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Review Article

A systematic review of the prevalence and incidence of prescribing errors with high-risk medicines in hospitals

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SUMMARY

What is known: **Prescribing errors are the most common type of error in the medication use process. However, there is a paucity of literature regarding the prevalence or incidence of prescribing errors in high-risk medicines (HRMs). HRMs bear a heightened risk of causing significant patient harm when they are used in error.**

Objective: **The aim of this research was to systematically investigate the literature regarding the prevalence and incidence of prescribing errors in HRMs in inpatient settings.**

Methods: **A search strategy was developed based on four categories of keywords: prescribing errors, HRMs, hospital inpatients, and prevalence or incidence. All keywords were searched for in Medline, Embase, Cochrane and the International Pharmaceutical Abstracts. The search was limited to English quantitative studies that reported the incidence or prevalence of prescribing errors by medical prescribers, whether they were seniors or juniors, since 1985.**

Results: **Of the 3507 records identified, nine studies met the review criteria. The most frequent denominator in the included studies was medication orders, in eight studies, ranged from 0·24 to 89·6 errors per 100 orders of HRMs. Two studies reported 107 and 218 errors per 100 admissions prescribed HRMs, and one study reported 27·2 errors per 100 prescriptions with a HRM. The incidence of prescribing errors could not be calculated.**

What is new and conclusion: **The prevalence of prescribing errors in HRMs in the inpatient setting has a very wide range that reflects the different data collection methods used within the included studies. Future studies in prescribing errors should use standardized approaches to enable comparison.**

WHAT IS KNOWN AND OBJECTIVE

Medications are a crucial part in the process of seeking health, when they are used wisely. However, medication errors, which are preventable by the definition of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) organization,[1] are one of the obstacles that face healthcare providers when keeping patients safe, particularly inpatients. Inpatient settings are vulnerable areas for medication errors,[2] which can increase the cost of patient care by increasing the length of stay in hospital, increasing pharmacy and laboratory costs, and doubling the patient mortality rate.[3]

Prescribing errors are the most frequent subtype of medication errors, occurring in 7% of medication orders, 50% of hospital admissions and 2% of inpatients.[4] The percentage of prescribing errors range from 29% to 56% of medication errors in adults,[5,6] and these figures have been found to be higher in children, with a range of 68–75%.[7,8]

Within the general medication classes, there are critical types of medications, termed high-risk medicines (HRMs), that are more likely to cause harm to a patient when they are used inappropriately compared to non-HRMs. HRMs have more potential to cause harm; thus, if they are prescribed erroneously, they can lead to a greater negative impact which can be associated with higher costs and increased mortality. The HRMs attracted the attention of well-known medication safety organizations and authors concerned about patient safety, because of the devastating harm caused to patients; hence, they addressed and specified HRMs to make it obvious to healthcare practitioners. Consequently, definitions and lists for HRMs were established by organizations such as the US Institute for Safe Medication Practices (ISMP)[9] and the UK National Health Service (NHS)[10] through the National Patient Safety Agency (NPSA). The ISMP uses the term high alert medications, whereas the NHS refers to high-risk medicines, but they are based on the same concept.

The ISMP established a list of HRMs, in acute care settings, which contains 22 classes of medications and 12 specific medications, based on its medication error reporting programme.[9] The NPSA has its own list that contains eight classes, based on 60 000 medication incidents reported to the National Reporting and Learning System (NRLS).[10] The eight classes within the NPSA list for HRMs are as follows: anticoagulants, injectable sedatives, opiates, insulin, antibiotics (allergy-related), chemotherapy, antipsychotics and infusion fluids. The ISMP list is broader than the NPSA list, apart from antibiotics (allergy-related), including antithrombotics rather than anticoagulants and antiarrhythmics, adrenergic agonists and antagonists, hypoglycaemic agents, and liposomal forms of drugs.[9]

It could be assumed that prescribing errors with HRMs have a lower rate of occurrence compared to non-HRMs. There are two reasons to support this assumption. Firstly, the focus and efforts provided by the aforementioned well-known medication safety organizations may increase prescribers' awareness of the risks associated with HRMs. Secondly, there are the catastrophic patient safety outcomes when HRMs are prescribed erroneously. Such

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devastating consequences might lead prescribers to apply caution when prescribing HRMs to patients. To investigate this assumption, there is a need to conduct an epidemiological study to investigate the rate of prescribing errors with HRMs.

The epidemiological parameters, prevalence and incidence, of prescribing errors in general medications have been studied extensively and systematically. Nevertheless, these important epidemiological parameters have not been studied systematically explicitly in HRMs. Due to the potential harm that errors with HRMs could generate, it is important to know to what extent they occur when compared to non-HRMs. Such findings might reveal a different picture to what we know already about non-HRMs. Therefore, this study aimed to systematically review the literature in order to report on the prevalence and incidence of prescribing errors in high-risk medicines in hospital inpatients.

METHODS

Search strategy

The detailed search strategies' keywords are available in the online appendix S1. In brief, the following categories of terms, and their synonyms, were initially used: prescribing error, HRMs, inpatients, and incidence or prevalence.

Keywords were searched through OvidSP; Ovid Technology Incorporated, New York, NY, USA: MEDLINE® (National Library of Medicine, Bethesda, MD, USA), Embase, Evidence Based Medicine Reviews: Cochrane Database of Systematic Reviews, and International Pharmaceutical Abstracts. Databases were searched from 1985 till May 2015, apart from the Cochrane Database of Systematic Reviews which was established in 2005.

The search strategy was then broadened by eliminating the search term 'high-risk medicines', in order to find studies that included HRMs in the text or contained HRMs without classifying medications using the terms HRMs and non-HRMs explicitly. In addition, studies included in Lewis *et al.*[4] systematic review were examined, which reviewed the prevalence and incidence of prescribing errors without distinguishing between HRMs and non-HRMs.

Inclusion and exclusion criteria

Inclusion criteria. Due to the difficulty in translation from other languages to English, the only papers written in English were included. Research on patient safety and medication errors largely started in 1985, [11] so studies published between then and May 2015 were included in the review.

Studies of prescribing for all ages were included in the literature review, that is children and adults. Only studies investigating prescribing by doctors, whether they were senior or junior, using handwritten prescriptions were included. The patient setting was restricted to hospital inpatients only, as this is different to the outpatient settings in terms of medication and error types.

All quantitative studies that reported incidence or prevalence of prescribing errors in HRMs were included. The included studies should have data that reported on the number of HRM prescriptions written with and without error. Rates of prevalence could be described in terms of a medication order that contained one HRM with one or more than one error, medication prescription that contained more than one medication order, of which at least one of them was a HRM that have an error or errors, or a hospital admission where the admitted patient had at least one HRM with one or more than one error. Hospital admission could be combined with time unit to become an incidence denominator. The review was not limited to the medications that included in the ISMP list or in the report of the NPSA for HRMs. Studies that utilized a different list of HRMs medication were eligible for inclusion.

Exclusion criteria. Non-medical prescribers such as independent pharmacists or nurse prescribers were excluded. Those prescribers may have different types of errors as they usually prescribe a limited number of medications and this type of practice is not recognized globally. In addition, studies conducted in primary care or outpatients were omitted from the review. Studies reporting on prescribing errors made using computerized physician order entry (CPOE) were excluded because it is associated with different types of errors than with handwritten prescriptions. Furthermore, handwritten prescriptions still dominate as the main method of prescribing in hospitals worldwide.

Abstracts of conferences or meetings, qualitative studies, or quantitative studies without prevalence or incidence were excluded. If a study only reported the proportion of HRM errors, in relation to the total number of non-high-risk medicines plus HRMs combined without recording the total number of HRM prescriptions written, then these were excluded as they would not allow the prevalence or incidence of HRM errors to be determined.

Study selection and data extraction

The selection and extraction process was performed independently by two members of the team. Any disagreements were resolved through consensus. A standardized data extraction form was used, based on the Cochrane checklist for Systematic Reviews of Interventions[12] and the third edition of the Centre for Reviews and Dissemination (CRD) guidance for undertaking systematic reviews.[13]

RESULTS

Nine studies met the inclusion criteria. Figure 1 depicts a flow diagram of this process.

Study characteristics

The oldest study[14] was published in 2008, whereas the others were published up to 2014.[15–22] More than half of the studies (5/9) were published in 2011.[15,16,20–22] Studies were predominantly conducted in the USA, with around 45% (4/9) of the studies from there.[15,17,20,22] Three were from Europe including the UK,[16] Germany[19] and Spain.[14] One study [21] was from Brazil and one[18] from Australia. Table 1 summarizes the data from the included studies. Each study had been conducted in a single teaching hospital,[14–22] which provided both adult and children services.

Fifty-five per cent (4/9) of the studies were in adult patients who were cared for in a variety of ward settings (surgery, medical, oncology, intensive unit and cardiology).[16,18–20] A third (3/9) of the studies were conducted solely in paediatric departments across both medical and surgical wards.[14,17,21] However, two studies (22%) did not specify the patient group and were based on pharmacist-intercepted errors databases.[15,22] The first study was in a hospital entirely for patients prescribed oral chemotherapeutic agents,[15] whereas the second study concentrated on analgesics.[22]

More than half of the studies, 55% (5/9),[14,17,19,21,22] had been carried out prospectively and 45% (4/9) retrospectively.[15,16,18,20]

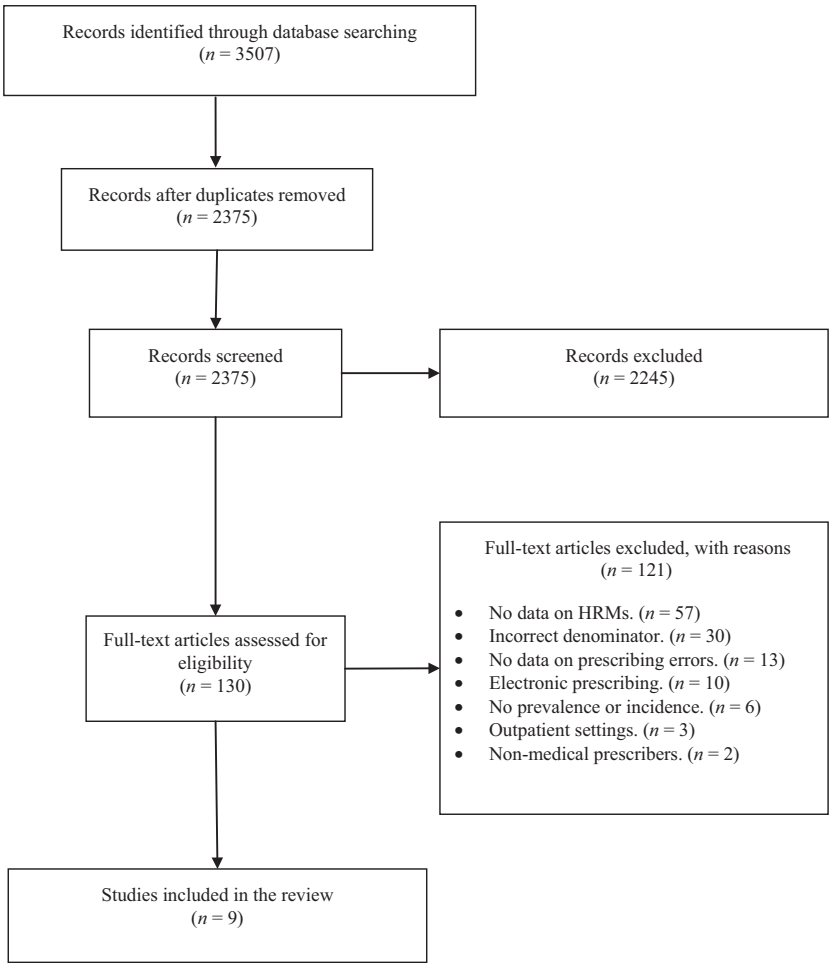

Fig. 1. Flow diagram of the screening process.

Data collection period ranged from 1 day to 5 years. The most frequent period was 2 years in three studies.[15,19,20]

Multidisciplinary teams and doctors were the data collectors in 33% (3/9) of studies, respectively.[15,17,19 14,16,20] Pharmacists were data collectors in two studies,[21,22] whereas in one study, the data collectors were research assistants who were not healthcare professionals.[18] Most studies (7/9) used the prescription review method.[14,16,17,19–22] The medical record review method was used in two studies,[18,20] as was a pharmacist-intercepted errors database.[15,22] Three studies used more than one method; combinations included prescription review with either medical record review, pharmacist-intercepted errors or discharge form review.[17,20,22]

Seven studies, 80%, did not validate the reported errors.[14,15,17,19–22] One study did partial validation of the reported errors, when one author independently randomly checked reported data[18] Another study validated all reported errors through a panel of senior doctors.[16]

Definitions

The definition of prescribing errors used varied between the studies. One study created its definition by combining Dean's definition[23] and Rosa *et al.*[24] classifications of prescribing errors with HRMs.[21] Another study used a combination of the ISMP list of error prone abbreviations[25] and its hospital formulary guidelines for good prescribing as a definition.[17] Three studies combined Dean's definition with other definitions.[14,15,21] The NCC MERP definition was used once.[18] In three studies, the authors conceived their own definitions.[16,19,22] One study did not use any definition for prescribing errors as it measured the prevalence of a single type of prescribing error, that is prescribing a contraindicated class of HRMs.[20]

In terms of the HRM list or definition used, two studies (22%) [18,21] used the ISMP list as a reference for HRMs and one study [16] used the NPSA recommendations for HRMs. The rest of the studies did not refer to any predefined list of HRMs.[14,15,17,19,20,22]

Prevalence and incidence of prescribing errors in HRMs

The prevalence of prescribing errors in HRMs was the only epidemiological measure that was found in the included studies, or could be calculated from the available data. There were three denominators used: medication orders, patient admissions and prescriptions. Medication orders as a denominator was the most frequent, used in 90% (8/9) of the studies.[14,15,17–22] The prevalence of errors in HRMs ranged from 0·24 to 89·6 errors per 100 orders of HRMs.[14,15,17–22] In two studies, errors were 107 errors or 218 errors per 100 admissions prescribed one or more HRMs.[17,18] One study

Table 1. Systematic review of prevalence and incidence of prescribing error in high-risk medicines: summary of included studies

Author/(year)	Country	Study site	Setting	Period	Adults/ Children	Type of study	Method of error detection	Total order/admissions/ patients/prescriptions	No. of PEs	Incidence or prevalence of HRM error
Collins, C. M. and Elsaid, K. A.[15] (2011)	USA	Tertiary academic hospital		2 years	No provided	R	Pharmacist intervention database	412 orders	39	9·47 error/ 100 orders
Davies, E. *et al.*[16] (2011)	UK	Multispeciality teaching hospital	Medical and surgical specialities	1 day	A	R	Prescription review	330 prescriptions	90	27·2 errors/ 100 prescriptions
Lee, B. H. *et al.*[17] (2009)	USA	Urban teaching hospital	Medical and surgical services	6 months	C	P	Prescription review and discharge form review	314 orders 241 patients (admission)	257	82 error/ 107 errors/100
Manias, E. *et al.*[18] (2014)	Australia	Tertiary care teaching hospital	CC, IC, EC, OC, PC	1 year	A	R	Medical record review	3492 orders 540 patients (admissions)	1176	33·7 errors 100 orders 218 errors/ 100 admissions
Markert, A. *et al.*[19] (2009)	Germany	University medical hospital	Haematology department	2 years	A	P	Prescription review	5250 orders	472	8·99 error 100 orders
Milani, R. V. *et al.*[20] (2011)	USA	Multispecialities academic hospital		2 years	A	R	Prescription review and medical record review	47 orders	8	17 error/ 100 order
Pallas C. R. *et al.*[14] (2008)	Spain	Urban teaching hospital	Neonatal unit	8 months	C	P	Prescription review	327 orders	172	52·60 error/ 100 order
Silva M. D. *et al.*[21] (2011)	Brazil	University hospital	Paediatric unit (60 beds) medical and surgical	30 days	C	P	Prescription review	705 orders	632	89·6 errors/ 100 orders
Smith H. S. and Lesar T. S.[22] (2011)	USA	Tertiary care teaching hospital		5 years	All	P	Pharmacist detected errors and prescription review	500 191 orders	1205	2·41 errors/ 1000 orders

HRMs, high-risk medicines; PE, prescribing error; A, adult; C, children; E, elderly; P, prospective; R, retrospective; pt., patient; CC, cardiac care; IC, intensive care; EC, emergency care; OC, oncology care; PC, perioperative care.

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expressed prescribing error prevalence using the denominator of prescription which was 27·2 errors per 100 prescriptions containing one or more HRMs.[16] The three highest prevalence rates (89·6%, 82% and 52·6%) in the medication order denominator were found in paediatric patients.[14,17,21] Pharmacist-intercepted errors databases were associated with the lowest and third lowest values of the prevalence.[15,22]

HRMs involved in prescribing error

Of the two studies that used the ISMP list of HRMs,[18,21] one found opioids were the most frequent class associated with prescribing error, followed by sedatives,[21] whereas the other study did not present data for individual classes or types of HRMs.[18] Opioids as a class of HRMs were found in more than the half of studies (5/9).[14,16,17,21,22] Two of the studies were solely about opioids,[16,17] whereas in the rest of the studies, opioids were part of a group of medications, whether these groups were only HRMs or non-HRMs.[14,21,22] One of the studies that discussed opioids chose them based on a NPSA recommendation as HRMs.[16] Chemotherapeutic agents were the only class investigated in two studies,[15,19] and one study only investigated antithrombotic agents.[20] The majority of the included studies, 66% (6/9), did not describe the medication explicitly as HRMs they merely used the drug class name or specific drug name.[14,15,18–20,22] Only three studies referred explicitly to the studied medication classes as being HRMs.[16,17,21]

Types of prescribing errors detected

Two studies did not give details as to the types of prescribing errors.[19,22] One of those studies did not distinguish the types of errors in HRMs from non-HRMs,[19] whereas the another did not describe the details at all.[22] Contraindicated drugs were the only type of prescribing errors that were studied in another study.[20] Dosage problems or wrong dosage was the most frequent type of prescribing errors detected in the studies with the highest percentage in 33% (3/9) of the studies[16,18,21] and the second highest in one study.[15] Prescription errors such as unclear prescription and incomplete information were found in high percentages in 33% (3/9) of the studies.[14,16,17] Missing weight or incorrect weight, which is necessary for paediatric patients especially with HRMs, was the most frequent type of error in children in one study.[17] Table 2 summarizes the prevalence of error types in descending pattern from the most frequent to the least frequent.

Table 2. Prevalence of detected types of prescribing errors

Type of errors	Range of prevalence, %	References
Dosage problems or wrong dosage	31–91	14–16,18,21
Prescription errors	31–59	14,16,17
Missing weight or incorrect weight	77	17
Prescribing policy not followed	38	15
Medications omissions	8	15
No or wrong prescription date	6	17
Drug–drug interaction, medications given to a known allergic patient, medication duplication	1–2	18

Severity of detected prescribing errors

Three studies (33%) did not report the severity or potential severity of the prescribing errors.[14,15,21] One study reported 87 actual severe adverse events regarding prescribing errors, but only one of them was in inpatients, were found in patients transferred to the ICU, this adverse event was the most frequent among the others with 44·8% (39/87) of the severe adverse events.[19]

Five studies (55%) clearly addressed the severity, whether it was actual or potential, of the prescribing errors.[16–18,20,22] However, each study used a different scale. Scales were established by the author or adapted from the literature. One study adapted an actual severity parameter, TIMI classification[26] of bleeding, used to classify the severity of bleeding whether it was major or minor that caused by prescribing error of antithrombotic agents.[20] Three studies (33%) adapted other authors' scales for potential severity.[16,17,22] The scales were adapted from the following: Overhage and Lukes scale's,[27] Leape *et al.* scale,[6] and Taylor *et al.* scale[28] that was itself adapted and modified from another author[29] scale. One study [18] used the NCC MERP scale [30] that evaluates the actual patient harm due to medication errors. In all scales used, the lowest percentages of adverse events were in the most harmful category.

DISCUSSION

This systematic review is the first to examine literature about the prevalence and incidence of prescribing errors with HRMs in inpatient settings. The prevalence of prescribing errors with HRMs expressed in rates of medication orders, medication prescriptions and hospital admissions was 0·24–89·6 errors per 100 orders, 27% and 107–218 errors per 100 admissions, respectively. The review did not find any available data to calculate the incidence.

The reported rates of errors in medication orders for HRMs had a very wide range that could be influenced by both the method used for error detection and the patient population. Pharmacy databases that described errors detected in the dispensary area gave small number of errors compared to other methods.[14,15,17,18,20–22] The small number of errors detected in the dispensary area would have omitted errors that had been intercepted by the medical team on the ward, or may be because pharmacists have limited access to the patients' medical records that could prevent them from identifying all errors. Children were more likely than adult patients to have prescribing errors with HRMs. This was concluded based on the finding that the three highest values for prevalence of prescribing errors in HRMs were in studies investigating prescribing for children. These results support the perception that children have more prescribing errors than adults.[7,8]

The method of error detection and study type has a substantial influence on the number of errors detected. Our results show the highest prescribing error rates were revealed using prospective prescription review. This method is thought to be the most comprehensive and accurate method to detect prescribing errors.[31] On the other hand, as mentioned above, pharmacist-intercepted errors in the dispensary area detected the least number of prescribing errors. For example, the lowest prescribing error prevalence was 0·24%, which expressed the pharmacist-intercepted errors.[22]

Dosage errors were the most frequent type of error reported. This result is consistent with other studies such as Lewis *et al.*,[4]

Ghaleb *et al.*,[32] and Winterstein *et al.*[33] In terms of definitions, prescribing error definitions were inconsistent in the included studies, and the majority were created by the authors or a combination of different authors' definitions. Moreover, HRM lists were undefined in more than the half of the studies. The heterogeneity in the definitions used was driven by authors' preferences, local definitions and the practice speciality. An example of that is one such study[15] combined Dean *et al.*[23] definition of prescribing errors with Ghaleb *et al.*[34] definition of errors in, and another[21] combined Dean *et al.*[23] definition with a local definition in Brazil, from Rosa *et al.*[24] There were no justified reasons given for these combinations or created definitions.

The severity of the detected HRM prescribing errors was evaluated in more than half of the studies. However, each study used a different scale to measure severity. This inconsistency made it difficult to draw any conclusions about the severity of errors in HRMs. However, regardless of the scale used, the lowest percentage of adverse events was in the most harmful category.

Nearly a quarter of the studies that went through the full-article review stage as part of the screening process were excluded because they did not have the right denominator to calculate the prevalence or incidence of prescribing errors with HRMs. Some of these excluded studies[5,35] were well known in the medication error field but were excluded from the review due to a lack of a denominator for HRMs; thus, the oldest study included was published in 2008. Many studies reported the proportion of prescribing errors rather than prevalence or incidence, where the denominator was the whole number of the medications prescribed without distinguishing between HRMs and non-HRMs.

In general, causes of prescribing errors could be categorized as prescribing mistakes, that is knowledge-based mistakes and rule-based mistakes, or slips and lapses.[36] Based on Reason's model,[37] the causes of prescribing errors have been studied with any medication type. The results of the study showed around 60% of prescribing errors discussed by doctors were considered prescribing mistakes and around 40% of prescribing errors were slips and lapses.[36] However, the causes of prescribing errors in HRMs specifically are unknown. Therefore, future research can focus on the causes of prescribing errors with HRMs and compare them to general medications. There is a variety of ways that can be used to explore the causes of prescribing errors such as observational techniques and interviews.[38, 39] Thus, a better understanding will be obtained to draw a clear picture about the future solutions that could be implemented.

Limitations

Several limitations to this systematic review study need to be acknowledged. The small number of included studies and the small sample size of some studies make it difficult to generalize the results. The current review has only examined studies that were written in English and that may lead to excluding valuable studies published in different languages. Despite the thorough review process, there were no data found about the incidence, and two of the prevalence denominators, hospital admission and prescriptions, were in limited studies that could make them unrepresentative when compared with other studies.

WHAT IS NEW AND CONCLUSIONS

The prevalence of errors in HRMs per medication order has a very wide range that reflect the inconsistency of the definition of prescribing errors, HRM lists, error detection techniques and the methods used to conduct studies; thus, a consistency in these parameters needs to be set in the future research. Opioids were the most frequently reported HRM associated with error and dosage errors were the most frequent type of prescribing error in HRMs. Errors with HRMs were found more frequently in children than adult patients. There was heterogeneity in different parameters such as prescribing error definitions, the HRM list used and error severity scales.

CONFLICT OF INTEREST

Nothing to declare.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Search strategy keywords details.

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