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Interventions to reduce the incidence of medical error and its financial burden in health care systems: A systematic review of systematic reviews

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Background and aim: Improving health care quality and ensuring patient safety is impossible without addressing medical errors that adversely affect patient outcomes. Therefore, it is essential to correctly estimate the incidence rates and implement the most appropriate solutions to control and reduce medical errors. We identified such interventions.

Methods: We conducted a systematic review of systematic reviews by searching four databases (PubMed, Scopus, Ovid Medline, and Embase) until January 2021 to elicit interventions that have the potential to decrease medical errors. Two reviewers independently conducted data extraction and analyses.

Results: Seventy-six systematic review papers were included in the study. We identified eight types of interventions based on medical error type classification: overall medical error, medication error, diagnostic error, patients fall, healthcare-associated infections, transfusion and testing errors, surgical error, and patient suicide. Most studies focused on medication error (66%) and were conducted in hospital settings (74%).

Conclusions: Despite a plethora of suggested interventions, patient safety has not significantly improved. Therefore, policymakers need to focus more on the implementation considerations of selected interventions.

KEYWORDS

medical error, financial burden, hospital, intervention, quality of care, public health

Introduction

A medical error is a preventable adverse effect of medical care (“iatrogenesis”). It can be defined as the “failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim” (1). As the associated burden is evident, medical errors have drawn considerable attention from academics, hospital managers, and major health stakeholders. Medical errors have a significant adverse impact on patients’ outcomes and workers’ mental health. They are associated with a considerable financial burden and undermine public trust in the health system (2–4). Medical errors, including healthcare-related adverse events, occur in 8–12% of hospitalisations in Europe (5). At least 50% of hospitalized patients’ harm could be preventable (6). Overall, healthcare-associated infections incidence is estimated at 4.1 million patients a year in Europe, with the four main types of error being urinary tract infections (27%), lower respiratory tract infections (24%), surgical site infections (17%), and bloodstream infections (10.5%) (5). In the US (2007), 1.7 million healthcare-associated infections occur annually. They result in excess healthcare costs of \$35.7–\$45 billion for inpatient hospital services (7, 8).

The medical errors can be classified based on their content or “what went wrong” (e.g., medication, surgical, transfusion, healthcare-associated infection) (9–15); location or “where did it happen” (e.g., intensive care unit, operation theater, emergency department, children’s ward) (15–18); staff or “who made an error” (e.g., doctor, pharmacists, nurse) (10, 19, 20); error’s severity or “how harmful was it” (e.g., error, no harm, near miss) (21–25); and “who was affected” (e.g., patient, family, medical staff) (26, 27). Depending on the type of medical errors, studies suggest various solutions, from simple activities (e.g., hand hygiene to prevent healthcare-associated infection) to more complex ones such as using technological instruments or methods to prevent retained surgical instruments errors (7, 15).

Despite the ongoing efforts to reduce and prevent the burden of medical errors and related patient harm, global efforts have not yet achieved substantial change over the past 15 years due to various reasons (6). Unclear policies, insufficient or unreliable data to drive patient safety improvements, unskilled health care professionals, lack of organizational leadership capacity, and non-participation of patients and families in the care process led to unsustainable and insignificant improvements in health care safety (2). Hence the primary goal of this article was to conduct a systematic review of systematic reviews to elicit interventions that can reduce medical errors or medical error costs in hospitals and analyse interventions implementation results where available. Specifically, we focused on interventions that can reduce health care costs, patient’s harm and death, improve health services quality, patient’s satisfaction, and safety.

Methods

Literature search and study selection

Inclusion criteria for articles considered in this review were as follows: (a) systematic reviews; (b) studies published in English language; (c) studies on solutions regarding medical error reduction or medical error costs; (d) studies on interventions in hospitals or the whole of the healthcare sector, which entered the study regardless of whether these reviews were based on reported errors, an examination of medical profiles, observational studies or other methods. We excluded studies (a) published in languages other than English; (b) studies conducted in settings other than the hospital; (c) studies focused only on a specific type of medical error/activity/patient subgroup, or a sporadic type of medical error (e.g., wrong-site surgery in neurosurgery); (d) studies focusing on a particular group of employees where generalisability to other groups would not be feasible (i.e., only nurses, physicians, pharmacists); (e) conference abstracts, narrative reviews, editorial and other types of studies but systematic reviews; (f) studies related to adverse events only; and (g) studies with no effect on medical errors.

Search strategy

To identify relevant interventions, we searched the four databases (PubMed, Scopus, Ovid Medline and Embase) from Oct 1977 until January 2021 and selected English-only publications. Multiple keywords related to medical errors were researched and customized for each database. We used the filters for searching papers on interventions to reduce medical error to maximize the sensitivity of our literature search. We did not make any limitations on the outcomes. Additionally, references from the included systematic reviews were checked and added to selected studies. Our search strategy was adjusted for each database accordingly. For example, following combination was used for Pubmed database: ((((((((((((((((((medical errors[MeSH Terms] OR “recording error”[Title/Abstract]) OR “no harm”[Title/Abstract] OR “patient fall*”[Title/Abstract]) OR “hospital infection”[Title/Abstract]) OR “transfusion error”[Title/Abstract]) OR “prescription error”[Title/Abstract]) OR “prescribing error”[Title/Abstract]) OR “CPR error”[Title/Abstract]))) OR “medication error”[Title/Abstract]) OR “near miss”[Title/Abstract]) OR “suicide”[Title/Abstract]) OR “sentinel event”[Title/Abstract]) OR “never event”[Title/Abstract]) AND systematic[sb]). An overview of the full search strategy can be found in [Appendix 1](#).

Data extraction

Two researchers independently extracted data from selected reviews. A third reviewer resolved any disagreements between the two reviewers. The following data were extracted: author, year, aim of the study, setting, medical error type, interventions, and the overall results if reported. Only reviews that met our selection criteria were extracted and analyzed.

Data analysis

The interventions of reviews were classified based on the medical error types. We additionally checked for the overlap between primary studies included in systematic reviews. Since there was no complete overlap between the reviews, none of the studies were excluded.

Results

Search results

The initial search provided 2108 records (Figure 1). After eliminating duplicate papers, titles and abstract screening, 181 reviews underwent the full-text assessment. In total 76 reviews met the inclusion criteria, 105 were excluded for various reasons (Figure 1).

Characteristics of the included systematic reviews

More than half of systematic reviews (67%) were published between 2013 and 2020 ($n = 51$). 66% of reviews were about medication error ($n = 49$), and 74% were related to all hospital settings ($n = 56$). The included studies reported on interventions for eight types of medical errors: overall medical error (13 interventions), medication error (37 interventions), patients' fall (11 interventions), healthcare-associated infections (21 interventions), diagnostic errors (7 interventions), transfusion and testing errors (8 interventions), surgical errors (3 interventions), and patients' suicide (13 interventions) (Table 1). Table 2 provides an overview of the impact of interventions on medical error reduction by intervention group. A more detailed overview of the impact of studies, including their aim, setting, and overall results can be found in Supplementary Table 1.

TABLE 1 Interventions to reduce medical error by medical error category.

Medical error category	Interventions groups	Number of interventions
Overall medical error (1–10)	Use of electronic systems	7
	Process interventions	4
	Patient-centered intervention	1
	Inter-professional education	1
Medication error (4, 5, 7, 11–57)	Use of electronic systems	10
	Pharmacists and clinical pharmacist role	1
	Process interventions	19
	Leadership or managerial manners and strategies	6
	Smart pumps impact	1
Patients' fall (5, 58–62)	Education and professional skills	3
	Methods/tools evaluating patients' fall risk	3
	Process and patient care programs	3
	Hourly rounding programs	1
	Organizational and workplace culture	1
Healthcare-associated infections (18, 21, 42, 58, 61, 63–69)	Caregivers' education and behavioral change interventions	4
	Process interventions	8
	Managerial and organizational interventions	5
	Use of medication interventions	3
	Environment/equipment cleaning	1
Diagnostic errors (5, 70, 71)	Digital and electronic interventions	3
	Patient identification and checking	2
	Quality improvement methodologies	2
Transfusion and testing errors (72, 73)	Identification of patients (labeling and barcoding)	8
Surgical errors (18, 42, 74, 75)	Use of checklists and counting materials	2
	Use of radio-frequency identification technology	1
Patients' suicide (76, 77)	Measures to reduce absconding and engagement with patient's family	2
	Contact interventions	3
	Process and patient care programs	8

TABLE 2 Impact of interventions on medical error reduction by intervention group.

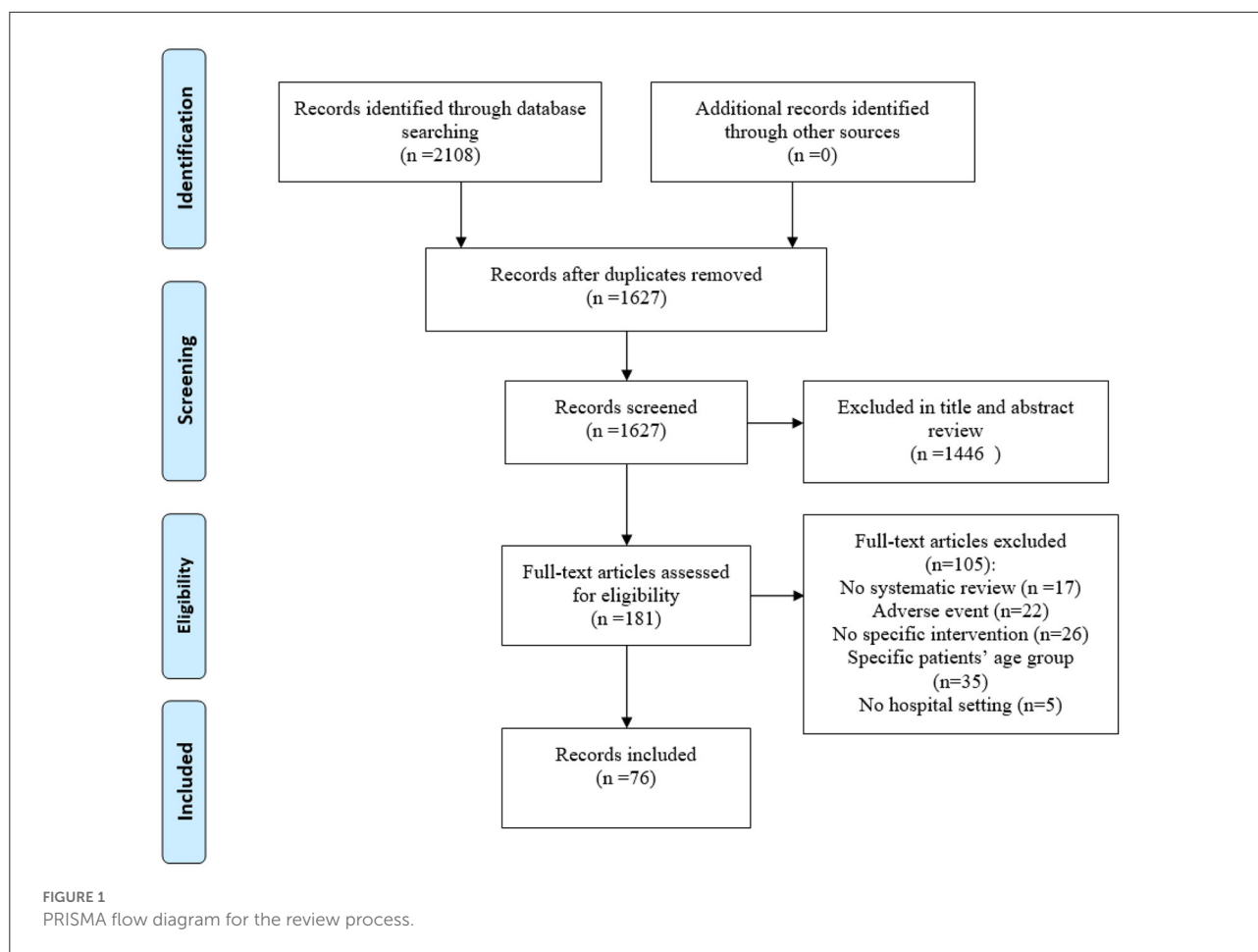
	Overall medical error	Medication error	Patients' fall	Healthcare-associated infections	Diagnostic error	Transfusion and testing errors	Surgical errors	Patients' suicide
Caregivers' education and behavioral change interventions				+ + 2 reviews (58, 64) + 2 reviews (65, 69)				
Digital and electronic						++1 review (5) + 1 review (70)		
Education and professional skills			+ + 2 reviews (58, 59) + 1 review (60)					
Use of electronic systems	+ + 2 reviews (3, 4) + 2 reviews (1, 2)	+ + 12 reviews (4, 22, 24–31, 56, 57) + 13 reviews (5, 34, 35, 44–53)						
Environment/equipment cleaning				++ 1 review (63)				
Identification of patients (labeling and barcoding)						++ 1 review (72) +1 review (73)		
Inter-professional education	+ + 1 review (9)							
Leadership or managerial manners and strategies		+ + 4 reviews (14, 17, 22, 23) + 1 review (21)						
Managerial and organizational interventions				++1 review (64) + 3 reviews (21, 61, 65)				
Measures to reduce absconding and engagement with patient's family								+ 1 review (76)
Methods/tools evaluating patients' fall risk			+ +1 review (59) + 1 review (5)					

(Continued)

TABLE 2 Continued

	Overall medical error	Medication error	Patients' fall	Healthcare-associated infections	Diagnostic error	Transfusion and testing errors	Surgical errors	Patients' suicide
Organizational and workplace cultures			+ 1 review (61)					
Patient identification					+ 1 review (70)			
Patient-centered interventions	+ 1 review (8)							
Pharmacists and clinical pharmacist role		++ 6 reviews (37–41, 43) + 7 reviews (5, 32, 33, 35, 36, 42)						
Use of checklists and counting materials							++ 2 review (18, 75) +1 review (42)	
Process and patient care interventions			++1 review (59)					++1 review (77)
Process interventions	++ 1 review (7) + 3 reviews (5, 6, 10)	++ 9 reviews (7, 13–20) + 4 reviews (5, 11, 12, 55)		++ 1 review (18) +2 reviews (42, 66)				
Quality improvement methodologies					+1 review (71)			
Smart pumps impact		+ 2 review (5, 54)						
Radio-frequency identification technology							+1 review (74)	
Contact interventions								++1 review (77)
Use of medication				++ 1 review (67) + 2 reviews (42, 68)				
Hourly rounding programs			++ 1 review (62)					

++ effective in reduction / significant reduction, + some evidence of reduction.



Interventions based on medical error types

Overall medical error

This group of interventions was not restricted to a specific medical error type. It included four intervention groups (i.e., use of electronic systems, patient-centered intervention, process interventions, and inter-professional education). In total, ten reviews focused on overall medical errors (28–37) and included 257 primary studies (Table 1). Five reviews focused on the use of electronic systems to reduce overall medical error levels using health information systems, computerized provider order entry systems combined with clinical decision support systems, diagnostic and clinical decision-making aids, error-resistant systems, computer-enabled discharge communication, personal digital assistants, human simulation training) (28–32). Four reviews presented the process interventions such as failure mode and effects analysis, proactive technique, systematic safety processes, teamwork and communication training interventions, and reactive systematic safety processes

in reducing risks, medical errors and adverse events (32–34, 37). One study referred to a patient-centered intervention, i.e., documentation through patient involvement and feedback on the medical file (35). Reeves et al. focused on inter-professional education (36) (Supplementary Table 1).

Reviews confirmed that using electronic systems could reduce (28, 29) or effectively and significantly (30, 31) reduce medical errors. For example, Charles et al. (29) stated that computerized provider order entry reduces medical error and adverse drug events. The effect would be more when combined with clinical decision support systems to alert healthcare providers of medical errors (29). Studies that focused on other intervention groups [i.e., process interventions (32–34, 37), patient-centered intervention (35), and inter-professional education (36)] presented some evidence of their potential to reduce medical errors (Table 2). For example, using process interventions minimizes risks and improves service quality (33). In contrast, inter-professional education could reduce medical errors and enhance behavior culture in the emergency department (36).

Medication error

This intervention group related to medication errors and specific subcategories (prescribing, dispensing, administering, transcription and dose errors). These interventions fell into five groups: use of electronic systems, pharmacists and clinical pharmacist involvement in the treatment process, process interventions, leadership or managerial manners, and strategies and smart pumps impact. Overall, 49 reviews focused on interventions to reduce medication errors. This was the most prominent intervention category, including 1,380 primary studies (Table 1). Twentyfive reviews focused on using electronic systems (14, 16, 31, 32, 38–58). Twelve reviews focused on pharmacists and clinical pharmacist involvement in the treatment process (13, 17, 32, 41, 59–66). Five reviews presented leadership or managerial manners interventions (12, 56, 67–69). The remaining 12 reviews stated process interventions (9, 12, 32, 34, 67, 70–76), and two reviews focused on smart pumps impact (32, 77) (Table 2).

Similarly to overall medical error interventions, reviews focusing on electronic systems provided evidence that they could reduce (14, 16, 32, 38–48) or effectively and significantly (31, 49–58) reduce medication errors. For example, the most significant results were noted for computerized provider order entry in 96% error interception and 90% reduction of medication errors (41, 44). There was evidence that leadership or managerial manners intervention could effectively and significantly reduce medication errors (12, 56, 67–69). For example, redesign of diabetes prescribing charts incorporating prescribing guidelines, diabetes prescription error management pathway, and mandatory e-learning reduced insulin prescription errors from 65 to 2% (67) (Table 2, Supplementary Table 1). Reviews on pharmacists and clinical pharmacist involvement in the treatment process presented evidence of some to a very effective and significant reduction on medical errors. For example, pharmacists' participation in medical treatment leads to a 43% reduction in prescribing errors and a 27% reduction in overall medication errors (63, 64). Most reviews on process interventions had also shown that such intervention could effectively and significantly reduce medication errors (9, 12, 34, 67, 70–74), with only a few (32, 75, 76, 78) presenting only some evidence of medication error reduction. For example, double-checking reduce medication error from 2.98 to 2.12 per 1,000 medication administered and dispensing error from 9.8 to 6 (73).

Patients' fall

This group of interventions focused on interventions that could reduce patients' falls by using four different categories of interventions (professional skills and education, methods/tools evaluating patients' fall risk, process and patient care programs, organizational and workplace culture). In total, six reviews (10, 26, 27, 32, 79, 80) focused on fall prevention and included

14 primary studies. Three reviews focused on using education and professional skills interventions (10, 27, 79). Two reviews presented using methods and tools evaluating patients' fall risk (27, 32). Cumbler et al. reported process and patient care programs as beneficial interventions (27). One study focused on hourly rounding programs (80), and Braithwaite et al. presented organizational and workplace culture interventions (26) (Table 2).

Based on the results of reviews, education and professional skills interventions effectively reduced or led to a significant reduction in patients' falls (10, 27, 80), while another review showed some evidence of a reduction in patients' falls (79). For example, there were patients' fall differences in intervention groups vs. control groups through patient-centered interventions (180 in intervention group vs. 319 in control group) (79). There was evidence that methods/tools evaluating patients' fall risk intervention could effectively and significantly reduce medical errors (27), and other reviews showed that could reduce patients' falls (32). For example, using the Morse fall scale decreased falls (27). Two remaining studies focused on effectively and significantly reducing patients' falls (27, 80), and the other had some evidence of reduction (26). For example, staff education, care planning, patient training in rehabilitation and nutritionist support lead to a reduction in falls from 16.28 to 6.29 per 1,000 patient days (27) (Table 2, Supplementary Table 1).

Healthcare-associated infections

Twelve reviews and 382 primary studies focused on five groups of interventions that could reduce healthcare-associated infections (caregivers' educational and behavioral change interventions, process interventions, managerial and organizational interventions, using medication interventions and environment/equipment cleaning) (Table 1). Four reviews focused on the caregivers' education and behavioral changes (10, 81–83). Three reviews focused on process interventions (65, 72, 84). Four reviews presented the managerial and organizational interventions (26, 69, 81, 83). Three reviews reported medication interventions (65, 85, 86). Schabrun et al. focused on equipment cleaning (87) (Table 2).

Caregivers' education and behavioral change effectively reduced healthcare-associated infections (10, 81), and the other two reviews showed some evidence of a reduction in healthcare-associated infections (82, 83). For example, hand-hygiene campaigns reduced nosocomial infection rates (median effect 49%) (81). Boyd et al. presented an effective or significant reduction in healthcare-associated infections (72), and two reviews showed that these interventions could reduce healthcare-associated infections (65, 84). For example, the Keystone intensive care unit intervention for central line-associated bloodstream infections and chlorhexidine for

vascular catheter site care economically reduced healthcare-associated infections (65). One review stated that managerial and organizational interventions are significant or effective in reducing healthcare-associated infections (81), while three studies have some evidence on reducing healthcare-associated infections (26, 69, 83). For example, antibiotic stewardship, antibiotic restriction, guidelines, education, and performance feedback showed a significant decrease ranging from 13 to 82% (81). One review of medication interventions reported a significant decline (28%) in surgical site infection using a chlorhexidine impregnated dressing that applied to the surgical site (86). Another review demonstrated an effective reduction (82.1%) in colony-forming units after cleaning pieces of equipment with alcohol (87).

Diagnostic error

Three studies that included 68 primary studies focused on three intervention categories (digital and electronic interventions, patient identification and checking and quality improvement methodologies) that affect diagnostic errors (2, 32, 88) (Table 1). Two studies presented the use of digital and electronic interventions (2, 32). One study focused on the use of patient identification (2). Amaratunga et al. focused on quality improvement methodologies (88). One review focused on digital and electronic interventions showed a significant effect of interventions to reduce diagnostic error. The other one presented some evidence of diagnostic error reduction (2, 32). For example, clinical decision support systems and a web-based diagnostic reminder system significantly reduced diagnostic errors (32). Zhou et al. (2) presented some evidence of a reduction in diagnostic error using patient identification. For example, the patient identification check, obtaining informed consent, verifying the correct side and site, and a final check by the radiologist decreased the incidence rate of diagnostic error from 0.03% (9 of 32,982) to 0.005% (2). Another review reported some evidence of a reduction in diagnostic error within radiology by lean and Six Sigma approaches as quality improvement methodologies (88).

Transfusion and testing errors

Two reviews included 26 primary studies focused on the identification of patients (labeling and barcoding) intervention (11, 89) (Table 1). The results of Snyder et al.'s review was effective in reducing transfusion and testing errors (89), and another review showed some evidence on reducing transfusion and testing errors (11) (Table 2). For example, labeling significantly reduces testing errors, so the most effective intervention in reducing transfusion and testing errors was

barcoding systems, which reduced 2.26 errors to 0.17 errors per 10,000 specimens (89).

Surgical errors

Four reviews included 38 primary studies focused on two intervention groups to reduce surgical errors (use of checklists and counting instruments and material and use of radio-frequency identification technology) (15, 65, 72, 90) (Table 1). Three reviews reported using checklists and counting materials interventions (65, 72, 90). Another review focused on radio-frequency identification technology (15) (Table 2). Two reviews showed an effective reduction in surgical errors (72, 90) while, Etchells et al.'s review had some evidence related to reducing surgical errors (65). For example, using checklists (or similar interventions) could reduce equipment errors in the operating room by 48.6% (90). One review showed some evidence to reduce retained surgical instrument errors, reduce the risk of counting errors, and improve workflow using radio-frequency identification technology (15) (Table 2).

Patients' suicide

Two reviews included 112 primary studies focused on reducing patients' suicide (91, 92) (Table 1). One review focused on reducing absconding and engagement with patient's family intervention (91). Doupnik et al., focused on process and patient care interventions and contact interventions (92) (Table 2). Bowers et al. reported measures to reduce absconding and engagement with patient's family intervention, showed some evidence to reduce absconding without locking the door and engage with patients' family problems to reduce patients' suicide (91). Another review focused on process, and patient care interventions and contact interventions showed significant reduction (pooled odds ratio, 0.69) in patients' suicide by using 11 interventions (i.e., telephone, postcard, letters, coordination between the mental health care team, and follow up mental health care team) (92) (Supplementary Table 1, Table 2).

Discussion

We systematically reviewed systematic reviews for interventions to reduce medical errors in hospitals. Studies related to preventing medication errors included approximately 35 interventions. We identified 21 groups of interventions falling into seven broader categories of medical errors. The least studied category of medical errors was related to patients' suicide and surgical errors. Our findings showed that among 101 presented interventions, the use of electronic systems intervention group, was included in most of the reviews

(27 reviews). This group included interventions that reduce medication and overall medical errors. Most interventions were related to the processing group (30 interventions). Also, this group had three types of errors (overall medical error, medication error, and healthcare-associated infections). The most effective interventions were related to medication errors among medical error types (27 reviews) and electronic systems among intervention groups (12 reviews).

Patient safety has several requirements such as safe infrastructure, technologies and medical devices, patient and staff education, information, professional participation in patient safety programs, and ensuring that all individuals receive secure health services, regardless of where they are delivered. This was reiterated in the resolution on “Global action on patient safety” in May 2019 (WHA72.6) (93). In particular, the resolution requests the World Health Organization’s Director-General to formulate a global patient safety action plan in consultation with the Member States, regional economic integration organizations and all relevant stakeholders, including in the private sector. As stated in the resolution, to achieve the highest level of patient safety and to be able to reduce medical error and adverse events, one needs to recognize patient safety as a health priority in health sector policies and programs, collaborate with other member states along with the improvement of national policies, programs, guidelines, strategies and tools.

There are several ways, policies and procedures to identify medical errors. Differences in error identification methods affect the incidence of errors and error reduction interventions. These methods include voluntary reporting, direct observation, patient and family reporting, and retrospective and prospective methods (cohort and cross sectional studies) and related techniques (e.g., failure mode, effects analysis, and root cause analysis) (94–99).

The most effective interventions related to patient satisfaction referred to managerial and process interventions that show patients do not have enough knowledge about medical issues. Process and administrative interventions increase their satisfaction as a perceived issue (70, 80). Effective interventions to reduce costs and increase efficiency were related to using electronic systems and processes and managerial or leadership strategies (9, 12, 54, 70). For example, electronic distribution drug systems decreased by €44,295 in a month (9). Effective interventions related to reducing death referred to the use of electronic systems and process interventions (16, 70). For example, commercial computerized provider order entry led to a 12% reduction in intensive care units mortality rates (16). Effective interventions for increasing health care quality were referred to as checklists and counting materials, environment/equipment cleaning, use of electronic systems, and process interventions (9, 54, 87, 90). Effective interventions related to patient safety were associated with the use of electronic systems, process, education and professional skills, methods/tools evaluating patients’ fall

risk, and process and patient care interventions groups (9, 27, 34, 51, 53, 58).

As we highlighted in our study findings, use of electronic systems has a wide effect on reduction of medical errors and related deaths, efficiency and effectiveness of services, and improvement of patient safety. Of course, when using electronic systems, like any other method, one must pay attention to its specific limitations and considerations. For example, implementation of computerized prescription order entry can lead to wrong drug selection from drop-down menus (49). Nonetheless, computerized prescription order entry systems are more effective to detect medical errors when they are bundled with clinical decision support systems, which has the potential to prevent errors of medication forms nearly completely (29, 100). Simulation systems prevent iatrogenic risk related to medication errors, if the program is well designed (14).

Our review has several limitations. One is that medical errors cover a very wide range of topics that cannot be addressed in one review article. For example, topics that were left outside the scope of this paper include error identification policies, procedures and methods, disclosure approaches, and incidence of medical errors. Another limitation is that we focused on the interventions in the hospital settings. Due to the high number of papers related to the effect of interventions on medical error, we restricted our analysis to documents that reported the positive impact of the intervention on medical error reduction. Also, our study was limited to systematic reviews that had different focus; hence, meta-analyses were not possible.

Conclusion

Prevention of medical errors is vital in reducing patient’s harm and improving overall patient outcomes. A review of the combined evidence of 73 systematic reviews found that a wide range of interventions could be used to prevent and decrease of incidence of medical errors. Process and managerial interventions, and use of electronic systems had a critical role in medical error reduction.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary material](#), further inquiries can be directed to the corresponding author/s.

Author contributions

EA-E and LD conceived the basic and original idea, outlined the study, literature review, data acquisition, data analysis, interpretation of data, and drafted the article. VS contributed to data acquisition, data analysis, interpretation of data, and

drafting and revising of manuscript. All authors participated in the final design, revision of the manuscript, and have read and approved the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fmed.2022.875426/full#supplementary-material>

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