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

Kuitunen, Sini; Airaksinen, Marja; Holmström, Anna-Riia

2024-06-01

Lippincott Williams and Wilkins Ltd.

http://hdl.handle.net/10138/576617

Kuitunen, S, Airaksinen, M & Holmström, A-R 2024, 'Evolution of Intravenous Medication Errors and Preventive Systemic Defenses in Hospital Settings - A Narrative Review of Recent Evidence', Journal of Patient Safety, vol. 20, no. 4, pp. E29-E39. https://doi.org/10.1097/PTS.0000000000001222

OPEN

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

(*J Patient Saf* 2024;20: e29–e39)

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

From the *HUS Pharmacy, Hospital Pharmacy of Helsinki University Hospital (HUS); and †Clinical Pharmacy Group, Division of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, University of Helsinki, Helsinki, Finland.

Correspondence: Anna-Riia Holmström, PhD (Pharm), Clinical Pharmacy Group, Division of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, University of Helsinki, PL 56 (Viikinkaari 5), 00014 Helsingin yliopisto, Helsinki, Finland (e-mail: anna-riia.holmstrom@helsinki.fi).

Sini Kuitunen had a PhD research grant from the University Pharmacy (Yliopiston Apteekki), which is a pharmacy corporation owned by the University of Helsinki, Finland. Open access funded by Helsinki University Library. The authors disclose no conflict of interests.

Sini Kuitunen received a PhD research grant from the University Pharmacy (Yliopiston Apteekki), which is a pharmacy corporation owned by the University of Helsinki. The funder had no input in the design, methods, data collection, analysis, or preparation of this paper.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.journalpatientsafety.com).

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)

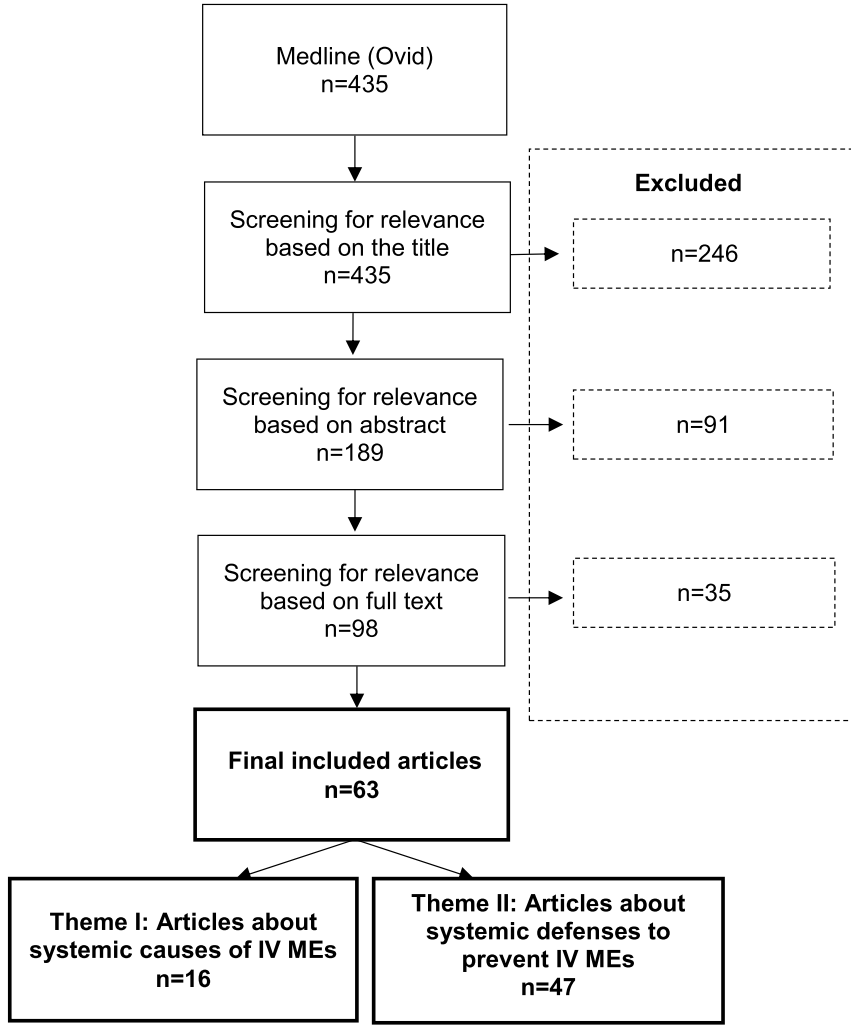

FIGURE 1. Flowchart of an updated literature search (conducted in October 2021).

(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 review[19] 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),[6,30,31,34,36,37,43] 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)[5,6,36,38–40,42] 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 review[19] 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

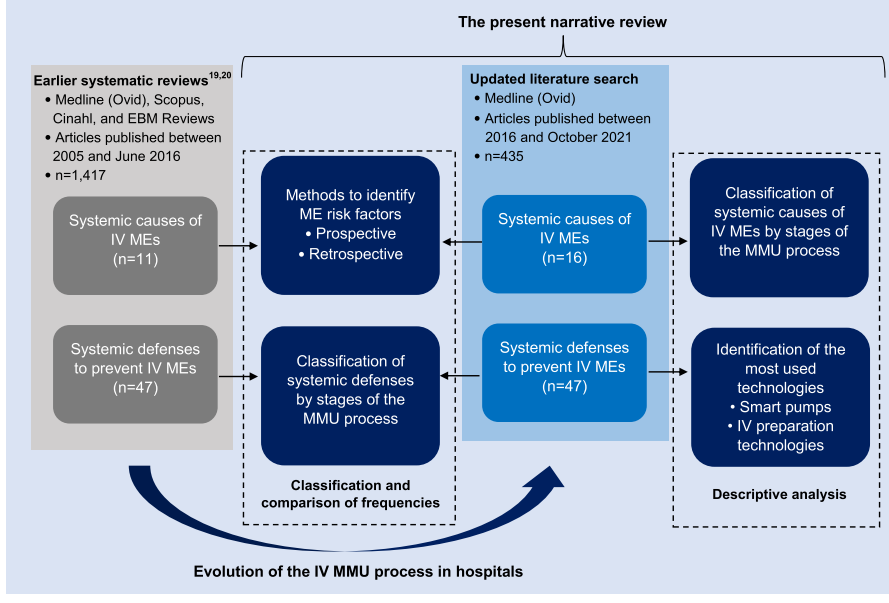

FIGURE 2. Outline of the narrative review process, analysis of the included articles (n = 63), and comparison to our previous systematic reviews.[19,20]

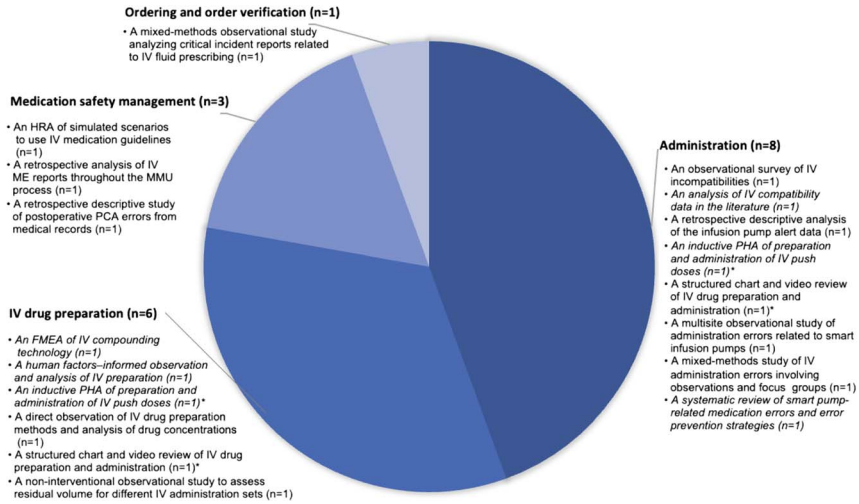

FIGURE 3. An overview of the studies focusing on systemic causes of IV MEs (n = 16).[6,30–44] The studies are categorized according to the MMU process stages they focused on. Two studies (*) were displayed in 2 categories. Studies aiming to identify ME risks prospectively (n = 5)[32,34,38,41,44] are 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]

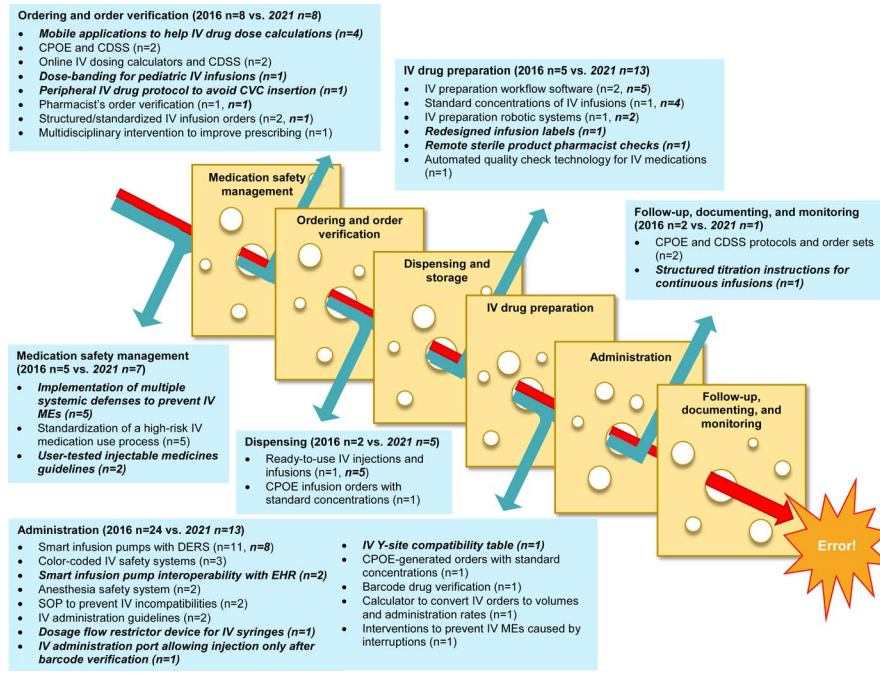

FIGURE 4. Evolution of systemic defenses to prevent IV MEs. The defenses identified in the articles (n = 47)[47–93] found in the updated literature search on Medline (Ovid) in 2021 are highlighted in red. For comparison, the defenses identified in our original systematic review are displayed in normal 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.

(Continued next page)

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 review[20] 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 FMEA[32] and inductive PHA[41] 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%) ($P < 0.05$). 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.

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.

REFERENCES

1. Keers RN, Williams SD, Cooke J, et al. Causes of medication administration errors in hospitals: a systematic review of quantitative and qualitative evidence. *Drug Saf*. 2013;36:1045–1067.
2. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA*. 2001;285:2114–2120.
3. Mcleod MC, Barber N, Franklin BD. Methodological variations and their effects on reported medication administration error rates. *BMJ Qual Saf*. 2013;22:278–289.
4. Sutherland A, Canobbio M, Clarke J, et al. Incidence and prevalence of intravenous medication errors in the UK: a systematic review. *Eur J Hosp Pharm*. 2020;27:3–8.
5. Lyons I, Furniss D, Blandford A, et al. Errors and discrepancies in the administration of intravenous infusions: a mixed methods multihospital observational study. *BMJ Qual Saf*. 2018;27:892–901.
6. Schnock KO, Dykes PC, Albert J, et al. The frequency of intravenous medication administration errors related to smart infusion pumps: a multihospital observational study. *BMJ Qual Saf*. 2017;26:131–140.
7. Institute for Safe Medication Practices. ISMP list of high-alert medications in acute care settings. Published 2018. Available at: https://www.ismp.org/recommendations/high-alert-medications-acute-list. Accessed November 27, 2022.
8. Vanderveen T. Intravenous infusion medication safety: the vision becomes reality. *Pat Saf Qual Healthc*. 2013;10:24–30. Accessed November 27, 2022. https://www.psqh.com/analysis/intravenous-infusion-medication-safety-the-vision-becomes-reality/.
9. Vanderveen T. From smart pumps to intelligent infusion systems—The promise of interoperability. *Patient Safety and Quality Healthcare*. Published 2014. Available at: https://www.psqh.com/analysis/from-smart-pumps-to-intelligent-infusion-systems-the-promise-of-interoperability/. Accessed November 27, 2022.

10. Institute for Safe Medication Practices. ISMP guidelines for optimizing safe implementation and use of smart infusion pumps; 2020. Available at: https://www.ismp.org/guidelines/safe-implementation-and-use-smart-pumps. Accessed November 27, 2022.
11. The Joint Commission. Sentinel event alert 53 managing risk during transition to new ISO tubing connector standards.; 2014. Available at: https://www.jointcommission.org/resources/sentinel-event/sentinel-event-alert-newsletters/sentinel-event-alert-53-managing-risk-during-transition-to-new-iso-tubing-connector-standards/. Accessed November 27, 2022.
12. Reason J. Human error: models and management. *BMJ*. 2000;320:768–770.
13. Kuitunen S. Medication safety in intravenous drug administration: error causes and systemic defenses in hospital setting. Doctoral thesis. University of Helsinki; 2022. Available at: http://urn.fi/URN:ISBN:978-951-51-8563-1. Accessed October 18, 2022.
14. Joint Commission International. *Joint Commission International Accreditation Standards for Hospitals*. 5th ed. Oakbrook Terrace, IL: Joint Commission Resources; 2020.
15. Institute for Safe Medication Practices. *ISMP Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology.*; 2022. Available at: http://www.ismp.org. Accessed November 27, 2022
16. Mcdowell SE, Mt-isa S, Ashby D, et al. Where errors occur in the preparation and administration of intravenous medicines: a systematic review and Bayesian analysis. *Qual Saf Health Care*. 2010;19:341–345.
17. Hedlund N, Beer I, Hoppe-Tichy T, et al. Systematic evidence review of rates and burden of harm of intravenous admixture drug preparation errors in healthcare settings. *BMJ Open*. 2017;7:e015912.
18. Hodkinson A, Tyler N, Ashcroft DM, et al. Preventable medication harm across health care settings: a systematic review and meta-analysis. *BMC Med*. 2020;18:313.
19. Kuitunen S, Niittynen I, Airaksinen M, et al. Systemic causes of in-hospital intravenous medication errors: a systematic review. *J Patient Saf*. 2021;17:e1660–e1668.
20. Kuitunen SK, Niittynen I, Airaksinen M, et al. Systemic defenses to prevent intravenous medication errors in hospitals: a systematic review. *J Patient Saf*. 2021;17:e1669–e1680.
21. Reason J. Understanding adverse events: human factors. *Qual Health Care*. 1995;4:80–89.
22. Council of Europe. Creation of a better medication safety culture in Europe: building up safe medication practices.; 2006. Available at: http://optimiz-sih-circ-med.fr/Documents/Council_of_Europe_Medication_Safety_Report_19-03-2007.pdf. Accessed November 27, 2022
23. Institute of Medicine, Kohn LT, Corrigan JM, Donaldson MS, eds. In: *To Err Is Human: Building a Safer Health System*. Washington, DC: National Academy Press; 2000.
24. Dückers M, Faber M, Cruijsberg J, et al. Safety and risk management interventions in hospitals: a systematic review of the literature. *Med Care Res Rev*. 2009;66(6 Suppl):90S–119S.
25. Rogers E, Griffin E, Carnie W, et al. A just culture approach to managing medication errors. *Hosp Pharm*. 2017;52:308–315.
26. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev*. 2019;4:5.
27. Billstein-Leber M, Carrillo CJD, Cassano AT, et al. ASHP guidelines on preventing medication errors in hospitals. *Am J Health Syst Pharm*. 2018;75:1493–1517.
28. Celikkayalar E, Myllyntausta M, Grissinger M, et al. Adapting and remodelling the US Institute for Safe Medication Practices' Medication Safety Self-assessment tool for hospitals to be used to support national medication safety initiatives in Finland. *Int J Pharm Pract*. 2016;24:262–270.
29. Institute for Safe Medication Practices. ISMP targeted medication safety best practices for hospitals 2022–2023.; 2022. Available at: https://www.ismp.org/guidelines/best-practices-hospitals. Accessed November 27, 2022.
30. Wolf ZR. Medication errors involving the intravenous administration route: characteristics of voluntarily reported medication errors. *J Infus Nurs*. 2016;39:235–248.
31. Marwitz KK, Giuliano KK, Su WT, et al. High-alert medication administration and intravenous smart pumps: a descriptive analysis of clinical practice. *Res Social Adm Pharm*. 2019;15:889–894.
32. Feemster AA, Augustino M, Duncan R, et al. Use of failure modes and effects analysis to mitigate potential risks prior to implementation of an intravenous compounding technology. *Am J Health-Syst Pharm*. 2021;78:1323–1329.
33. Cole JB, Knack SK, Karl ER, et al. Human errors and adverse hemodynamic events related to "push dose pressors" in the emergency department. *J Med Toxicol*. 2019;15:276–286.
34. Kirkendall ES, Timmons K, Huth H, et al. Human-based errors involving smart infusion pumps: a catalog of error types and prevention strategies. *Drug Saf*. 2020;43:1073–1087.
35. Conn RL, McVea S, Carrington A, et al. Intravenous fluid prescribing errors in children: mixed methods analysis of critical incidents. *PloS One*. 2017;12:e0186210.
36. Cooper DM, Rassam T, Mellor A. Non-flushing of IV administration sets: an under-recognised under-dosing risk. *Br J Nurs*. 2018;27:S4–S12.
37. Furniss D, Lyons I, Franklin BD, et al. Procedural and documentation variations in intravenous infusion administration: a mixed methods study of policy and practice across 16 hospital trusts in England. *BMC Health Serv Res*. 2018;18:270.
38. Jones MD, Clarke J, Feather C, et al. Use of pediatric injectable medicines guidelines and associated medication administration errors: a human reliability analysis. *Ann Pharmacother*. 2021;55:1333–1340.
39. Rashed AN, Tomlin S, Aguado V, et al. Sources and magnitude of error in preparing morphine infusions for nurse-patient controlled analgesia in a UK paediatric hospital. *Int J Clin Pharmacol*. 2016;38:1069–1074.
40. Maison O, Tardy C, Cabelguenne D, et al. Drug incompatibilities in intravenous therapy: evaluation and proposition of preventive tools in intensive care and hematology units. *Eur J Clin Pharmacol*. 2019;75:179–187.
41. Hfaiedh N, Kabiche S, Delescluse C, et al. Performing a preliminary hazard analysis applied to administration of injectable drugs to infants. *J Eval Clin Pract*. 2017;23:875–881.
42. Gilbert RE, Kozak MC, Dobish RB, et al. Intravenous chemotherapy compounding errors in a follow-up pan-Canadian observational study. *J Oncol Pract*. 2018;14:E295–E303.
43. Lee Y, Kim K, Kim M. CE: Original Research: errors in postoperative administration of intravenous patient-controlled analgesia: a retrospective study. *Am J Nurs*. 2019;119:22–27.
44. Fernández-Peña A, Katsumiti A, de Basagoiti A, et al. Drug compatibility in neonatal intensive care units: gaps in knowledge and discordances. *Eur J Pediatr*. 2021;180:2305–2313.
45. Nerich V, Limat S, Demarchi M, et al. Computerized physician order entry of injectable antineoplastic drugs: an epidemiologic study of prescribing medication errors. *Int J Med Inform*. 2010;79:699–706.
46. White R, Cassano-Piché A, Fields A, et al. Intravenous chemotherapy preparation errors: patient safety risks identified in a pan-Canadian exploratory study. *J Oncol Pharm Pract*. 2014;20:40–46.
47. Bucci TG, Hedrick TL, Roberts PA, et al. Evaluation of gravimetric-based technology-assisted workflow for nonhazardous sterile product preparation. *Am J Health Syst Pharm*. 2019;76:1071–1077.
48. Burger M, Degnan D. Comparative safety, efficiency, and nursing preference among 3 methods for intravenous push medication

preparation: a randomized crossover simulation study. *J Patient Saf*. 2019; 15:238–245.

49. Cape KM, Jones LG, Weber ML, et al. Implementation of a protocol for peripheral intravenous norepinephrine: does it save central line insertion, is it safe? *J Pharm Pract*. 2020;35:347–351.
50. Chen A, Vogan E, Foglio J, et al. Effect of detailed titration instructions on time to hemodynamic stability in ICU patients requiring norepinephrine. *Jt Comm J Qual Patient Saf*. 2019;45:606–612.
51. Eckel SF, Higgins JP, Hess E, et al. Multicenter study to evaluate the benefits of technology-assisted workflow on i.v. room efficiency, costs, and safety. *Am J Health-Syst Pharm*. 2019;76:895–901.
52. Erwin BL, Denaburg MA, Cortopassi JB, et al. Improving the medication-use process for 23.4% sodium chloride. *Am J Health-Syst Pharm*. 2019;76:50–56.
53. Estock JL, Murray AW, Mizah MT, et al. Label design affects medication safety in an operating room crisis: a controlled simulation study. *J Patient Saf*. 2018;14:101–106.
54. Fell GL, O'Loughlin AA, Nandivada P, et al. Methods to reduce medication errors in a clinical trial of an investigational parenteral medication. *Contemp Clin Trials Commun*. 2016;4:64–67.
55. Giuliano KK, Su WT, Degnan DD, et al. Intravenous smart pump drug library compliance: a descriptive study of 44 hospitals. *J Patient Saf*. 2018;14:e76–e82.
56. Hertig JB, Degnan DD, Scott CR, et al. A comparison of error rates between intravenous push methods: a prospective, multisite, observational study. *J Patient Saf*. 2018;14:60–65.
57. Higgins JP, Hardt S, Cowan D, et al. Multicenter study to evaluate the benefits of technology-assisted workflow on i.v. room efficiency, costs, and safety in small community hospitals. *Am J Health-Syst Pharm*. 2019; 76:964–969.
58. Jean SJ, Francart SJ, Eckel SF, et al. Evaluation of telepharmacy and the use of a gravimetric technology–assisted workflow system for remote sterile product pharmacist checks. *Am J Health-Syst Pharm*. 2020;77: 560–567.
59. Lin AC, Deng Y, Thaibah H, et al. The impact of using an intravenous workflow management system (IVWMS) on cost and patient safety. *Int J Med Inform*. 2018;115:73–79.
60. Pang B, Earl M, Knoer S, et al. Comparison of IV oncology infusions compounded via robotics and gravimetrics-assisted workflow processes. *Am J Health-Syst Pharm*. 2021;78:122–134.
61. Schnock KO, Dykes PC, Albert J, et al. A multi-hospital before–after observational study using a point-prevalence approach with an infusion safety intervention bundle to reduce intravenous medication administration errors. *Drug Saf*. 2018;41:591–602.
62. Wei W, Coffey W, Adeola M, et al. Impact of smart pump-electronic health record interoperability on patient safety and finances at a community hospital. *Am J Health Syst Pharm*. 2021;zxab287.
63. Jani YH, Chumbley GM, Furniss D, et al. The potential role of smart infusion devices in preventing or contributing to medication administration errors: a descriptive study of 2 data sets. *J Patient Saf*. 2021;17:e1894–e1900.
64. Rashed AN, Whittlesea C, Davies C, et al. Standardised concentrations of morphine infusions for nurse/patient-controlled analgesia use in children. *BMC Anesthesiol*. 2019;19:26.
65. Perkins J, Aguado-Lorenzo V, Arenas-Lopez S. Standard concentration infusions in paediatric intensive care: the clinical approach. *J Pharm Pharmacol*. 2017;69:537–543.
66. Jones MD, Franklin BD, Raynor DK, et al. Costs and cost-effectiveness of user-testing of health professionals' guidelines to reduce the frequency of intravenous medicines administration errors by nurses in the United Kingdom: a probabilistic model based on voriconazole administration. *Appl Health Econ Health Policy*. 2022;20:91–104.
67. Jones MD, McGrogan A, Raynor DK, et al. User-testing guidelines to improve the safety of intravenous medicines administration: a randomised in situ simulation study. *BMJ Qual Saf*. 2021;30:17–26.
68. Arenas-López S, Stanley IM, Tunstell P, et al. Safe implementation of standard concentration infusions in paediatric intensive care. *J Pharm Pharmacol*. 2017;69:529–536.
69. Furniss D, Dean Franklin B, Blandford A. The devil is in the detail: how a closed-loop documentation system for IV infusion administration contributes to and compromises patient safety. *Health Informatics J*. 2020; 26:576–591.
70. Jackson A, Little M. Electronic intravenous N-acetyl cysteine ordering tool: a retrospective review. *Emerg Med Australas*. 2020;32:267–270.
71. Karande IS, Goff Z, Kewley J, et al. Dose-banding of intravenous piperacillin-tazobactam in pediatric surgical inpatients. *J Pediatr Pharmacol Ther*. 2017;22:364–368.
72. Cree ML, Stocker CF, Tu QM, et al. Adherence to standard medication infusion concentrations and its impact on paediatric intensive care patient outcomes. *Aust Crit Care*. 2018;31:213–217.
73. Araújo ES, Modesto ACF, Ferreira TXAM, et al. Pharmaceutical intervention in the rational use of intravenous omeprazole. *Einstein (Sao Paulo)*. 2020;18:eAO4433.
74. Silva RCLD, QuinellatoLouro T, Peregrino AAF, et al. Cost-effectiveness of infusion pumps to reduce errors in a pediatric ICU. *Rev Bras Enferm*. 2019;72:617–623.
75. Moreira APA, Carvalho MF, Silva RCLD, et al. Handling errors in conventional and smart pump infusions: a systematic review with meta-analysis. *Rev Esc Enferm*. 2020;54:e03562.
76. Manrique-Rodríguez S, Heras-Hidalgo I, Pernia-López MS, et al. Standardization and chemical characterization of intravenous therapy in adult patients: a step further in medication safety. *Drugs R D*. 2021;21: 39–64.
77. Manrique-Rodríguez S, Sánchez-Galindo AC, Fernández-Llamazares CM, et al. Safe intravenous administration in pediatrics: a 5-year pediatric intensive care unit experience with smart pumps. *Med Intensiva*. 2016;40: 411–421.
78. Castells Lao G, Rodríguez Reyes M, Roura Turet J, et al. Compatibility of drugs administered as Y-site infusion in intensive care units: a systematic review. *Med Intensiva*. 2020;44:80–87.
79. Palacios Rosas E, Soria-Cedillo IF, Puértolas-Balint F, et al. Impact of implementing smart infusion pumps in an intensive care unit in Mexico: a pre-post cost analysis based on intravenous solutions consumption. *Hosp Pharm*. 2019;54:203–208.
80. Ibarra-Pérez R, Puértolas-Balint F, Lozano-Cruz E, et al. Intravenous administration errors intercepted by smart infusion technology in an adult intensive care unit. *J Patient Saf*. 2021;17:430–436.
81. AlGoraini Y, Hakeem N, AlShatarat M, et al. Designing and evaluating an automated intravenous dosage medication calculation tool for reducing the time of stat medication administration in a pediatric emergency department. *Heliyon*. 2020;6:e04140.
82. Waterson J, Al-Jaber R, Kassab T, et al. Twelve-month review of infusion pump near-miss medication and dose selection errors and user-initiated "good save" corrections: retrospective study. *JMIR Hum Factors*. 2020; 7:e20364.
83. Khan SA, Khan S, Kothandan H. Simulator evaluation of a prototype device to reduce medication errors in anaesthesia. *Anaesthesia*. 2016;71: 1186–1190.
84. Ng YYY, Wan PW, Chan KP, et al. Give intravenous bolus overdose a brake: user experience and perception of safety device. *J Patient Saf*. 2021;17:108–113.
85. Pinkney SJ, Fan M, Koczmara C, et al. Untangling infusion confusion: a comparative evaluation of interventions in a simulated intensive care setting. *Crit Care Med*. 2019;47:e597–e601.

86. Li G, Xu B, He RX, et al. Using healthcare failure mode and effect analysis to reduce intravenous chemotherapy errors in Chinese hospitalized patients. *Cancer Nurs*. 2017;40:88–93.
87. Benhamou D, Piriou V, de Vaumas C, et al. Ready-to-use pre-filled syringes of atropine for anaesthesia care in French hospitals – a budget impact analysis. *Anaesth Crit Care Pain Med*. 2017;36:115–121.
88. Baumann D, Dibbern N, Sehner S, et al. Validation of a mobile app for reducing errors of administration of medications in an emergency. *J Clin Monit Comput*. 2019;33:531–539.
89. Amodeo I, Pesenti N, Raffaeli G, et al. Robotic therapy: cost, accuracy, and times. New challenges in the neonatal intensive care unit. *Front Pharmacol*. 2019;10:1431.
90. Larmené-Beld KHM, Spronk JT, Luttjeboer J, et al. A cost minimization analysis of ready-to-administer prefilled sterilized syringes in a Dutch hospital. *Clin Ther*. 2019;41:1139–1150.
91. Siebert JN, Ehrler F, Combescure C, et al. A mobile device application to reduce medication errors and time to drug delivery during simulated paediatric cardiopulmonary resuscitation: a multicentre, randomised, controlled, crossover trial. *Lancet Child Adolesc Health*. 2019;3:303–311.
92. Hua X, Li C, Pogue JM, et al. ColistinDose, a mobile app for determining intravenous dosage regimens of colistimethate in critically ill adult patients: clinician-centered design and development study. *JMIR Mhealth Uhealth*. 2020;8:e26593.
93. Terkola R, Czejka M, Bérubé J. Evaluation of real-time data obtained from gravimetric preparation of antineoplastic agents shows medication errors with possible critical therapeutic impact: results of a large-scale, multicentre, multinational, retrospective study. *J Clin Pharm Ther*. 2017; 42:446–453.
94. Koyama AK, Maddox CSS, Li L, et al. Effectiveness of double checking to reduce medication administration errors: a systematic review. *BMJ Qual Saf*. 2020;29:595–603.
95. Westbrook JI, Li L, Raban MZ, et al. Associations between double-checking and medication administration errors: a direct observational study of paediatric inpatients. *BMJ Qual Saf*. 2021;30: 320–330.
96. American Society for health System Pharmacists. Adult continuous infusion standards.; 2020. Available at: https://www.ashp.org/pharmacy-practice/standardize-4-safety-initiative. Accessed November 27, 2022.
97. American Society for health System Pharmacists. Pediatric continuous infusion standards.; 2020. Available at: https://www.ashp.org/pharmacy-practice/standardize-4-safety-initiative. Accessed November 27, 2022.
98. Shah PK, Irizarry J, O'Neill S. Strategies for managing smart pump alarm and alert fatigue: a narrative review. *Pharmacotherapy*. 2018;38:842–850.
99. Ohashi K, Dalleur O, Dykes PC, et al. Benefits and risks of using smart pumps to reduce medication error rates: a systematic review. *Drug Saf*. 2014;37:1011–1020.
100. The Joint Commission. Optimizing smart infusion pump safety with DERS. Sentinel Event Alert. Published 2021. Available at: https://www.jointcommission.org/-/media/tjc/documents/resources/patient-safety-topics/sentinel-event/sea-63-smart-infusion-pumps-w-ders-final.pdf. Accessed November 27, 2022.
101. Institute for Safe Medication Practices. Survey results: smart pump data analytics pump metrics that should be monitored to improve safety. Published 2018. Available at: https://www.ismp.org/resources/survey-results-smart-pump-data-analytics-pump-metrics-should-be-monitored-improve-safety. Accessed November 27, 2022.
102. Suess TM, Beard JW, Ripchinski M, et al. Smart pump–electronic health record (EHR) interoperability with auto-documentation is associated with increased submission of infusion-therapy billing claims at a community hospital. *Pharmacoecon Open*. 2019;3:619–629.
103. Howlett MM, Breatnach C, Brereton E, et al. Direct observational study of interfaced smart-pumps in pediatric intensive care. *Appl Clin Inform*. 2020;11:659–670.
104. Biltoft J, Finneman L. Clinical and financial effects of smart pump-electronic medical record interoperability at a hospital in a regional health system. *Am J Health-Syst Pharm*. 2018;75:1064–1068.
105. Marwitz KK, Fritschle AC, Trivedi V, et al. Investigating multiple sources of data for smart infusion pump and electronic health record interoperability. *Am J Health-Syst Pharm*. 2020;77:1417–1423.
106. Joseph R, Lee SW, Anderson SV, et al. Impact of interoperability of smart infusion pumps and an electronic medical record in critical care. *Am J Health Syst Pharm*. 2020;77:1231–1236.
107. Suess TM, Beard JW, Trohimovich B. Impact of patient-controlled analgesia (PCA) smart pump-electronic health record (EHR) interoperability with auto-documentation on chart completion in a community hospital setting. *Pain Ther*. 2019;8:261–269.