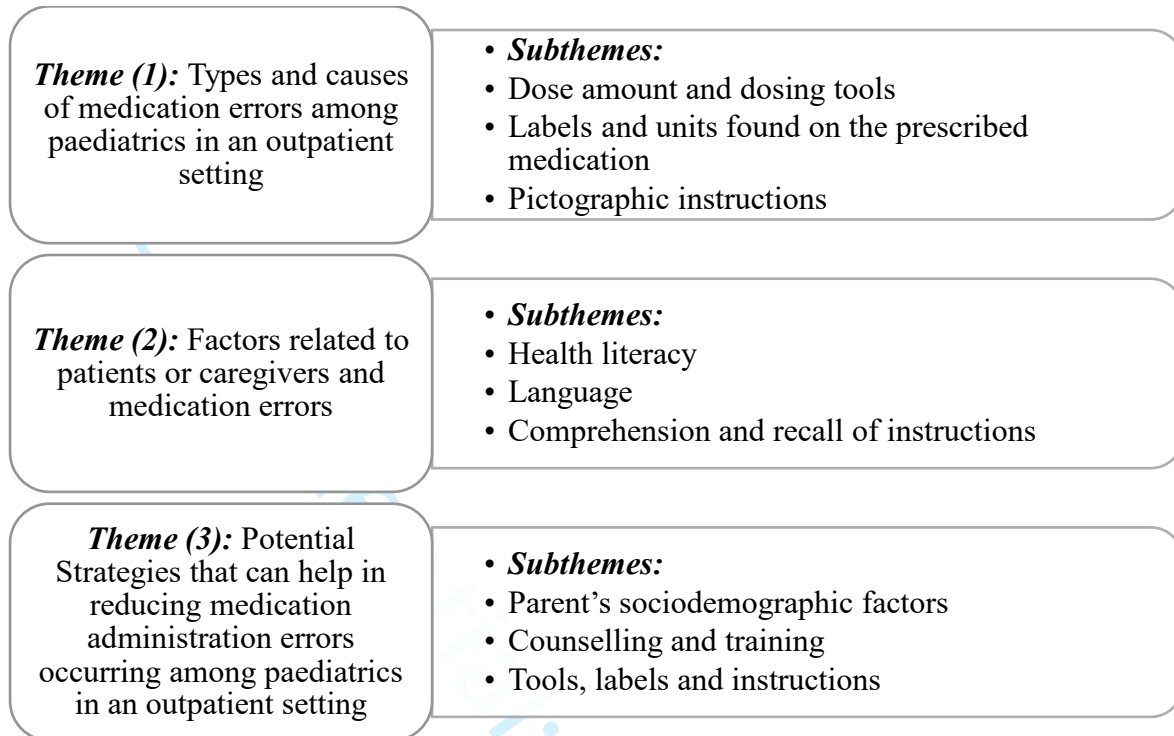


Table S1: Search Strategy for Systematic Review per database

Database	Search strategy
1- PubMed	<p>1- (((child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or teenager* or youth or infant* or newborn* or neonate*))) AND</p> <p>2- (("medical error*" or "medication error*" or "medication administration error*" or "drug administration error*" or "medicine administration error*" or "medication safety" or "optimisation" or "optimization" or "dosing error*")) AND</p> <p>3- (("health literacy" or "literacy" or "literate")).</p>
4- Scopus	<p>1- (child OR children OR pediatric* OR paediatric* OR toddler* OR adolescent* OR baby OR babies OR teen* OR teenager* OR youth OR infant* OR newborn* OR neonate*) AND</p> <p>2- (health AND literacy OR literacy OR literate) AND</p> <p>3- (medical AND error* OR medication AND error* OR medication AND administration AND error* OR drug AND administration AND error* OR medicine AND administration AND error* OR medication AND safety OR optimisation OR optimization OR dosing AND error*)</p>
5- Web of Science	<p>1- TOPIC: (child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or youth* or infant* or newborn* or neonate*) <i>AND</i></p> <p>2- TOPIC: ("health literacy" or "literacy" or "literate") <i>AND</i></p> <p>3- TOPIC: ("medical error*" or "medication error*" or "medication safety" or "medication administration error*" or "medicine administration error*" or "drug administration error*" or "dosing error*" or "optimisation" or "optimization")</p>
6- Cochrane Library	<p>1- "health literacy" or "literacy" or "literate" in Title Abstract Keyword AND</p> <p>2- "medication error" or "medical error" or "medication administration error" or "medicine administration error" or "drug administration error" or "dosing error" or "medication safety" or "optimisation" or "optimization" in Title Abstract Keyword AND</p> <p>3- child or children or pediatric or paediatric or toddler or adolescent or baby or babies or teen or teenager or youth or infant or newborn or neonate in Title Abstract Keyword - (Word variations have been searched)</p>

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Table S2: Excluded studies at full text stage with reasons for exclusion:

Author	Study Title	Reason For Exclusion
Almazrou, S. (2014)	Ability of Saudi mothers to appropriately and accurately use dosing devices to administer oral liquid medications to their children	The study conducted in Saudi Arabia. The study was designed to assess Saudi mother's experiences with measuring cups, syringes and droppers for oral liquid medications, and compared the accuracy of dosing across these devices. The study looked at the educational level as a factor that might influence dose accuracy and did not assess the health literacy levels of participants.
Boztepe, H. (2016)	Administration of oral medication by parents at home	The study was conducted in Turkey. The study aimed at determining the practices and difficulties experiences by the parents at home when administering oral medication to their children. However, the study did not assess the health literacy levels of the participants.
Brass, E. P. (2018)	Medication Errors With Pediatric Liquid Acetaminophen After Standardization of Concentration and Packaging Improvements	The study used poison control centre data to assess if the mitigation efforts by industry, have affected the rate of medication errors involving liquid acetaminophen products in children.
Chan, H. K. (2017)	Influences of pictogram-based instructions in paediatric drug labelling on dosing accuracy among caregivers: a pilot study from Malaysia	The study was conducted in Malaysia. The study investigated the influence if pictographic dosing instructions used in paediatric drug labelling on dose accuracy. The study did not assess the participant's health literacy levels.
Chew, C. C. (2019)	Medication Safety at Home: A Qualitative Study on Caregivers of Chronically Ill Children in Malaysia	The study was conducted in Australia. The study assessed the health literacy skills of parents and caregivers of children using a hypothetical dosing scenario of a child with fever. However, the study did not assess the literacy levels of

		participants or considered the tasks done by parents in order to prepare the dose is enough.
Emmertson, L. (2014)	Management of children's fever by parents and caregivers: Practical measurement of functional health literacy	The study did not state the health literacy tool.
Erickson, S. R.	Health literacy and medication administration performance by caregivers of adults with developmental disabilities	The study looked at medication administration in adults with disabilities not within the age range of this review.
Freedman, R. B.(2012)	Influence of Parental Health Literacy and Dosing Responsibility on Pediatric Glaucoma Medication Adherence	The study was conducted in the USA. The study examined medication adherence not administration.
Glick, A. F. (2020)	Accuracy of Parent Perception of Comprehension of Discharge Instructions: Role of Plan Complexity and Health Literacy	No medication administration related information more about parent's perception of comprehension of discharge instructions.
Huang, W. T. (2015)	Immigrant mothers' knowledge of medication safety and administration for young children	The study did not access the health literacy levels of the participants.
Joshi, P. (2019)	Liquid Drug Dosage Measurement Errors with Different Dosing Devices	The study was carried out to determine the magnitude of dosing errors made by parents of children aged under 5 years old, the most preferred drug delivery device and its association with age, gender, education of caregivers and number of children. However, health literacy levels was not associated with these errors.
Lee, C. H. (2017)	Inappropriate self-medication among adolescents and its association with lower medication literacy and substance use	The study was conducted in Taiwan. The study assessed inappropriate self-medication among adolescent and examines the relationships among medication literacy, substance use, and inappropriate self-medication.

		The study did not assess the health literacy levels of the participants and used previous studies that state that children and adults in Taiwan have low health literacy levels.
Lubrano, R. (2016)	Acetaminophen administration in pediatric age: An observational prospective cross-sectional study	The study was conducted in Italy. The study evaluated the appropriateness of the dosage of acetaminophen administered to children with fever, and the factors that may influence dosage accuracy. The study did not assess the health literacy levels of parents.
Manchanayake, M. G. C. A. (2018)	Patients' ability to read and understand dosing instructions of their own medicines - A cross sectional study in a hospital and community pharmacy setting	The study was conducted in Sri Lanka, looking at adult's participants and their overall knowledge in regards to written dosing instructions provided by the pharmacists on dispensing labels. Hence, it was excluded as the targeted population was not parents or young people. In addition, data for young people aged 18 years old was not stratified from others.
Ryu, G. S. (2012)	Analysis of liquid medication dose errors made by patients and caregivers using alternative measuring devices	The study was conducted in south Korea. The study was designed to understand the various factors that might affect liquid medication measurement. However, the study did not assess the health literacy levels of recruited participants.
Shone, L. P. (2011)	Misunderstanding and potential unintended misuse of acetaminophen among adolescents and young adults	The study was conducted in USA. The study identified gaps in evidence about unintentional misuse among adolescents. Although young people were recruited but data for young people was not stratified from the adult data.
Sil, A.(2017)	A study of knowledge, attitude and practice regarding administration of pediatric	The study was conducted in India, to assess the knowledge, attitude and practices regarding medicine

	dosage forms and allied health literacy of caregivers for children	administration and literacy. After a careful consideration, the study was excluded as the study looked at the participant's level of education to assess for health literacy levels.
Solanki, R. (2017)	Medication errors by caregivers at home in neonates discharged from the neonatal intensive care unit	The study did not access the health literacy levels of the participants.
Tanner, S.(2014)	Parents' understanding of and accuracy in using measuring devices to administer liquid oral pain medication	The study looked at dosing accuracy when parents used various measuring devices and aimed at identifying risk factors associated with dosing errors. However, they have not looked at health literacy levels among their selected population.
Taybeh, E. (2020)	The awareness of the Jordanian population about OTC medications: A cross-sectional study	The study evaluated the knowledge and attitudes towards the use of OTC products. The targeted population was adults and not within the specific age group that this review was aimed at.
Tobaiqy, M. (2020)	Parental Experience of Potential Adverse Drug Reactions Related to Their Oral Administration of Antipyretic Analgesic Medicines in Children in Saudi Arabia	The study was conducted in Saudi Arabia. The study explored parent's experience of potential adverse drug events after administering antipyretic analgesics. The study looked at adverse drug events after administering analgesics to children. However, The study did not assess the health literacy levels of parents.
Walsh, K. E. (2011)	Medication errors in the homes of children with chronic conditions	The study observed medication errors occurring at home. Parents and children from infants through 20 years old were recruited. the results of the children could not be stratified from the younger people.
Walsh, K. E. (2013)	Medication errors in the home: A multisite study of children with cancer	The study observed medication errors occurring at home among infants through 20 years old. The results of the children

		could not be stratified from the younger people.
You, M. A. (2015)	Parental experiences of medication administration to children at home and understanding of adverse drug events	The study was conducted in Korea. The study described parent's administration of medications to their children at home and their understanding to adverse drug events. The study briefly reported some practices that parents committed in regards to medication administration at home but the was not the aim of the study. In addition to that, health literacy levels of the parents was not assessed.

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Table S3: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Randomised Controlled Trials Research Checklist.⁽¹³⁾

CASP Question Number	Authors and date					
	Yin (2017) ⁽²³⁾	Harris et al. (2017) ⁽²¹⁾	Shonna Yin et al. (2016) ⁽²⁴⁾	Yin et al. (2008) ⁽²⁵⁾	Yin et al. (2011) ⁽²⁶⁾	Wallace et al. (2012) ⁽²²⁾
1. Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the assignment of patients to treatments randomised?	Yes	Yes	Yes	Yes	Yes	Yes
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes	Yes	Yes	Yes	Yes	Yes
4. Were patients, health workers and study personnel 'blind' to treatment?	No	No	No	No	No	No
5. Were the groups similar at the start of the trial	Yes	Can't Tell	Yes	Yes	Yes	Yes
6. Aside from the experimental intervention, were the groups treated equally?	No	Yes	Yes	Yes	Yes	Yes
7. How large was the treatment effect? ^a	Yes	Uncertain	Yes	Yes	Yes	Uncertain
8. How precise was the estimate of the treatment effect? ^b	Yes	Yes	Yes	Yes	Yes	Yes
9. Can the results be applied to the local population, or in your context?	No	No	No	No	No	No
10. Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes	Yes	Yes
11. Are the benefits worth the harms and costs?	Yes	Yes	Yes	Yes	Yes	Yes

^a Based on the power calculation of the sample size and the primary outcomes results stated clearly.

^b Based on the extract ρ value and CI value of the primary outcome.

Table S4: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Quality Research Checklist.⁽¹⁴⁾

CASP Question Number	Authors and date							
	Williams et al. (2019) ⁽²⁷⁾	Torres et al. (2018) ⁽²⁸⁾	Morrison et al. (2017) ⁽²⁰⁾	Shonna Yin et al. (2014) ⁽²⁹⁾	Samuels- Kalow et al. (2013) ⁽¹⁸⁾	Yin et al. (2007) ⁽¹⁷⁾	Yin et al. (2010) ⁽¹⁶⁾	Yin et al. (2014) ⁽¹⁵⁾
1. Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the data collected in a way that addressed the research issues?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Has the relationship between researcher and participants been adequately considered?	Yes	Yes	Can't Tell	Can't Tell	Yes	Yes	Yes	Can't Tell
7. Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Is there a Value of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

BMJ Paediatrics Open

A Literature review of medication administration problems in paediatrics by parent/caregiver and the role of health literacy

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Complete List of Authors:	Dahmash, Dania; Aston University, Pharmacy Shariff, Zakia; Aston University Kirby, Daniel ; Aston University Terry, David; Aston University, School of Pharmacy Huynh, Chi; Aston University
Keywords:	Pharmacology, Qualitative research, Health services research

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4 1 **A Literature review of medication administration problems in**
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6 2 **paediatrics by parent/caregiver and the role of health literacy**
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8 3 Dania Dahmash, MSc, Aston University, Aston Pharmacy School

9 4 Zakia Shariff, MPharm, Aston University, Aston Pharmacy School

10 5 Dr. Daniel Kirby, PhD, Aston Pharmacy School

11 6 Dr. David Terry, PhD, Aston Pharmacy School

12 7 Dr. Chi Huynh, PhD, Aston Pharmacy School

13
14
15
16
17
18 9 **Corresponding author;**

19
20 10 Dr. Chi Huynh, c.huynh3@aston.ac.uk, Work: - 0121 204 3231

21
22 11 **List of key words not in the title;**

23 12 Systematic Review; Children; Medication Error

24
25 13 **Reprint request;**

26
27 14 Dr. Chi Huynh, PhD, Aston University, Birmingham, United Kingdom, E-mail:
28 15 c.huynh3@aston.ac.uk.

29
30 16 **Source of funding and conflict of interest statement, if applicable;**

31
32 17 Aston University, Birmingham, United Kingdom is funding Dania Dahmash PhD project, which as
33 18 part of her project this review was conducted.

34
35 19 The review preliminary results was published on the BMJ (Archives of Disease in childhood) after an
36 20 abstract was submitted for the NPPG 2018 conference for the purpose of poster presentation.

37
38 21 The authors declare no conflicts of interest.

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40 22

23 ABSTRACT

24 **Objective:** To identify studies that highlighted medication administration problems experienced by
25 parents and children, which also looked at health literacy aspect using a validated tool to assess for
26 literacy.

27 **Study design:** Ten electronic databases were systematically searched and supplemented by hand
28 searching through reference lists using the following search terms: i) paediatric ii) medication error
29 including dosing error, medication administration error, medication safety and medication optimisation
30 and iii) health literacy.

31 **Results:** Of the (1,230) records screened, fourteen studies were eligible for inclusion. Three analytical
32 themes emerged from the synthesis. The review highlighted that frequencies and magnitudes of dosing
33 errors varies by the measurement tools used, the dose prescribed and by the administration instruction
34 provided. Parent's sociodemographic; such as health literacy and language, is a key factor to be
35 considered when designing an intervention aimed at averting medication administration errors at home.
36 The review summarised some potential strategies that could help in reducing medication administration
37 errors among children at home. Among these recommendations is to show the prescribed dose to the
38 parents or young people along with the verbal instructions, as well as to match the prescribed dose with
39 the measuring tool dispensed, to provide an explicit dose intervals and pictographic dosing instructions.

40 **Conclusion:** The findings suggest that in order to optimise medication use by parents, further work is
41 needed to address the nature of these issues at home. Counselling, medication administration
42 instructions and measurement tools are some of the areas in addition to the sociodemographic
43 characteristics of parents and young people that need to be considered when designing any future
44 potential intervention aimed at reducing medication errors among children and young people at home.

45

46

47 INTRODUCTION

48 When it comes to medication administration for children at home, a significant burden of responsibility
49 relays on the on parents or on the patients themselves.⁽¹⁾ It's been documented that medication
50 administration among children are well known to occur⁽²⁾. Previous studies recognised that more than
51 40% of parents and caregivers make dosing errors in an outpatient setting.^(3,4)The inability to administer
52 medication correctly may result in adverse drug events and poor patient clinical outcomes.⁽⁵⁾ Causes of
53 medication administration problems at home are multifactorial and potentially depend on various
54 factors. ⁽²⁾ So in order to improve medication administration by parents and patients, an initial
55 assessment of the current problems and factors that may contribute to this issue must be identified first.
56 Previous studies have recognised potential factors that can contribute to clinician led medication
57 administration errors in children, but there have been no studies recording both the types and risk factors
58 that can contribute towards caregiver's medication administration problems as well as young people. ⁽⁶⁾
59 ⁷⁾ According to the European Health Literacy Survey (HLS-EU), conducted across eight different
60 countries, the prevalence of low health literacy levels varies from 29% to 62%.^(8,9)

61 Owing to this high prevalence of low health literacy levels and its potential association with medication
62 administration issues among children. This review aimed at identifying studies that highlighted
63 medication administration problems experienced by parents and children, which also looked at health
64 literacy aspect using a validated tool to assess for literacy. In this systematic review, the common
65 medication administration problems occurring at home as well as the potential causalities and risk
66 factors other than health literacy that further could contribute to medication administration errors have
67 been highlighted.

68 METHODS

69 This review was conducted in accordance with the Cochrane Handbook for Systematic Reviews, and
70 followed PRISMA reporting guidelines^(10, 11) The review protocol is registered on PROSPERO (ID:
71 CRD42018091590).

72 **Patient and Public Involvement**

73 There was no patient and public involved in the design, or conduct, or reporting, or dissemination of
74 this review.

75 **Eligibility Criteria**

76 Studies were eligible for inclusion if they were related to medication administration errors among
77 children and adolescent between the ages of 0 to 18 years old as per the World Health Organisation
78 definition of population age group. This includes studies reporting medication related problems outside
79 the clinical setting; where the parent or the child is responsible for administering or taking the
80 medication. Studies must have assessed the health literacy levels of the participants using a validated
81 health literacy assessment tool. Any study that looked only at education levels of the participants
82 without assessing the literacy levels was excluded. There were no restrictions on the date of publication,
83 only English language articles studies where included.

84 **Search Strategy**

85 The search strategy was designed initially by the research team and verified by an information specialist
86 using the Population, Intervention, Comparison and Outcomes (PICO) model. The reviewer (D.D.)
87 systematically searched PubMed, Scopus, Web of Science, Cochrane Library, OpenGrey, NHS Digital
88 Department of Health Office for National Statistics, BBC News, Bielefeld Academic Search Engine
89 (BASE), E-thesis Online Service (EThOS) and Conference proceedings through Web of Science for
90 studies from database inception to September 2020.

91 Search terms summarised in *(Table S1; supplementary material)* included a comprehensive list of
92 synonyms and multiple Boolean operators relating to: i) paediatric ii) medication error including dosing
93 error, medication administration error, medication safety and medication optimisation and iii) health
94 literacy. (D.D.) further performed reference tracking of all included studies to identify any potential
95 studies to be included in the review.

96 **Study selection**

1
2
3 97 Two reviewers (D.D., Z.S.) independently evaluated each study for eligibility to reduce bias using the
4
5 98 inclusion criteria above. The titles and/or abstracts of all identified studies were reviewed
6
7 99 independently, and full manuscripts that appeared to potentially relevant.
8
9

10 **Data extraction process and synthesis**

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12
13 101 Two reviewers (D.D. and Z.S.) independently extracted data using a standardised predefined
14
15 102 spreadsheet. Inconsistencies in extracted data were resolved through consensus discussion by a third
16
17 103 reviewer (C.H.), if necessary. Results were synthesised and summarised according to analytical themes.
18
19 104 Thematic analysis was opted by the research team as it's known for its flexibility and ability of
20
21 105 identifying patterns of meaningful information within the data. ⁽¹²⁾
22
23

24 **Quality appraisal**

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27 107 The quality of the included papers was independently assessed by two reviewers (D.D., Z.S.) using
28
29 108 Critical Appraisal Skills Programme (CASP) checklists.^(13, 14) Discrepancies were resolved through
30
31 109 discussion and consensus.
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33

34 **RESULTS**

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38 110 A total of 672 citations were retrieved from the database and other searches. After screening titles and
39
40 111 abstracts, 38 publications were obtained in full text and assessed for suitability. Of which, 14 met the
41
42 112 inclusion criteria and were included in the analysis (*See Figure 1 for PRISMA flow chart*).⁽¹⁵⁻²⁸⁾ See
43
44 113 (*Table S2; supplementary material*) for reasons of exclusion.
45

46
47 114 The details of the 14 studies are presented in (*Table 1 and 2*).⁽¹⁵⁻²⁸⁾ The majority of the included studies
48
49 115 were published in the last 12 years. All of the studies (n=14) took place in the United States of America.

50
51 116 Overall, eleven studies recruited parents or caregivers of children aged between 30 days to less than 9
52
53 117 years old, two studies had recruited parents with no age limitations of the child and one study recruited
54
55 118 only women of childbearing age. The majority of the studies (n=13) did report the ethnic composition
56
57 119 of their recruited sample and they were vastly Hispanic or black African American parents or caregivers.
58
59 120 One study had only exclusively recruited women from a white ethnic background. ⁽²²⁾
60

121 **Quality appraisal**

122 The results from the quality appraisal are shown in (*Table S3 and Table S4; supplementary material*).

123 All identified studies were included in the final synthesis with a greater emphasis on the higher quality
124 studies.

125 **Synthesis of results**

126 The data from the 14 studies were analysed and three analytical themes emerged from the analysis and
127 a summary of the review results are demonstrated in (*Figure 2*).

128 **Types and causes of medication administration errors among children led by parents or child** 129 **outside a clinical setting:**

130 Eight of the included studies indicated that paediatric dosing errors are among the most common
131 medication errors made by parents. ^(15, 18-21, 23, 24, 26) Among these studies, two randomised trials identified
132 that overdosing errors are more common among parents. ^(23, 24) While another cross sectional study
133 looking at parents with child on a short course prescribed medication reported that the majority of the
134 parents measured below the prescribed dose. ⁽¹⁵⁾ A study by Morrison *et al.* reported that parents who
135 made under-dosing errors made more dosage errors and frequency errors compared with those who
136 made an overdosing error. ⁽²⁰⁾

137 From the included studies, it was noticed that the magnitude and frequency of dosing errors by parents
138 were influenced by two factors: measurement tool used by parents and the dose volume (amount) . In
139 one study, parents stated that non-standardised kitchen spoon was their primary dosing tool. ⁽¹⁷⁾ Two
140 studies reported that errors were more common with measuring cups than with syringes, in particularly
141 with small dose volumes (amounts). ^(21, 24) In a cross sectional study conducted in the USA, the majority
142 66% of the parents considered oral syringes are the best tool for dosing accuracy, while 23.5% believed
143 that cups were the best, however, few 10.1% believed that dosing spoon, measuring spoon, kitchen
144 teaspoon and droppers were the best. ⁽²⁷⁾ Another study reported that larger dosing errors; (>40%
145 deviation of the recommended dose) were made by parents using cups with printed marking and etched
146 markings, this was thought to be due to confusion about teaspoon vs tablespoon instructions,

1
2
3 147 assumptions that the cup is the unit of measure and the full cup is the dose. ⁽¹⁶⁾ Labels and units of the
4
5 148 prescribed medication were contributing factors to dosing errors.⁽²⁴⁾ Parents made significant dosing
6
7 149 errors when the units found on the medication bottle label were not similar to the units used on the
8
9 150 dosing tool.⁽²⁴⁾ Parents who used teaspoon/tablespoon units were likely to use a non-standardised dosing
10
11 151 instrument and make errors in measuring the prescribed and intended dose. ⁽¹⁹⁾The final potential factor
12
13 152 was the type of instructions provided. For liquid medication, less errors were seen among parents who
14
15 153 were provided with text-plus-pictogram instructions 43.9% compared with text-only instructions 59.0%
16
17 154 and this group were also less likely to make overdosing errors. ⁽²⁶⁾ Parents who received standard
18
19 155 medication counselling were 47.8% more likely to make dosing errors when compared with parents
20
21 156 who received pictogram instruction (5.4%).⁽²⁵⁾

25 157 **Factors related to patients or caregivers and medication errors**

27 158 *Health Literacy*

29
30 159 Health literacy of caregivers in the studies were assessed, six conducted further analyses of its influence
31
32 160 on dose accuracy and other co-factors related to medication errors. Yin *et al.* reported that caregivers
33
34 161 with inadequate or marginal health literacy were more likely to use a non-standardised dosing
35
36 162 instrument and further lacked knowledge on weight based dosing for over the counter medication when
37
38 163 compared with caregivers with adequate health literacy. ⁽¹⁷⁾ Another study by Yin *et al.*, found a
39
40 164 significant association between health literacy and dosing errors using cups and dosing spoons. ⁽¹⁶⁾In
41
42 165 adjusted analysis conducted by Williams *et al.*, they found that there was a strong association between
43
44 166 health literacy levels and measurement tool preference in particular cups, parents with limited literacy
45
46 167 reported that dosing cups were the tool of choice most of the time (aOR=2.4).⁽²⁷⁾ The use of a
47
48 168 teaspoon/tablespoon was associated with errors in the intended dose for those with low health literacy
49
50 169 but not for those with adequate health literacy.⁽¹⁹⁾ Harris *et al.* identified that parents with limited health
51
52 170 literacy and Limited English Proficiency (LEP) made the most dosing errors. ⁽²¹⁾ Similarly, Kalow *et*
53
54 171 *al.* revealed that parents with inadequate and marginal health literacy committed dosing errors, but the
55
56 172 sample size of this group was small compared with the adequate health literacy group. ⁽¹⁸⁾

173 *Language*

174 Association between health literacy and lack of knowledge of weight-based dosing varied by English
175 speaking caregiver's. For English speaking caregivers 88.6% of inadequate or marginal health literacy
176 caregivers were unaware of weight based dosing in comparison to 54.1% of caregivers with adequate
177 health literacy.⁽¹⁷⁾ In contrast, Yin *et al.* found that there was no significant relation between dosing
178 error and (LEP).⁽²⁶⁾ However, there were some differences in teaspoon-associated errors in measurement
179 by language.⁽¹⁹⁾

180 *Comprehension and recall of instructions in relation to parent sociodemographic status*

181 Yin *et al.* reported that parents from a low sociodemographic status who were prescribed a daily dose
182 and who received a simple language, pictogram instructions sheets, were less likely to make errors in
183 knowledge of dose frequency and dose accuracy compared with the control group who received
184 standard medication counselling (0% vs 15.1%).⁽²⁵⁾ Participants among the interventional group were
185 less likely to report incorrect medication preparation related to shaking the medication before
186 administration for both daily doses (10.9% vs 28.3% $P= 0.04$) and as needed medication (21.5% vs
187 43.0%).⁽²⁵⁾ Participants in the interventional group were less likely to use a non-standardised
188 measurement tool compared with the parents in the standard group (daily dose: 93.5% vs 71.7%; as
189 needed: 93.7% vs 74.7%).⁽²⁵⁾ Torres *et al.* a cross-sectional study that analysed data from a randomised
190 control study, looked at parents preference and perceptions in regards to units of measurements. It was
191 found that over 80% of the parents perceived a change to millilitre only instructions would be easy in
192 comparison to 14% found it some how hard and 4.1% very hard.⁽²⁸⁾

193 **Interventions aimed at reducing medication administration errors occurring among children** 194 **outside a clinical setting**

195 *Parent's sociodemographic factors*

196 Four studies suggested that parental sociodemographic risk factors should be considered when
197 designing an intervention aimed at averting medication administration errors.^(16, 17, 21, 26) Amongst these
198 factors were parents' health literacy as well as language. Kalow and his colleagues suggested that efforts

199 to streamline interpreter services must be continued as well, to having a more formalised approach in
200 place to elucidate the patient's preferred language for communication. ⁽¹⁸⁾

201 *Counselling and training*

202 Three studies suggested that provisional dose counselling (showing the patient how to prepare the dose)
203 in combination with verbal counselling could be associated with less dosing errors. ^(15, 17, 23) A study by
204 Yin *et al.* indicated that errors occur across different counselling approaches, and they have
205 recommended developing new strategies to ensure that parents understand medication instructions as
206 well as the need for further research to identify the best counselling strategies and how to incorporate
207 these within clinical practice. ⁽¹⁵⁾ Yin *et al.* suggested the need for intensive teaching, training and
208 coaching programmes that can accommodate for different parental health literacy levels. ⁽²⁴⁾

209 *Tools, labels and instructions*

210 Yin *et al.* suggested a promising strategy that could potentially help to reduce paediatric-dosing errors,
211 which was to match the dosing tool with the prescribed dose volume and move towards more simplified
212 numerical markings on the measurement tools as well as to move to millilitre-only units. ^(24, 26, 28) Wallace
213 *et al.* indicated in his study that some parents would prefer instructions with explicit dosage intervals
214 with the exact time and dose to be specified on the label. ⁽²²⁾ Harris *et al.* suggested improving the
215 availability of language concordant labels that could accommodate for different health literacy levels. ⁽²¹⁾
216 Three studies from this review strongly suggested the importance of utilising pictographic dosing
217 instructions and how it could be a positive aid in reducing paediatric dosing errors. ^(23, 25, 26) Majority of
218 parents would be comfortable with millilitre dosing instructions only.

219 **DISCUSSION**

220 The results of this study suggest that parents appear to make a range of medication errors, particularly
221 with liquid medications as documented by prior studies that were conducted also in the USA as well as
222 studies from this review. ^(2, 4, 23, 25) The majority of the included studies indicated that dosing errors were
223 amongst the most common medication errors made by parents, which is consistent with another study,

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2
3 224 which was conducted on Spanish –speaking Latino parents.^(15, 19, 21, 25, 29)This review identified possible
4
5 225 causality behind parents dosing errors other than just the effect of health literacy; these errors could be
6
7 226 linked to the: dose volume prescribed, measurement tools used, units used on the labels and the
8
9 227 instructions provided.

11
12 228 Although standardised measurement tools are usually dispensed with the prescribed liquid medications
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14 229 in the UK, this review identified that the studies published in the USA indicated that parents still use
15
16 230 non-standardised liquid dosing tools as their primary measuring tool; this has been previously linked
17
18 231 with medication administration errors by both Yaffe *et al.* and McMahon *et al.*.^(30, 31) The review found
19
20 232 that pairing the medication labels to the closest measurement tool size, particularly for millilitre-only
21
22 233 labels and tools, could be associated with a reduction in parent dosing and administrating error rates, as
23
24 234 well as a decrease in the likelihood of parents using non-standardised measurement tools as suggested
25
26 235 by another research.^(19, 32)

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28
29 236 The review showed that the use of simple pictographic based medication instructions with explicit
30
31 237 dosage intervals could reduce dosing errors by parents. This finding was consistent with previous
32
33 238 existing data from both South and West Africa as well as the USA regarding the use of pictographic
34
35 239 illustrations as a supportive tool to aid parents in administering medication to their children correctly.
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37 240⁽³³⁻⁴¹⁾ Potentially this could benefit both parents and caregivers with limited or low health literacy levels.

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41 241 Our findings are consistent with prior USA studies investigating the link between adult's
42
43 242 sociodemographic factors, particularly health literacy, and medication administration problems.⁽⁴²⁻⁴⁵⁾
44
45 243 Four studies explicitly highlighted that sociodemographic factors, such as health literacy and language,
46
47 244 must be incorporated into any future intervention that aims to reduce parental dosing and administration
48
49 245 errors.

50
51
52 246 The results of the review highlighted several interventions to aid parents and patients to potentially
53
54 247 reduce medication administration errors at home. This include the use of plain language combined with
55
56 248 provision of using the dosing tool provided as well as incorporating pictographic instructions which
57
58 249 were consistent in four of the included studies.^(15, 23, 25, 26) Pictographic-plain instructions significantly
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250 improve the accuracy of dosing and administering medication to children especially for those parents
251 with insufficient health literacy. ^(25, 26)

252 This study emphasised potential areas that could be incorporated into real practice that could help with
253 reducing medication administration errors done by parents/caregivers and patients. Potential strategies
254 include personalised training and coaching that accommodate different health literacy levels and
255 languages as well as the possibility to match the dosing tool with the prescribed volume alongside the
256 use of millilitre units.

257 Our review is subject to several limitations. There were two major limitations to our study. Firstly, we
258 only included studies in English, so publication bias may exist and non-English studies that are related
259 to this topic might have been missed. Secondly, we only included studies that evaluated literacy using
260 a validated tool. This resulted in only studies from the USA being included. The excluded studies that
261 are of relevance to the topic, but outside the scope of this review are listed in (**Table S2**). Literacy is a
262 problem worldwide, but of greater importance in low and middle-income countries. Future reviews
263 should include these studies by broadening the search strategy.

264 Furthermore, although the study aimed at including medication administration challenges for younger
265 people aged between 16 and 18 years old, however, none was included, as they did not pass the
266 eligibility criteria for this review. Future research are needed where younger people aged 16 to 18 years
267 old are included as participants. In addition, the generalisability of the study results maybe low, this is
268 because the majority of the studies were conducted in the USA and emerged from the same research
269 group Yin *et al.* This research group, have highlighted in their studies several limitations, such as the
270 use of hypothetical scenarios that might not be a true reflection on how parents measure the dose at
271 home. ^(16, 23, 24, 26) For some randomised trial studies in this review, it was difficult for the research team
272 to maintain blindness as some of the participants revealed their allocated group, while for the cross
273 sectional studies, no conclusion of the causes could be drawn. ^(17, 19, 25) Finally, the date of publication
274 for one of the studies was 13 years old ⁽¹⁷⁾, which would not take into account the changes that have
275 occurred in terms of interventions that would vary locally, nationally and internationally. However, this

276 review highlights that non-standard dosing still occurs to date due to parent preference based on recent
277 evidence in 2018 ⁽²⁸⁾.

278

279 **Conclusions**

280 The findings suggest that in order to optimise medication use by parents, further work is needed to
281 address the nature of these issues at home. Counselling, medication administration instructions and
282 measurement tools are some of the areas in addition to the sociodemographic characteristics of parents
283 and young people are among the factors to be considered when designing any future potential
284 intervention aimed at reducing medication errors among children and young people at home.

285 **No grant/award information in the Funding information**

286 This study was not funded. It's done as part of the author (DD) PhD research project.

287 **What is known about this topic?**

- 288 1- Medication administration errors occur frequently among children.
- 289 2- Parent's health literacy could be associated with medication administration problems in
290 children.
- 291 3- Studies examining parent administrator paediatric medicine accuracy were mainly from one
292 particular research group in the USA with participant parents using non-standardised
293 measuring tools

294 **What this study adds:**

- 295 1- The nature of medication administration error's happening at home are not well documented
296 across each age group.
- 297 2- The need to explore parents and patients perspective in regards to medication administration
298 challenges happening at home.

Table 1 : Characteristics of the observational included studies in the review (listed by health literacy test).

Study Information		Participants Characteristics			Findings		
First Author (Year)	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Morrison et al. (2017) ⁽²⁰⁾	Outpatient clinic and emergency department	Interviews and applied assessment	To examine the association between parent health literacy and pain medication knowledge and applied skills in parents of children with sickle cell disease.	Parents of children 1 to 12 years old.	100	Newest Vital Sign (NVS)	Parents with low health literacy made more under dose frequency errors on the pain treatment skills. Health literacy was not associated with errors on the applied treatment skills. Parents recalled under-dosing of medication (both dose and frequency). On the applied pain treatment skills, parents made both underdosing and overdosing errors.
Torres et al. (2018) ⁽²⁸⁾	Paediatric outpatient clinics	Cross sectional analysis	Sought to examine the interrelationships between parents' preferences and perceptions regarding unites of measurement, parents millilitre dosing experiences, and parent health literacy.	Parents or legal guardian of children ≤ 8 years old.	493	Newest Vital Sign (NVS)	Parents preferred the millilitre dosing to be easy; few 11.5% prefers teaspoon units. Parents with low health literacy levels had a higher odd of having a teaspoon preference and greater odds of perceiving difficulty with the millilitre only dosing.
Williams et al. (2019) ⁽²⁷⁾	Outpatient clinics	Cross sectional analysis	To assess parent decision-making regarding dosing tools, a known contributor to medication dosing errors, by evaluating parent dosing tool use, beliefs, and access, and the role of health literacy, with a focus on dosing cups, which are associated with an increased risk of multi-fold overdose.	Parents or legal guardians of children aged ≤ 8 years old.	473	Newest Vital Sign (NVS)	Health literacy is one of the factors that could be associated with the dosing tool choice. Parents with limited health literacy reported that dosing cups were the tool used most of the time.
Yin et al. (2010) ⁽¹⁶⁾	Pediatric clinic	Observational	To assess parents' liquid medication administration errors by dosing instrument	Parents of children with no specific age limitation.	302(287 mothers, 8 fathers, 7	Newest Vital Sign (NVS)	Health literacy was significantly related to doing errors with the cups as well as the dosing spoon, while non-significant trend was seen for the dropper and the oral syringes with the bottle adaptor.

			type and to examine the degree to which parents' health literacy influences dosing accuracy.		legal guardians)		
Samuels-Kalow et al. (2013) ⁽¹⁸⁾	Tertiary	Prospective observational	To examine language-based disparities in discharge communication and parental understanding of discharge instructions.	Parents of children 2 to 24 months.	145	Short Test of Functional Health Literacy (S-TOFHLA)	Parents had acetaminophen dosing errors. There is significant association between language and dosing errors. Parents with marginal or inadequate health literacy had dosing errors compared with adequate health literacy.
Yin et al. (2014) ⁽¹⁵⁾	Paediatric emergency department	Interviews and observations	To examine the degree to which recommended provider-counselling strategies, including advanced communication techniques and dosing instruments provision, are associated with reductions in parents liquid medication dosing errors.	Parents of children aged < 8 years old.	287	Short Test of Functional Health Literacy (S-TOFHLA)	Majority of the patents made underdoing errors as well as few made overdosing errors. Recipients of at least one advanced counselling were less likely to make a dosing error compared with those who did not report received advanced counselling. Parent who received dosing instrument from the emergency department made fewer errors. For adequate health literacy levels was significantly associated with fewer errors when they have received advanced counselling in combination with instrument provision but not the low literacy.
Shonna Yin et al. (2014) ⁽¹⁹⁾	Emergency department	Interviews and observations	To examine the association between unit used and parent medication errors and whether nonstandard instruments mediate the relationship.	Parents of children aged <9 years old.	400	Short Test of Functional Health Literacy in Adults (S-TOFHLA)	Parents made different kind of error in measurement. 1 in 6 parents used kitchen spoon rather than a standard instrument. Parents did not used the unit listed on the prescription or label.
Yin et al. (2007) ⁽¹⁷⁾	Pediatric emergency department.	Interviews	To assess whether low caregiver health literacy was related to risk factors for liquid medication dosing errors, including reported use of non-standardised dosing tools and lack of knowledge about weight based dosing.	Parents and caregivers of children aged between 30 days to 8 years old.	292	Test of Functional Health Literacy in Adults (TOFHLA)	Low health literacy, particularly reading comprehension, was associated with reported use of non-standardised dosing instruments and lack of knowledge regarding weight based dosing. In addition, this has been found previously to be associated with decreased dosing accuracy.

Table 2: Characteristics of the randomised controlled experiment included in the review (listed alphabetically according to first author).

Study Information		Participants Characteristics			Findings		
First Author (Year)	Setting	Methods	Aim	Age of the recruited sample	Sample Size	Health Literacy test used	Outcomes and gaps
Wallace et al. (2012) ⁽²²⁾	Outpatient clinic	Randomized Controlled Trial	To address the gap by addressing whether instructions wording that implicit versus explicit dosage intervals was associated with participant's ability to describe and correctly measure a dose of a commonly prescribed liquid pediatric prescription medication.	Women of childbearing age.	193	Estimated using three established items: -How often do you have problems learning about your medical condition because of difficulty understanding written information? - How often do you have someone help you read hospital martials? - How confident are you filling out medical forms by yourself?	One third of the participants (32.1%) were able to describe and measure the dose accurately. Participants with inadequate health literacy skills were one third as likely to measure a dose of the medication correctly.
Shonna Yin et al. (2016) ⁽²⁴⁾	Pediatric clinic	Randomized controlled experiment	Hypothesized that unit concordance would be associated with fewer errors and that parents would measure most accurately with syringes we also sought to examine differences in impact by parents health literacy and language because low health literacy and limited English proficiency are factors known to place children at risk for errors.	Parents of children aged \leq 8 years old.	2099 parents	Newest Vital Sign (NVS)	Nearly all parents (99.3%) measured \geq 1 dose that was not the exact amount. Overdoing (8.0%) was the majority of the errors. Dose amount of 2.5 and 7.5 mL was associated with more errors when compared with 5 mL (2.5 vs 5 mL adjusted odds ratio [aOR]=4.2; 95% CI,3.8-4.6; 7.5 vs 5 mL [aOR]=2.4;95%CI, 1.2-1.5).
Harris et al. (2017) ⁽²¹⁾	Outpatient	Randomized Controlled Experiment	To examine the association between health literacy and limited English proficiency and	Hispanic parents of children <8 years old.	1126 parents	Newest Vital Sign (NVS)	80% of the recruited parents had Limited English Proficiency (LEP), 82.7% had limited literacy. Of parents who had Limited English

			liquid medication dosing errors in Hispanic parents				Proficiency (LEP) 88.8% had limited and 1.2% adequate health literacy. 3.1% of parents made a dosing error at least one out of the nine dosing trials. Parents with limited health literacy and with limited English Proficiency (LEP) made the most dosing error and errors varied by dose amount and tool type.
Yin et al. (2011) ⁽²⁶⁾	Outpatient pediatric clinic	Randomized Controlled Trail	To sought whether a pictographic dosing diagram included as part of written instructions can decrease parent errors in dosing infant acetaminophen as well as whether pictogram benefit varies by parent health literacy level.	Parents or caregiver of a child with no specific age limitation.	299 parents were assessed	Newest Vital Sign (NVS)	Both groups were associated with poor dosing with the tendency for the parents who have received text plus pictogram significantly less likely to make dosing error (0.6%) compared with parents who received text only instructions (5.6%). Parents with low literacy who received the text plus pictogram instructions were significantly less likely to make errors in dosing compared with who received text only instructions (50.4% vs 66.4%; $P=.02$).
Yin et al. (2017) ⁽²³⁾	Pediatric outpatient clinic	Randomized controlled experiment	To examine the degree to which errors could be reduced with pictographic diagrams, millilitre-only units, and provision of tools more closely matched to prescribed volumes	Parents of children aged \leq 8 years old.	2099 for all arms	Newest Vital Sign (NVS)	Majority of the parents (99.3%) made dosing errors. More errors with the 2 and 7.5 mL dosing amount when compared with the 10 mL dosing amount (10 mL vs 2 mL aOR =3.7; 7.5 mL vs 10 mL aOR= 1.4). Parents who received text and pictogram dosing instructions with mL only labels and tools had decreased odds of making a dosing error compared with received mL/tsp labels and tools with or without pictographic dosing instructions.
Yin et al. (2008) ⁽²⁵⁾	Pediatric emergency department	Randomized Controlled Trial	To evaluate the efficacy of a pictogram based health literacy intervention to decrease liquid medication administration errors by caregivers of young children.	Parents and caregivers of children aged 30 days to 8 years.	245	Test of Functional Health Literacy in Adults (TOFHLA)	Caregiver's dose accuracy was higher among the intervention group prescribed daily and as needed medications regardless of the cut-off point was 20% or 40%. 4% of the intervention caregivers whose children had been prescribed daily doses gave inaccurate dose at the 20% cut-off point, compared with 47.8% of control caregivers. The study suggested that there is no health literacy association with the dosing errors.

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Figure 1: Flow diagram for the study selection based on PRISMA flow diagram

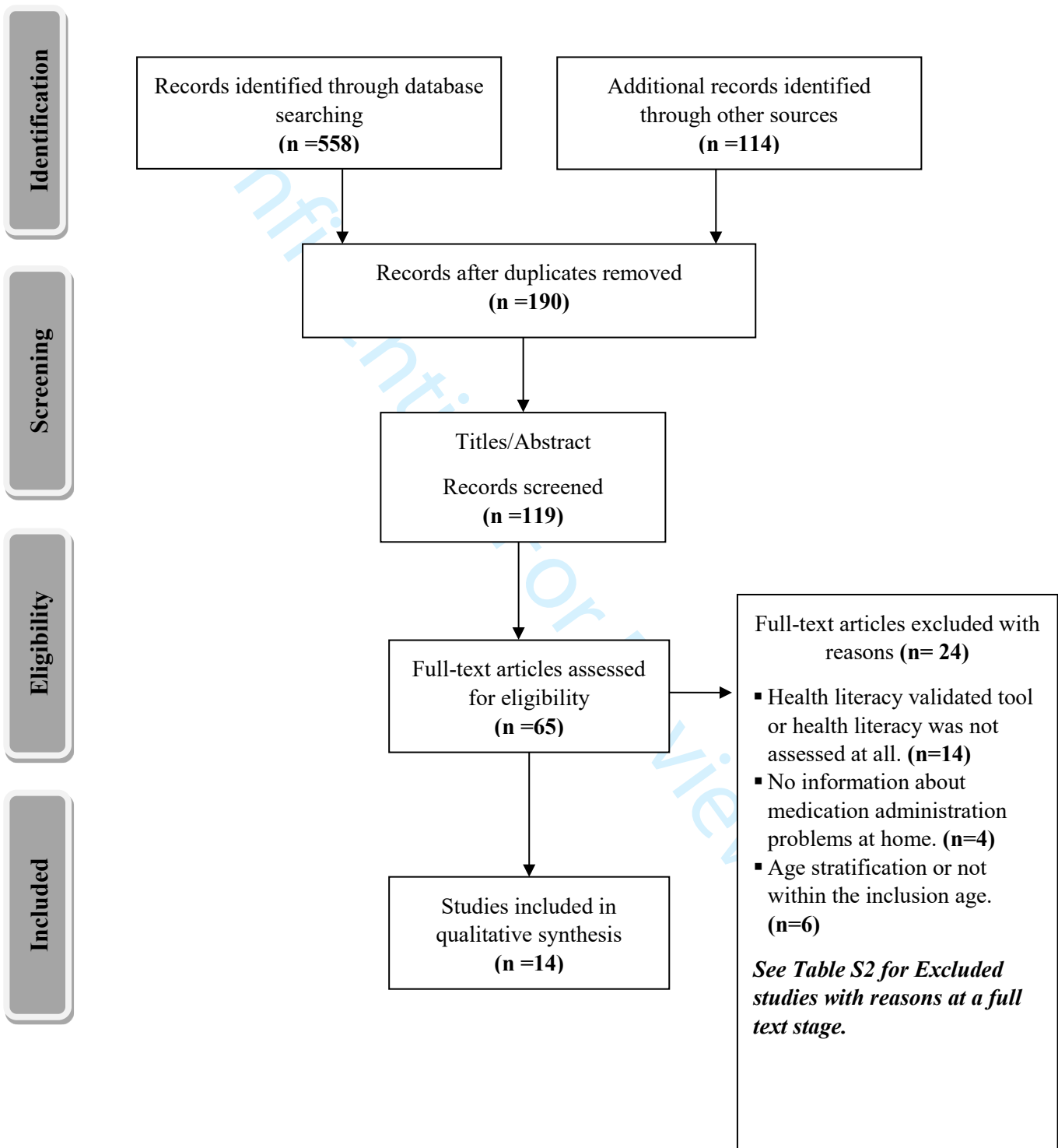


Figure 2: list of the review results

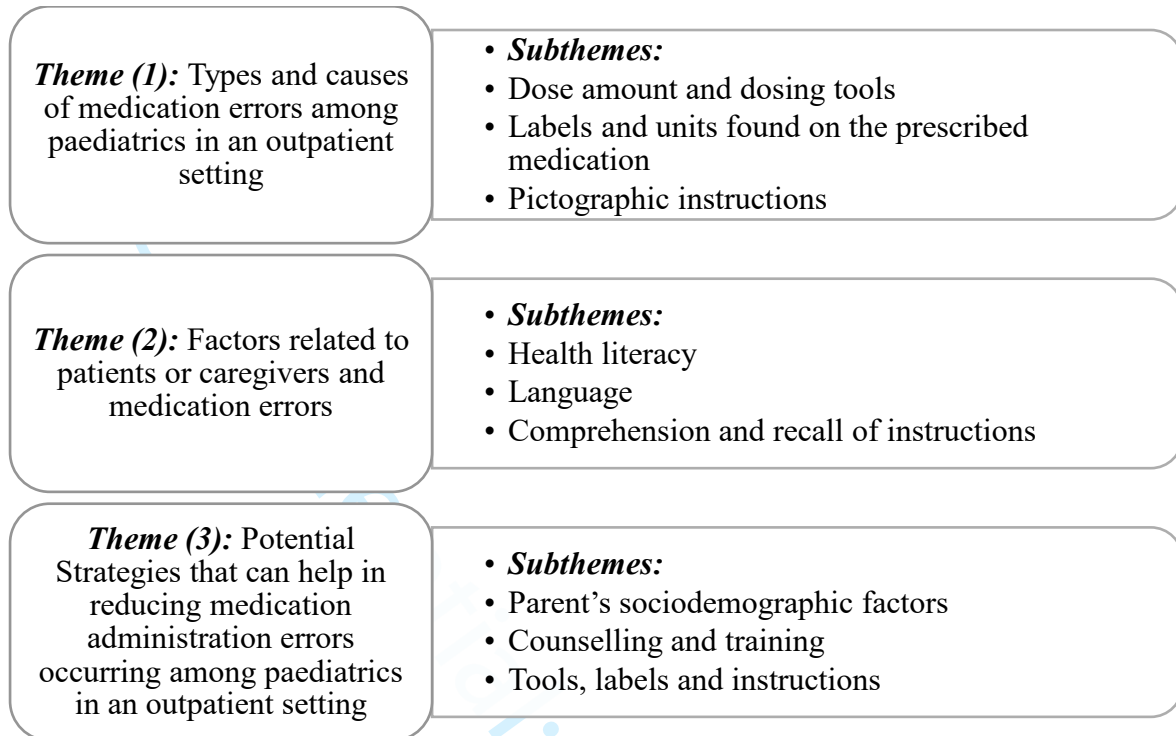


Table S1: Search Strategy for Systematic Review per database

Database	Search strategy
1- PubMed	<p>1- (((child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or teenager* or youth or infant* or newborn* or neonate*))) AND</p> <p>2- (("medical error*" or "medication error*" or "medication administration error*" or "drug administration error*" or "medicine administration error*" or "medication safety" or "optimisation" or "optimization" or "dosing error*")) AND</p> <p>3- (("health literacy" or "literacy" or "literate").</p>
4- Scopus	<p>1- (child OR children OR pediatric* OR paediatric* OR toddler* OR adolescent* OR baby OR babies OR teen* OR teenager* OR youth OR infant* OR newborn* OR neonate*) AND</p> <p>2- (health AND literacy OR literacy OR literate) AND</p> <p>3- (medical AND error* OR medication AND error* OR medication AND administration AND error* OR drug AND administration AND error* OR medicine AND administration AND error* OR medication AND safety OR optimisation OR optimization OR dosing AND error*)</p>
5- Web of Science	<p>1- TOPIC: (child or children or pediatric* or paediatric* or toddler* or adolescent* or baby or babies or teen* or youth* or infant* or newborn* or neonate*) <i>AND</i></p> <p>2- TOPIC: ("health literacy" or "literacy" or "literate") <i>AND</i></p> <p>3- TOPIC: ("medical error*" or "medication error*" or "medication safety" or "medication administration error*" or "medicine administration error*" or "drug administration error*" or "dosing error*" or "optimisation" or "optimization")</p>
6- Cochrane Library	<p>1- "health literacy" or "literacy" or "literate" in Title Abstract Keyword AND</p> <p>2- "medication error" or "medical error" or "medication administration error" or "medicine administration error" or "drug administration error" or "dosing error" or "medication safety" or "optimisation" or "optimization" in Title Abstract Keyword AND</p> <p>3- child or children or pediatric or paediatric or toddler or adolescent or baby or babies or teen or teenager or youth or infant or newborn or neonate in Title Abstract Keyword - (Word variations have been searched)</p>

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Table S2: Excluded studies at full text stage with reasons for exclusion:

Author	Country of Origin	Study Title	Aim of the Study	Reason For Exclusion
Almazrou, S. (2014)	Saudi Arabia	Ability of Saudi mothers to appropriately and accurately use dosing devices to administer oral liquid medications to their children	The study was designed to assess Saudi mother's experiences with measuring cups, syringes and droppers for oral liquid medications, and compared the accuracy of dosing across these devices	Health literacy levels was not tested.
Huang, W. T. (2015)	Taiwan	Immigrant mothers' knowledge of medication safety and administration for young children	The study aimed at comparing immigrant (Southeast Asian and Chinese) and non-immigrant (Taiwanese) mothers' knowledge of medication safety and administration for children, and to reveal how the accessibility of medical resources could affect immigrant mothers' medication administration.	Health literacy levels was not tested.
Boztepe, H. (2016)	Turkey	Administration of oral medication by parents at home	The study aimed at determining the practices and difficulties experiences by the parents at home when administering oral medication to their children.	Health literacy levels was not tested.
Chan, H. K. (2017)	Malaysia	Influences of pictogram-based instructions in paediatric drug labelling on dosing accuracy among caregivers: a pilot study from Malaysia	The study investigated the influence if pictographic dosing instructions used in paediatric drug labelling on dose accuracy.	Health literacy levels was not tested.
Chew, C. C. (2019)	Malaysia	Medication Safety at Home: A Qualitative Study on Caregivers of Chronically Ill Children in Malaysia	The study designed to specifically explore the issues related to out-of-hospital medication safety among the pediatric outpatients in Malaysia from the caregivers' perspective.	Health literacy levels was not tested.
Emmertson, L. (2014)	Australia	Management of children's fever by parents and caregivers: Practical measurement of functional health literacy	The study assessed the health literacy skills of parents and caregivers of children using a hypothetical dosing scenario of a child with fever.	Health literacy levels was not tested.
Joshi, P. (2019)	Mumbai	Liquid Drug Dosage Measurement Errors	The study was carried out to determine the magnitude of dosing errors made by parents of	Health literacy levels

		with Different Dosing Devices	children aged under 5 years old, the most preferred drug delivery device and its association with age, gender, education of caregivers and number of children.	was not tested.
Lee, C. H. (2017)	Taiwan	Inappropriate self-medication among adolescents and its association with lower medication literacy and substance use	The study assessed inappropriate self-medication among adolescents and examines the relationships among medication literacy, substance use, and inappropriate self-medication.	Health literacy levels was not tested.
Lubrano, R. (2016)	Italy	Acetaminophen administration in pediatric age: An observational prospective cross-sectional study	The study evaluated the appropriateness of the dosage of acetaminophen administered to children with fever, and the factors that may influence dosage accuracy.	Health literacy levels was not tested.
Ryu, G. S. (2012)	South Korea	Analysis of liquid medication dose errors made by patients and caregivers using alternative measuring devices	The study was designed to determine the rate and magnitude of liquid medication dose errors that occur with patient/caregiver use of various measuring devices in a community pharmacy.	Health literacy levels was not tested.
Sil, A.(2017)	India	A study of knowledge, attitude and practice regarding administration of pediatric dosage forms and allied health literacy of caregivers for children	The study assessed the knowledge, attitude and practices regarding medicine administration and literacy.	Health literacy levels was not tested.
Solanki, R. (2017)	India	Medication errors by caregivers at home in neonates discharged from the neonatal intensive care unit	The study determined the frequency of medication errors by caregivers at home in neonates discharged from the neonatal intensive care unit and to identify the associated risk factors.	Health literacy levels was not tested.
Tanner, S.(2014)	USA	Parents' understanding of and accuracy in using measuring devices to administer liquid oral pain medication	The study looked at dosing accuracy when parents used various measuring devices and aimed at identifying risk factors associated with dosing errors.	Health literacy levels was not tested.
Tobaiqy, M.	Saudi Arabia.	Parental Experience of Potential Adverse Drug	The study explored parent's experience of potential adverse drug events after administering	Health literacy levels

(2020)		Reactions Related to Their Oral Administration of Antipyretic Analgesic Medicines in Children in Saudi Arabia	antipyretic analgesics. The study looked at adverse drug events after administering analgesics to children.	was not tested.
You, M. A. (2015)	Korea	Parental experiences of medication administration to children at home and understanding of adverse drug events	The study described parent's administration of medications to their children at home and their understanding to adverse drug events.	Health literacy levels was not tested.
Glick, A. F. (2020)	USA	Accuracy of Parent Perception of Discharge Instructions: Role of Plan Complexity and Health Literacy	The study compared parents' perceived and actual comprehension of discharge instructions as well as assessed association between plan complexity and parent's health literacy with overestimation of comprehension.	No medication administration related information.
Brass, E. P. (2018)	USA	Medication Errors With Pediatric Liquid Acetaminophen After Standardization of Concentration and Packaging Improvements	The study assessed the impact of the 2011 changes in paediatric single-ingredient liquid acetaminophen product packaging and standardization of the acetaminophen concentration on poison control centre exposure due to medication errors.	The study did not examine medication administration challenges, however, looked at reported medication errors on poison control centre.
Freedman, R. B. (2012)	USA	Influence of Parental Health Literacy and Dosing Responsibility on Pediatric Glaucoma Medication Adherence	The study assessed glaucoma medication adherence in children, hypothesising that poor parental health literacy and eye drop instillation by the child are associated with worse adherence.	The study examined medication adherence not administration errors.
Erickson, S. R.	USA	Health literacy and medication administration performance by caregivers of adults	The study determined the association between health literacy and a medication administration task assessment, as well as to identify caregiver characteristic associated with higher health literacy and medication administration task.	The study looked at medication administration in adults

		with developmental disabilities		with disabilities not within the age range of this review.
Taybeh, E. (2020)	Jordan	The awareness of the Jordanian population about OTC medications: A cross-sectional study	The study evaluated the knowledge and attitudes towards the use of OTC products.	The targeted population was adults and not within the specific age group that this review was aimed at.
Walsh, K. E. (2011)	USA	Medication errors in the homes of children with chronic conditions	The study observed and described the types of medication errors occurring at home of children with chronic disease.	Unable to extract data for children aged 0 to 18 years old from the final analysis, which included adult data.
Walsh, K. E. (2013)	USA	Medication errors in the home: A multisite study of children with cancer	The study described the types of errors occurring in the home medication management of children with cancer.	Unable to extract data for children aged 0 to 18 years old from the final analysis, which included adult data.
Shone, L. P. (2011)	USA	Misunderstanding and potential unintended misuse of acetaminophen among adolescents and young adults	The study assessed adolescents' s (ages 16 to 23 years) health literacy, knowledge about acetaminophen, recent use of over the counter medicines and understanding of medication dosing instructions.	Unable to extract data of children aged between 16 and 18 years old from the adult data.
Manchana yake, M.	Sri Lanka	Patients' ability to read and understand dosing	Looking at adult's participants and their overall knowledge in regards to written dosing	Younger people aged

G. C. A. (2018)		instructions of their own medicines - A cross sectional study in a hospital and community pharmacy setting	instructions provided by the pharmacists on dispensing labels.	18 years old data was no stratified from the adult data.
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Table S3: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Randomised Controlled Trials Research Checklist.⁽¹³⁾

CASP Question Number	Authors and date					
	Yin (2017) ⁽²³⁾	Harris et al. (2017) ⁽²¹⁾	Shonna Yin et al. (2016) ⁽²⁴⁾	Yin et al. (2008) ⁽²⁵⁾	Yin et al. (2011) ⁽²⁶⁾	Wallace et al. (2012) ⁽²²⁾
1. Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the assignment of patients to treatments randomised?	Yes	Yes	Yes	Yes	Yes	Yes
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes	Yes	Yes	Yes	Yes	Yes
4. Were patients, health workers and study personnel 'blind' to treatment?	No	No	No	No	No	No
5. Were the groups similar at the start of the trial	Yes	Can't Tell	Yes	Yes	Yes	Yes
6. Aside from the experimental intervention, were the groups treated equally?	No	Yes	Yes	Yes	Yes	Yes
7. How large was the treatment effect? ^a	Yes	Uncertain	Yes	Yes	Yes	Uncertain
8. How precise was the estimate of the treatment effect? ^b	Yes	Yes	Yes	Yes	Yes	Yes
9. Can the results be applied to the local population, or in your context?	No	No	No	No	No	No
10. Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes	Yes	Yes
11. Are the benefits worth the harms and costs?	Yes	Yes	Yes	Yes	Yes	Yes

^a Based on the power calculation of the sample size and the primary outcomes results stated clearly.

^b Based on the extract ρ value and CI value of the primary outcome.

Table S4: Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Quality Research Checklist.⁽¹⁴⁾

CASP Question Number	Authors and date							
	Williams et al. (2019) ⁽²⁷⁾	Torres et al. (2018) ⁽²⁸⁾	Morrison et al. (2017) ⁽²⁰⁾	Shonna Yin et al. (2014) ⁽²⁹⁾	Samuels- Kalow et al. (2013) ⁽¹⁸⁾	Yin et al. (2007) ⁽¹⁷⁾	Yin et al. (2010) ⁽¹⁶⁾	Yin et al. (2014) ⁽¹⁵⁾
1. Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the data collected in a way that addressed the research issues?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Has the relationship between researcher and participants been adequately considered?	Yes	Yes	Can't Tell	Can't Tell	Yes	Yes	Yes	Can't Tell
7. Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Is there a Value of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes