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Evolution of Intravenous Medication Errors and Preventive Systemic Defenses in Hospital Settings—A Narrative Review of Recent Evidence

Sini Kuitunen, PhD (Pharm),* Marja Airaksinen, PhD (Pharm),† and Anna-Riia Holmström, PhD (Pharm)†

Objectives: Intravenous drug administration has been associated with severe medication errors in hospitals. The present narrative review is based on a systematic literature search, and aimed to describe the recent evolution in research on systemic causes and defenses in intravenous medication errors in hospitals.

Methods: This narrative review was based on Reason's theory of systems-based risk management. A systematic literature search covering the period from June 2016 to October 2021 was conducted on Medline (Ovid). We used the search strategy and selection criteria developed for our previous systematic reviews. The included articles were analyzed and compared to our previous reviews.

Results: The updated search found 435 articles. Of the 63 included articles, 16 focused on systemic causes of intravenous medication errors, and 47 on systemic defenses. A high proportion ($n = 24$, 38%) of the studies were conducted in the United States or Canada. Most of the studies focused on drug administration ($n = 21/63$, 33%) and preparation ($n = 19/63$, 30%). Compared to our previous review of error causes, more studies ($n = 5/16$, 31%) utilized research designs with a prospective risk management approach. Within articles related to systemic defenses, smart infusion pumps remained most widely studied ($n = 10/47$, 21%), while those related to preparation technologies ($n = 7/47$, 15%) had increased.

Conclusions: This narrative review demonstrates a growing interest in systems-based risk management for intravenous drug therapy and in introducing new technology, particularly smart infusion pumps and preparation systems, as systemic defenses. When introducing new technologies, prospective assessment and continuous monitoring of emerging safety risks should be conducted.

Key Words: intravenous drugs, medication errors, defenses, hospitals, systems approach

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Intravenous (IV) drug administration has been associated with a high risk of medication errors (MEs) and other adverse drug

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events in hospital settings.^{1–4} Observational multisite studies have reported a high prevalence of MEs and procedural failures,^{5,6} while some have estimated that up to 10% of IV medication administrations include an error.⁴ When compared to other administration routes, it has been found that errors are as much as five times more likely to occur when an IV route is used.³ Moreover, many intravenously administered drugs are high-alert medications, bearing a heightened risk of causing significant patient harm if used in error.⁷ Consequently, effective interventions to highlight and eliminate IV MEs within the medication management and use (MMU) process are needed to ensure medication safety in hospital settings.^{8–15}

Studies have found preparation and administration errors to be the most common IV ME types, probably due to these phases of the MMU process being the most widely studied.^{4,16,17} However, the number of IV prescribing errors is likely to be higher as, when also considering other administration routes, prescribing and monitoring are associated with the highest prevalence rates of preventable MEs.¹⁸ Wrong administration rate errors have been identified as the most common error type in IV drug administration, followed by the wrong time of administration, and the remaining error types include administration of wrong dose, inputting wrong pump settings, and dose omission.⁴ When considering error defenses, a systematic review exploring IV preparation errors compared incidence by preparation site and/or method, finding the error incidence to be lower for doses prepared within a central pharmacy versus the nursing ward and lower for automated preparation versus manual preparation.¹⁷ In the same study, the error types and reported rates were found to vary substantially.

In 2016, we conducted systematic reviews exploring systemic causes of,¹⁹ and systemic defenses to prevent,²⁰ IV MEs. Insufficient actions to secure safe use of IV high-alert medications, lack of knowledge of the drug, calculation tasks, failure in double-checking procedures, and confusion between look-alike sound-alike medications were identified as the leading causes of IV MEs.¹⁹ Most studies exploring systemic defenses to prevent IV MEs focused on the administration stage, with smart infusion pumps being the most widely studied systemic defense.²⁰ A limited number of studies explored other stages of the MMU process, which represented a crucial area for future research. Moreover, most of the systemic defenses involved new technological solutions and features related to closed-loop medication management systems. The aim of the present narrative review was to describe the recent evolution of research on systemic causes of, and defenses to prevent, IV MEs in the MMU process in hospitals. A specific emphasis was to investigate whether the research on systemic causes has shifted more toward prospective risk management, and what the phases are of the IV MMU process to which the studied systemic defenses have been integrated.

METHODS

Theoretical Framework

The theoretical framework of the present narrative review was psychologist James Reason's (1995, 2000) systems-based risk

management theory on preventing human errors, which has been widely applied in patient and medication safety research.^{12,21–23} In health care, risk management is defined as “clinical and administrative activities undertaken to identify, evaluate, and reduce the risk of injury to patients, staff, and visitors and the risk of loss to the organization itself.”²² These activities or measures aim to prevent, remedy, or mitigate the occurrence or reoccurrence of an actual or potential patient safety event.²⁴ The starting point of the theory is that errors are inevitable when human action is involved, which is why systems relying on perfect performance by individuals to prevent errors are doomed to fail. Hospitals are considered as high-reliability organizations which should introduce safety culture to learn from errors and to implement systemic defenses for ensuring safer care.^{12,21,23} In recent decades, medication risk management has evolved from retrospective error detection and a person-centered approach toward prospective risk management and a just culture environment, where the accountability of errors is divided between the systems and the individuals.^{12,21,22,24,25}

Search Strategy and Study Selection

This narrative review was carried out according to the Scale for the Assessment of Narrative Review Articles (SANRA), which is a brief critical appraisal tool for the assessment of nonsystematic

review articles (Supplementary File 1, <http://links.lww.com/JPS/A611>).²⁶ A systematic literature search was performed on Medline (Ovid) in October 2021. We used the same search strategy as in our previous publications^{19,20} to review the most recent evidence. Medline (Ovid) was selected as a source of information as it represents a key database for medication safety research. Studies published within the period from 2016 to October 2021 were included. One reviewer (SK) selected the studies based on titles, abstracts, and full texts (Fig. 1). The PICO tool (participants, interventions, comparison, and outcomes) developed for our earlier publications^{19,20} was used to select studies for inclusion. The search found 435 articles, of which 63 articles were included in the narrative review.

Data Extraction and Analysis

One author (SK) carried out the data extraction and analysis, and the results were carefully reviewed by the other authors (A-RH, MA). At first, reference, country, study design, setting, and the main results of the included studies were extracted to 2 tables (Supplementary Files 2, <http://links.lww.com/JPS/A612>, and 3, <http://links.lww.com/JPS/A613>). After that, a classification and comparison of frequencies were performed to summarize key findings of the articles included in this narrative review (n = 63)

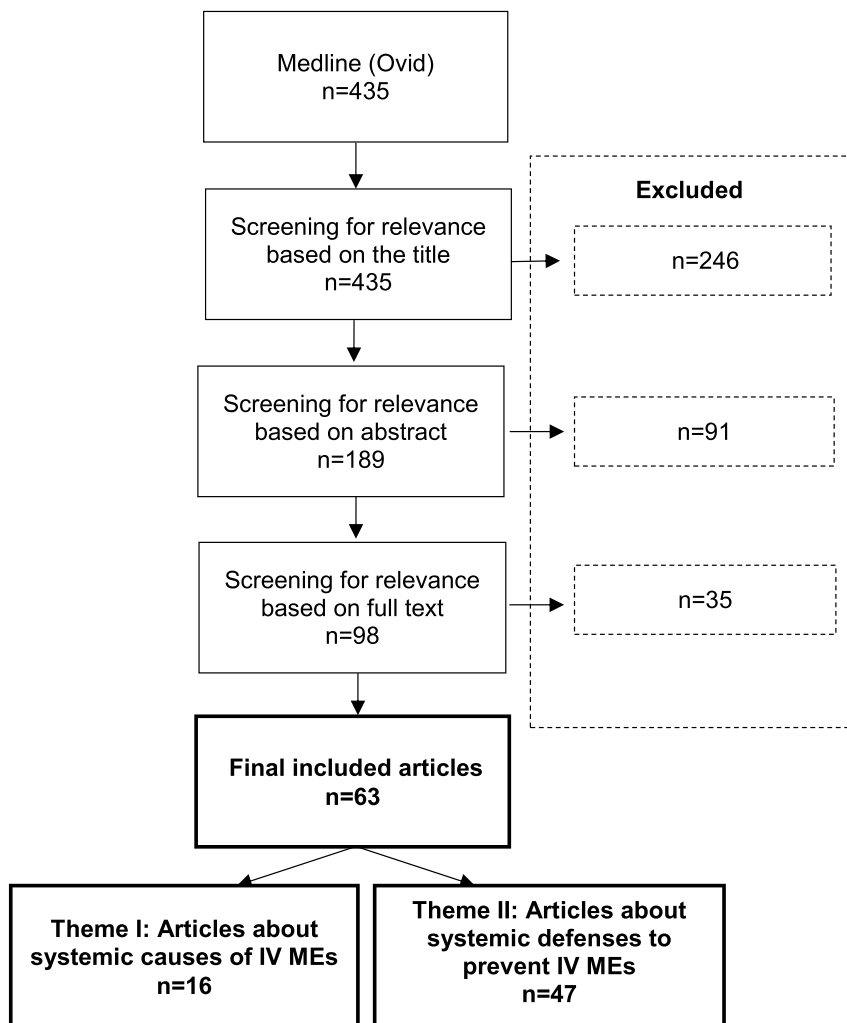


FIGURE 1. Flowchart of an updated literature search (conducted in October 2021).

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(Fig. 2). Finally, the key findings were compared to our previous systematic reviews^{19,20} to illustrate the evolution of the IV medication MMU process in hospitals.

The articles on systemic causes of IV MEs (n = 16) were classified according to the stages of the MMU process they focused on (Fig. 2). The study designs employed in the articles were analyzed to recognize whether the studies aimed to identify ME risks prospectively or retrospectively (Fig. 2).^{12,24} Study designs focusing on learning from previous incidents to minimize similar errors in the future were defined as retrospective risk management (e.g., retrospective analysis of ME reports, observations, and medical records, or interviewing healthcare professionals about MEs they have encountered).^{12,24,27} On the contrary, studies with a purpose to identify and prevent MEs before they occur were considered as prospective risk-management (accomplished by, e.g., identifying medication safety risks from the literature or by utilizing proactive risk management activities, such as failure mode and effects analysis (FMEA) or medication safety self-assessment tools).^{27–29} The number of studies utilizing a design considered as prospective risk management was compared between our earlier systematic review¹⁹ and the present narrative review (Fig. 2).

The articles on systemic defenses to prevent IV MEs (n = 47) were classified according to the MMU process stages they focused on and compared to our earlier systematic review (Fig. 2).²⁰ The evolution of systemic defenses was described using the “Swiss cheese model” comprising a central component of the systems-based risk management theory by James Reason (2000).¹² Finally, the main findings related to the most studied medication management technologies within all the included articles were summarized in 2 tables.

RESULTS

Description of Studies Exploring Systemic Causes of IV MEs (n = 16)

Our systematic search on Medline (Ovid) found 16 articles describing systemic causes of IV MEs published between June 2016 and October 2021 (Supplementary file 2, <http://links.lww.com/>

JPS/A612). These studies were conducted in the following 6 countries: United States (n = 6),^{6,30–34} United Kingdom (n = 5),^{35–39} France (n = 2),^{40,41} Canada (n = 1),⁴² South Korea (n = 1),⁴³ and Spain (n = 1).⁴⁴ Most of the studies were carried out in a hospital setting without a specification of a specialty area (n = 7), whereas some were conducted in a pediatric hospital setting (n = 3),^{35,39,41} hospital pharmacy (n = 2),^{32,42} emergency department (n = 1),³³ intensive care unit (ICU) and hematology sterile unit (n = 1),⁴⁰ neonatal intensive care unit (NICU) (n = 1),⁴⁴ and a simulated pediatric medical facility (n = 1).³⁸ There was a lot of variation between the study designs and research methods; the most used methods were observation (n = 7),^{5,6,30,31,34,36,37,43} and retrospective analysis of ME reports (n = 2).^{30,35} Other methods included a systematic review (n = 1),³⁴ analysis of IV compatibility data in literature (n = 1),⁴⁴ failure mode and effects analysis (FMEA) (n = 1),³² inductive preliminary hazard analysis (PHA) (n = 1),⁴¹ retrospective analysis of smart pump alert log data (n = 1),³¹ retrospective analysis of medical records (n = 1),⁴³ and structured chart and video review (n = 1).³³

All studies focused on a specific phase of the IV MMU process (Fig. 3). Most of the studies concerned administration (n = 8, 50%)^{6,31,33–35,40,41,44} or preparation (n = 6, 38%)^{32,33,36,39,41,42} phases. Up to 31% (n = 5)^{32,34,38,41,44} of the studies utilized research designs that could be interpreted as proactive risk management, while in our earlier systematic review¹⁹ features of prospective risk management could be identified only in 2 studies (18%).^{45,46}

Description of Studies Exploring Systemic Defenses to Prevent IV MEs (n = 47)

The systematic search on Medline (Ovid) found 47 articles describing systemic defenses to prevent IV MEs published between June 2016 and October 2021 (Supplementary file 3, <http://links.lww.com/JPS/A612>). The studies were conducted in the United States (n = 16),^{47–62} the United Kingdom (n = 7),^{63–69} Australia (n = 3),^{70–72} Brazil (n = 3),^{73–75} Spain (n = 3),^{76–78} Mexico (n = 2),^{79,80} Saudi Arabia (n = 2),^{81,82} Singapore (n = 2),^{83,84} Canada (n = 1),⁸⁵ China (n = 1),⁸⁶ France (n = 1),⁸⁷ Germany (n = 1),⁸⁸ Italy (n = 1),⁸⁹ Netherlands (n = 1),⁹⁰ and Switzerland

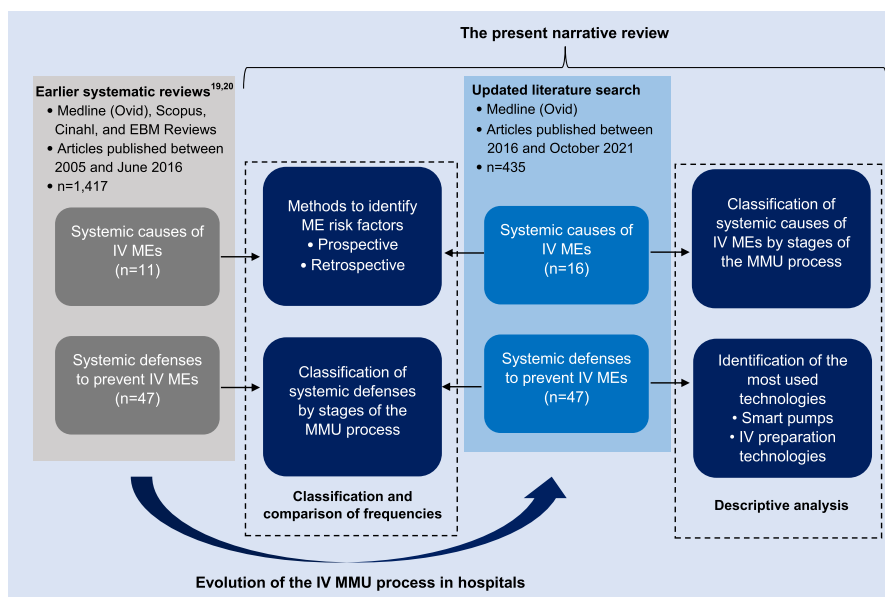


FIGURE 2. Outline of the narrative review process, analysis of the included articles (n = 63), and comparison to our previous systematic reviews.^{19,20}

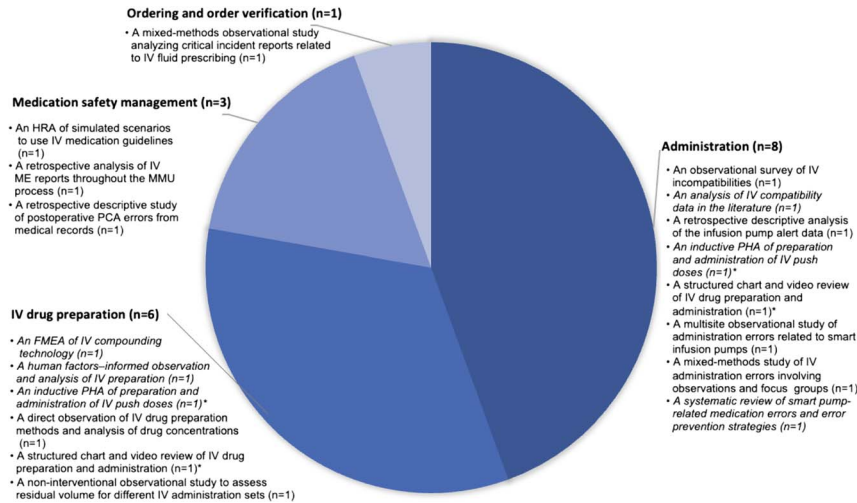


FIGURE 3. An overview of the studies focusing on systemic causes of IV MEs (n = 16).^{6,30–44} The studies are categorized according to the MMU process stages they focused on. Two studies (*) were displayed in 2 categories. Studies aiming to identify ME risks prospectively (n = 5)^{32,34,38,41,44} are highlighted in red. HRA, human reliability analysis; PCA, patient-controlled analgesia.

(n = 1).⁹¹ Some studies (n = 2) were carried out in multiple countries.^{92,93} The studies were conducted in hospital settings without a specification of a specialty area (n = 10),^{55,56,61–63,66,73,76,82,90} adult ICU (n = 9),^{49,50,52,69,75,78–80,92} hospital pharmacy (n = 7),^{47,51,57–60,93} pediatric intensive care unit (n = 5),^{65,68,72,74,77} pediatric hospital (n = 3),^{54,64,71} emergency department (n = 2),^{70,84} anesthesia department (n = 1),⁸⁷ cancer hospital (n = 1),⁸⁶ and pediatric emergency department (n = 1).⁸¹ Some studies (n = 8) were carried out in simulated environments comprising an anesthesia setting

(n = 2),^{83,88} hospital setting (n = 2),^{48,67} ICU (n = 1),⁸⁵ NICU (n = 1),⁸⁹ operating room (n = 1),⁵³ and pediatric emergency department (n = 1).⁹¹

A lot of variation between the study designs and research methods was identified (Supplementary file 3, <http://links.lww.com/JPS/A613>). The designs used in more than one study were observational simulation studies (n = 8),^{48,53,67,83,85,88,89,91} retrospective analysis of drug preparation reports (n = 6),^{47,51,57,59,60,93} mixed-methods studies (n = 5),^{63,64,68,69,76} observational studies (n = 5),^{49,50,56,58,81}

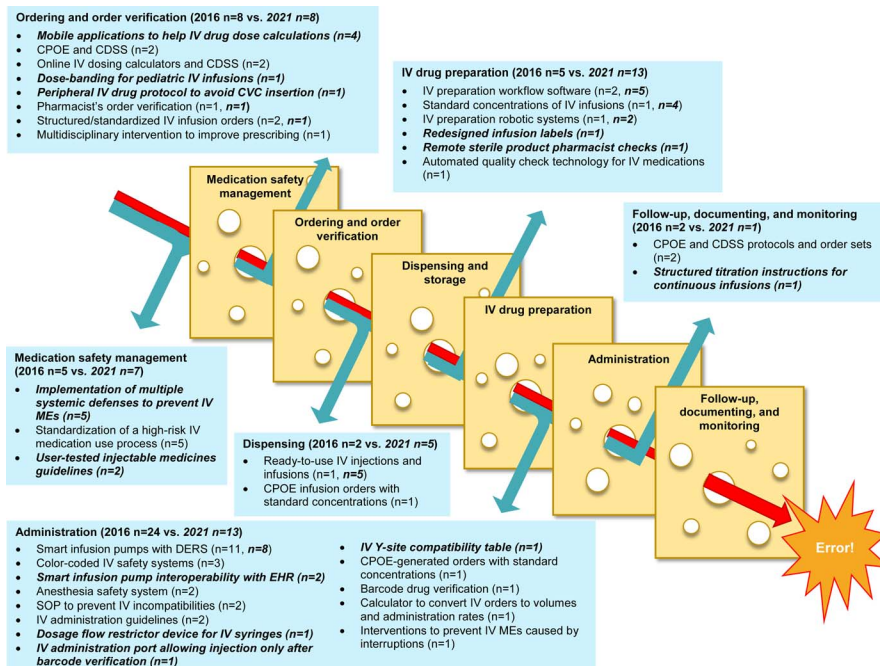


FIGURE 4. Evolution of systemic defenses to prevent IV MEs. The defenses identified in the articles (n = 47)^{47–93} found in the updated literature search on Medline (Ovid) in 2021 are highlighted in red. For comparison, the defenses identified in our original systematic review are displayed in normal text.²⁰ The defenses are classified according to the stages of the MMU process and presented using the “Swiss cheese model” by Reason (2000).¹² CDSS, clinical decision support system; CPOE, computerized prescriber order entry; CVC, central venous catheter; DERS, dose error reduction software; SOP, standard operating procedure.

TABLE 1. A Summary of the Key Findings of Studies Investigating Smart Infusion Pumps (n = 13)^{6,31,34,55,62,63,69,74,75,77,79,80,82}

Reference	Study Design	Objectives	Key Findings
Systemic causes of IV MEs related to smart infusion pumps (n = 3 studies)			
Kirkendall et al, 2020 ³⁴	A systematic review.	To identify the types of human based MEs and associated error prevention strategies related to smart pump use.	Smart pumps produce new previously unknown classes of MEs associated with their use. Extraction of error types and prevention strategies resulted in the identification of 18 smart pump-specific error types (e.g., drug library errors and programming errors), 21 error subtypes, and 10 prevention strategies (e.g., technological integration of systems and uniform pump brand/function).
Marwitz et al, 2019 ³¹	A retrospective descriptive analysis of the infusion pump alert data.	To use the REMEDI dataset, an aggregate, multihospital database inclusive of smart pump analytics, to improve the current understanding of clinical practices for IV HAM administration.	Over 70% of smart pump alerts were bypassed by clinicians in 17 hospitals, which is a symptom of alert fatigue.
Schnock et al, 2017 ⁶	A multisite study using the prospective point prevalence approach.	To investigate the types and frequency of intravenous medication errors associated with smart pumps in the USA.	60% of the observed infusions in 10 hospitals were associated with one or more MEs. The MEs were predominantly associated with violations of hospital policy (e.g., labeling errors, bypassing the smart pump and the drug library).
Smart infusion pumps with DERS as a systemic defense (n = 8)			
Giuliano et al, 2018 ⁵⁵	A retrospective one-way analysis of variance and a descriptive overview of smart pump alerts.	To improve the overall understanding of IV smart pump drug library compliance by using the REMEDI data set to describe end-user compliance.	There are differences in IV smart pump compliance both within and between hospital systems. IV smart pump type and the number of drug library profiles may be influencing factors for smart pump compliance.
Ibarra-Perez et al, 2021 ⁸⁰	A descriptive retrospective analysis of the smart pump alert reports.	To investigate the efficacy of IV smart pumps with drug libraries and DERS to intercept programming errors entailing high risk for patients in an adult ICU.	Drug library compliance was 70%. MEs were intercepted in 30% of infusions when using a drug library. Upper hard limit alerts accounted for 26% of pump reprogramming events.
Jani et al, 2020 ⁶³	A retrospective review of ME reports and observed MEs.	To explore the role of smart infusion devices in preventing or contributing to medication administration errors using retrospective review of 2 complementary data sets.	Smart pumps both prevent and contribute to MEs. Using any infusion device rather than gravitational administration may have prevented 8–13% of MEs. EHR-integrated pumps could have prevented 52–73% of MEs.
Manrique-Rodriguez et al, 2016 ⁷⁷	A prospective, observational interventional study with analytical components.	To estimate the impact of smart pump implementation in a PICU in terms of number and type of administration errors intercepted.	Drug library compliance was 84% and 283 MEs were intercepted for a study period of 62 months. A high-risk drug was involved in 58% of prevented MEs, which is why smart pump implementation was proven effective in intercepting programming errors of high-risk drugs.
Moreira et al, 2020 ⁷⁵	A systematic review and meta-analysis.	To identify the scientific evidence for the frequency of handling errors of conventional and smart pump infusions in IV insulin therapy in ICUs.	An error rate of 10%–40% was associated with conventional pumps and 0–14% with smart pumps. Meta-analysis of 2 studies favored smart pumps to reduce the relative risk of programming errors by 51%.
Palacios Rosas et al, 2019 ⁷⁹	A retrospective observational study with a pre-post design.	To evaluate the economic impact of the implementation of smart infusion pumps in the consumption of IV solutions in an ICU.	Implementation of smart infusion pumps allows savings by reducing the annual consumption of IV solutions measured in both units (18%) and liters (22.3%).
Silva et al, 2019 ⁷⁴	A mathematical modeling for economic analysis to analyze cost-effectiveness.	To analyze cost-effectiveness and to calculate incremental cost-effectiveness ratio of the use of infusion pumps with drug library to reduce errors in IV drug administration in pediatric and neonatal patients in ICUs.	Infusion pump with a drug library may be the best strategy to avoid IV administration errors. Although it has the lowest cost, the conventional pump also has lower effectiveness.

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TABLE 1. (Continued)

Reference	Study Design	Objectives	Key Findings
Waterson et al, 2020 ⁸²	A retrospective review of drug library reports.	To establish baseline data to show how metrics in the set-up and programming phase of IV medication administration can be produced from medication library near-miss error reports from infusion pumps.	Drug library compliance was 74%. Wrong drug selections (LASA errors) represented 3% of drug library alerts and 22% of canceled infusions. Wrong dose selection was responsible for 3% of alerts and 19% of canceled infusions.
Smart infusion pump interoperability with EHR as a systemic defense (n = 2)			
Furniss et al, 2020 ⁶⁹	A sociotechnical investigation utilizing in-depth qualitative observations and interviews.	To gain an in-depth understanding of the patterns of working that had evolved in an ICU where a closed-loop IV medication administration documentation system had been implemented and of the consequent effects on patient safety.	Several benefits were identified (e.g., hard and soft limits for different drugs, bolus limits for certain drugs, automatic recording of drug administration). Challenges included inadequate and outdated drug libraries, pump or medications not mapped with the EHR system, and inconsistency in dosing units between the drug library, EHR and usual pump-programming practices.
Wei et al, 2021 ⁶²	Retrospective analysis of infusion pump log data.	To describe the patient safety and financial impact of pump-EHR interoperability at a community hospital.	Pump-EHR interoperability leads to safer administration of IV medications based on improved drug library compliance (74% versus 83%) and more accurate smart pump programming (infusions generating alerts 4% versus 3%).

DERS, dose error reduction software; LASA, look alike sound alike; ME, medication error; PICU, pediatric intensive care unit; REMEDI, Regenstrief National Center for Medical Device Informatics.

retrospective analysis of smart infusion pump alert log data (n = 5),^{55,62,77,80,82} studies measuring costs or cost effectiveness of the studied defense (n = 4),^{66,74,87,90} observational intervention studies (n = 3),^{61,71,73} retrospective or observational studies measuring drug consumption (n = 2),^{52,79} chart reviews (n = 2),^{70,72} and studies to design and develop systemic defenses (n = 2).^{65,92} Other methods included an analysis of administration error reports (n = 1),⁵⁴ a survey study (n = 1),⁸⁴ healthcare failure mode and effects analysis (HFMEA) (n = 1),⁸⁶ a systematic review (n = 1),⁷⁸ and a systematic review with a meta-analysis (n = 1).⁷⁵

The evolution of systemic defenses to prevent IV MEs between our previous systematic review²⁰ and the present narrative review (n = 47 articles) is presented in Figure 4. A growing research interest in systemic defenses related to IV preparation (n = 13)^{47,51,53,57–60,65,68,72,76,89,93} and ready-to-use IV drugs (n = 5)^{48,56,64,87,90} was identified. Administration remained the most widely studied phase of the MMU process (n = 13),^{55,62,63,69,74,75,77–80,82–84} Overall, research of systemic defenses to secure IV medication safety has shifted more toward introduction of new technologies, especially in IV preparation and administration.

The Most Studied Technological Solutions to Secure Safe IV MMU Process

The most studied medication management technologies in all the included articles (n = 63) were smart infusion pumps (n = 13, 21%)^{6,31,34,55,62,63,69,74,75,77,79,80,82} (Table 1) and IV preparation workflow systems (n = 8, 13%)^{32,47,51,57,59,60,89,93} (Table 2). Most of these studies were focused on investigating smart pumps and IV preparation workflow systems as systemic defenses (n = 17),^{47,51,55,57,59,60,62,63,69,74,75,77,79,80,82,89,93} while only some explored the causes of MEs related to implementation and use of these technologies (n = 4).^{6,31,32,34} The studies of smart infusion pumps focused on pump compliance,^{55,77,80,82} cost-effectiveness,^{74,79} the ability of smart pumps to prevent IV MEs,^{63,75} and interoperability with electronic health record (EHR)

system (Table 1).^{62,69} IV preparation workflow systems were examined from 2 different perspectives: prospective risk management in system implementation,³² and to describe the benefits of these systems in terms of preventing preparation errors (Table 2).^{47,51,57,59,93} In addition, 2 studies investigated feasibility and effectiveness of IV robotic system as a systemic defense.^{60,89}

DISCUSSION

Our narrative review demonstrated a recent expansion of, and growing interest in, research related to medication safety of IV drug therapy. When compared to our previous systematic reviews,^{19,20} the present updated literature search resulted in similar numbers of publications, although the search timeframe was shorter than in the original search, and the current search was conducted only in one database. While our previous review of systemic causes of IV MEs highlighted the need for more research into prescribing, preparation, and administration phases,¹⁹ the present narrative review indicated that research interest in drug preparation and administration has remained, but research into causes of prescribing errors is still lacking. In addition, the transition from using retrospective research methods and study designs toward prospective risk management was identified in studies investigating systemic causes of IV MEs, because methods such as FMEA³² and inductive PHA⁴¹ were increasingly used in recent studies. This may represent a currently increasing trend of study focus in preventive IV medication risk management and has not been demonstrated in such an extent in previous literature.

In relation to studying systemic defenses to IV MEs, the stages of prescribing, preparation, and administration remained dominant.²⁰ However, the identified widely expanding research interest in systemic defenses to secure safe IV drug preparation represents a key finding. This is central, as manual IV drug preparation has been identified as an especially high-risk task.^{4,16,17} If an IV workflow management system is not available, it is recommended that a second individual performs an independent verification of

TABLE 2. A Summary of the Key Findings of Studies Investigating IV Preparation Workflow Technologies or IV Robotic Systems (n = 8)^{32,47,51,57,59,60,89,93}

Reference	Study Design	Objectives	Key Findings
Systemic causes of MEs related to IV preparation workflow software (n = 1 study)			
Feemster et al, 2021 ³²	FMEA.	To identify potential failure points in a new chemotherapy preparation technology and to implement changes that prevent or minimize the consequences of those failures before they occur.	FMEA is useful for risk mitigation and workflow optimization prior to the implementation of an IV compounding technology. The chemotherapy workflow was defined as a 41-step process with 16 failure modes.
IV preparation workflow software as a systemic defense (n = 5)			
Bucci et al, 2019 ⁴⁷	A retrospective analysis of TAWF error reports and manual error reports.	To evaluate the impact of a gravimetric-based TAWF system on the nonhazardous compounded sterile product error capture rate, production times, and pharmacy staff perceptions of compounding methods.	IV preparation with a gravimetric TAWF system is slower than manual volumetric preparation but can improve the error capture rate (41% versus <1%). Staff perceived the TAWF method to be the safest and most accurate.
Eckel et al, 2019 ⁵¹	A retrospective analysis of TAWF error reports and manual error reports.	To evaluate the benefits of TAWF compared with manual workflow (non-TAWF) on IV room efficiency, costs, and safety at hospitals with more than 200 beds.	The use of TAWF in the IV room was associated with detecting 14 times more MEs than the use of non-TAWF, demonstrating the different frequency of error in the results. TAWF also led to a faster preparation time with a lower cost.
Higgins et al, 2019 ⁵⁷	A retrospective analysis of TAWF error reports and manual error reports.	To evaluate the benefits of TAWF compared to manual workflow (non-TAWF) on IV room efficiency, costs, and safety at community hospitals with less than 200 beds.	The TAWF sites detected errors at a significantly higher rate (4%) compared to the non-TAWF sites (<1%) (<i>P</i> < 0.05). The top error-reporting category for the TAWF sites was incorrect medication (72%). The use of TAWF may be associated with a decrease in turnaround time and a decrease in overall cost.
Lin et al, 2018 ⁵⁹	A retrospective analysis of the error report sample hospital information system database.	To determine the financial costs associated with wasted and missing doses before and after the implementation of an IVWMS and to quantify the number and the rate of detected IV preparation errors.	The adoption of the IVWMS significantly reduced the amount of wasted and missing IV doses from 21% to 7%. The overall cost savings of using the system was \$144,000 over three months. The total number of MEs detected was 1,160 (1%) after using the IVWMS.
Terkola et al, 2017 ⁹³	A large-scale, multicenter, multinational, retrospective study of preparation error reports.	To detect medication errors with possible critical therapeutic impact as determined by the rate of prevented medication errors in chemotherapy compounding after implementation of gravimetric measurement.	A gravimetric IV workflow system detected and prevented MEs that would not have been recognized with traditional methods. Eight percent of the antineoplastic drug doses had ME levels outside the accepted tolerance range. The proportion of doses with deviations >10% ranged from 0%–5% (mean 2.25%), and >20% ranged from 0%–1% (mean 0.71%).
IV preparation robotic system as a systemic defense (n = 2)			
Amodeo et al, 2019 ⁸⁹	A simulated experimental controlled observational study.	To analyze the advantages of using the IV robotic system, compared to the manual preparation of injectable drugs in terms of accuracy, cost, and time in NICU.	The median error observed during reconstitution, dilution, and final therapy of the drugs prepared by the IV robotics ranged within ±5% accuracy, with narrower ranges of ME compared to manual preparation. The IV robotics consumed fewer materials, reduced costs, decreased preparation time, and optimized the medication process.
Pang et al, 2021 ⁶⁰	A retrospective analysis of preparation reports from the IV preparation system's internal database.	To compare an IV gravimetric TAWF platform to an IV robotic system.	Implementing either an IV gravimetric TAWF system or an IV robotics system will result in similar compounding accuracy and precision. Preparation time was less with the use of the IV gravimetric TAWF versus the IV robotic system, but the IV robotic system required less human intervention.

FMEA = failure mode and effects analysis, IV = intravenous, IVWMS = intravenous workflow management system, ME = medication error, TAWF = technology-assisted workflow.

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manual additions to ensure that the proper medications (and diluents) are added, including confirmation of the proper volume of each medication (and diluent) before its addition to the final container.¹⁵ However, without technological assistance, manual double-check procedures have been recognized as complex, laborious, and rarely executed to full extent.^{94,95} Our present review identified a growing interest in IV preparation workflow software and robotic systems that could secure and, at least to some extent, replace risky manual work steps.^{47,51,57,59,60,89,93} Implementation of these systems has also been highlighted elsewhere, accompanied by technology utilized in telepharmacy operations.^{15,27}

In addition to streamlining the preparation workflow and equipment, standardizing IV infusions is one of the key components of error prevention both in adult and pediatric populations.^{10,65,68,72,76,96,97} However, the most powerful safeguard against preparation errors is to dispense IV medications in ready-to-administer packaging without further manipulation by the person administering the medication (e.g., withdrawing doses from containers or reconstituting powdered drug products).^{27,96,97} This trend was also noticeable in our review, as safety and cost-effectiveness of ready-to-use IV injections and infusions represented a new individual research area.^{48,56,64,87,90} Overall, our work shows that several alternative systemic defenses to secure safe preparation of IV medications are available, with the aim to either reduce or secure risky manual work steps. When it comes to IV medication guidelines, user-testing seems to be worthwhile to ensure practical and easy-to-understand instructions.³⁸

Smart infusion pumps remained one of the most widely studied technological defense in IV drug therapy.^{55,63,74,75,77,79,80,82} Examples of new perspectives include studies employing larger datasets collected from multiple hospitals^{31,55} and smart infusion pump cost-effectiveness.⁷⁴ In the literature, smart infusion pumps have been associated with alert fatigue resulting in insufficient compliance with drug library use and high override rates of soft limits.^{10,20,98,99} Other barriers include limitations in pump capabilities, availability of pumps in clinical care areas, unfunctional programming workflow, risks associated with secondary infusions, pump data analysis not utilized in quality improvement purposes, and deficiencies in drug library use and updates (e.g., omitting specific drugs or IV fluids).^{10,100,101} Despite these challenges, the use of smart pumps with dose-error reduction software is recommended for every drug infusion in all care settings as they may serve as an effective defense if their use is optimized.^{10,29}

However, implementation of new technologies may also create new, unexpected risks.^{10,15,27,100} This was observed in studies focusing on smart infusion pumps,^{6,31,34} as well as IV workflow systems,³² and patient-controlled analgesia.⁴³ Especially smart pumps were found to introduce their own class of MEs that have not been considered in taxonomies of current ME reporting systems, which may hinder their detection.³⁴ Consequently, it is important to evaluate possible new medication safety risks caused by defense implementation, as well as to improve and monitor their usability, which helps to avoid creation of risky shortcuts.^{10,15,27,100} A new area of research interest was smart infusion pump interoperability with EHR,^{62,69} also identified as an important area of development elsewhere.^{8–10,29} Nonetheless, during the analysis process we observed that the current search strategy was not sensitive enough to detect all studies related to the EHR interoperability with smart infusion pump^{102–106} and patient-controlled analgesia pumps.¹⁰⁷ Therefore, more targeted research objectives and search strategies are needed in future systematic reviews of new technologies to secure safe IV MMU process.

The findings of the present review are preliminary and indicative in nature, as the literature search was performed in only one database. Because of the increased use of technological solutions

and closed-loop medication management systems, there is a continuous need to explore the emerging new risks throughout the IV MMU process. Moreover, it will be important to investigate effectiveness of systemic defenses in stronger outcomes research designs able to provide high quality evidence, both in terms of medication safety and cost effectiveness. As more data is available from technology integrated into MMU systems (e.g., compounding error reports within IV workflow management systems, smart pump alert log data, reports of EHR system-generated alerts), it is essential to use this information in academic research, practice development, and in knowledge-based leadership within hospital organizations. There is also a need for further studies to explore safety of IV drug administration in other settings apart from inpatient care. This would be crucial as IV medications are commonly administered in ambulatory settings, such as home infusion chemotherapy, pain management, and antimicrobial therapy.

CONCLUSIONS

This narrative review demonstrates that interest is still growing in systems-based risk management for IV drug therapy. The use of study designs and methods based on prospective risk management has increased in studies investigating systemic causes of IV MEs. This is a reasonable direction for development as safeguarding the IV MMU process has shifted toward application of technologies to replace or support manual error-prone work steps, which, in turn, may create new unexpected risks. In relation to studying systemic defenses to IV MEs, the stages of prescribing, preparation, and administration remained dominant. However, monitoring the usability of new defenses is recommended to ensure their feasible use and to avoid the development of shortcuts posing unnecessary safety risks.

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