

REVIEW



Understanding and mitigating medication errors associated with patient harm in adult intensive care units: a scoping review

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Abstract

Purpose: Medication interventions are fundamental to the care of the critically ill patient in the intensive care unit (ICU), relying on effective and appropriate delivery of the medication use process. Medication errors affect a high proportion of patients in the ICU. This scoping review maps the literature pertaining to medication errors and preventable adverse drug events in the adult ICU.

Methods: We searched seven electronic databases (PubMed, MEDLINE, EMBASE, CINAHL, Web of Science, Cochrane, Google Scholar), identifying 2960 records. After screening against predefined eligibility criteria, 48 records were included for data extraction.

Results: A high variation in incidence of medication errors and preventable adverse drug events were reported, reflecting the heterogeneity in study designs, surveillance methods and preventability assessments. Associated risks factors include patient (high severity of illness, older age), clinical (renal dysfunction, prolonged ICU stay), staff (staff inexperience, role overload), environmental (interruptions, transfer of care) in addition to high-risk medications. The rate of serious or life-threatening harm was low at 1–5% of all medication errors. Half ($n = 11$, 55%) of the interventions or mitigation practices were focused on the medication prescription phase.

Conclusion: Most medication errors in ICU are identified and intercepted by systems and staff. A minority lead to preventable patient harm and increased length of stay. Decision support embedded in e-prescribing systems, medication reconciliation and review processes and clinical pharmacist activities reduce medication errors and patient harm.

Keywords: Adverse drug events, Medication errors, Mitigating strategies, Safety, Quality improvements

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Introduction

Medication is the most common intervention intensive care unit (ICU) patients receive. In turn, ICU patients are particularly vulnerable to medication errors (MEs) contributing to preventable adverse drug events (ADEs) [1, 2]. While MEs are defined as errors or irregularities occurring in the medication-use process including medication prescribing, transcription, dispensing, administration and monitoring [3–5], an ADE refers to any patient harm or negative impact in the health process related to medication exposure. Some patients will experience an ADE even when the medication is prescribed, administered and used correctly, these are considered adverse drug reactions or non-preventable ADEs. In contrast, ADEs related to MEs are regarded as preventable ADEs. Many MEs are intercepted by staff or systems (e.g. organized practices/frameworks designed to minimize risks) before they can affect a patient or cause a preventable ADE, referred to as being potential ADEs, which do not result in patient harm. However, when the ME reaches the patient, harm can occur with the most severe patient impact of MEs and ADEs leading to prolonged organ dysfunction or death [6]. Mitigating practices are therefore essential for high quality ICU care.

In the ICU setting, medication-related risks include high medication exposure, and the hazards related to preparation, weight-based dosing or titration to response. Critical illness, including multi-organ failure, alters medication pharmacokinetics and predisposes to increased volume of distribution and reduced medication clearance [7], potentially increasing medication exposure with risk of toxicity and increased ICU and hospital length of stay. The complex environment of a modern ICU, where fast-paced and dynamic processes of care are provided by teams of healthcare professionals in a technologically rich system only increases this risk further [8, 9], while patients may not be able to effectively contribute to their own safety when sedated or delirious. Finally, lack of continuity of care following step down from ICU is a well-recognised problem that places ICU patients at risk of medication transfer errors as they continue their recovery on the hospital ward and beyond [10].

Previous systematic reviews described the broad domain of MEs and ADEs in the ICU [6, 11, 12]. However, much of the literature to date has been heterogeneous in both definition and approach to describing MEs and ADEs in an ICU setting, and a knowledge gap exists regarding mitigating practices and future avenues for research. By utilizing scoping review methodology, the breadth of evidence in this domain can be mapped to better understand current inadequacies in methodology and identify areas where future research should be

Take-home message

Medication errors are common in ICU and while the majority are identified and intercepted by safety systems and staff, a small proportion lead to patient harm with resulting increased length of stay. Interventions such as clinical decision support embedded in e-prescribing systems, medication reconciliation and review processes, and clinical pharmacists can help to mitigate the risks and reduce patient harm.

targeted. The purpose of the current scoping review is to describe the incidence and types of MEs that occur in the adult ICU environment, the nature of adverse patient and health system consequences, and potential mitigation measures.

Methods

Design

Our protocol was developed using the scoping review framework provided by the Joanna Briggs Institute [13] and further refined following feedback from the research team. Scoping reviews are useful tools to broadly explore concepts and related aspects in a rigorous and transparent method to ensure that the results are trustworthy. The “population, concept and context” framework was used to identify relevant studies. Our population were human adult ICU patients; concept was any description of medication error frequency, risk factors, consequences or mitigation measures; and, context was original research articles limited to developed countries. Reporting is in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews [14]. The multiprofessional research team was composed by methodologists and specialists in intensive care and expert in patient safety, on behalf of the European Society of Intensive Care Medicine (ESICM) [15].

Eligibility criteria

We included original research set in adult ICUs that evaluated MEs and potential or preventable ADEs and reported any of the following: (1) any measure of frequency or incidence (with numerical results and denominators); (2) demographic features or risk factors; (3) consequences (impact on patient or staff); or, (4) mitigation measures or interventions evaluated to minimise errors. We excluded publications where: (1) the setting was not adult ICU; (2) MEs and potential or preventable ADEs were not identifiable from the results; (3) only incidence data was provided without numerical results or denominators; (4) publication date was prior to 1st January 2000; (5) editorials, review articles or conference abstracts; or (6) language other than English. It became

clear that the problems encountered in a low- or middle-income country [16] were very different to that experienced in high income country ICUs, and a decision was taken to exclude articles describing ME and ADEs in low- or middle-income countries.

Information sources

Comprehensive literature searches were conducted by an expert information specialist in consultation with two authors (MvM, RB) and reviewed by the research team prior to translation into other databases [17]. We searched the following seven electronic databases from 1st January 2000 until 1st January 2024: PubMed, MEDLINE, EMBASE, CINAHL, Web of Science, Cochrane, Google Scholar. The search strategy utilized is available in Supplemental file 1.

Study selection

The search strategy identified 2960 records. These were screened by the research team through a two-person blinded review of titles/abstracts using Covidence [18]. In Step one, it was assessed whether the paper pertained to medical errors or preventable ADEs in adult ICUs. This led to exclusion of 2427 records leaving a remaining 533 [19]. Step two review was undertaken with two-person abstract review (KP, MvM) to identify records

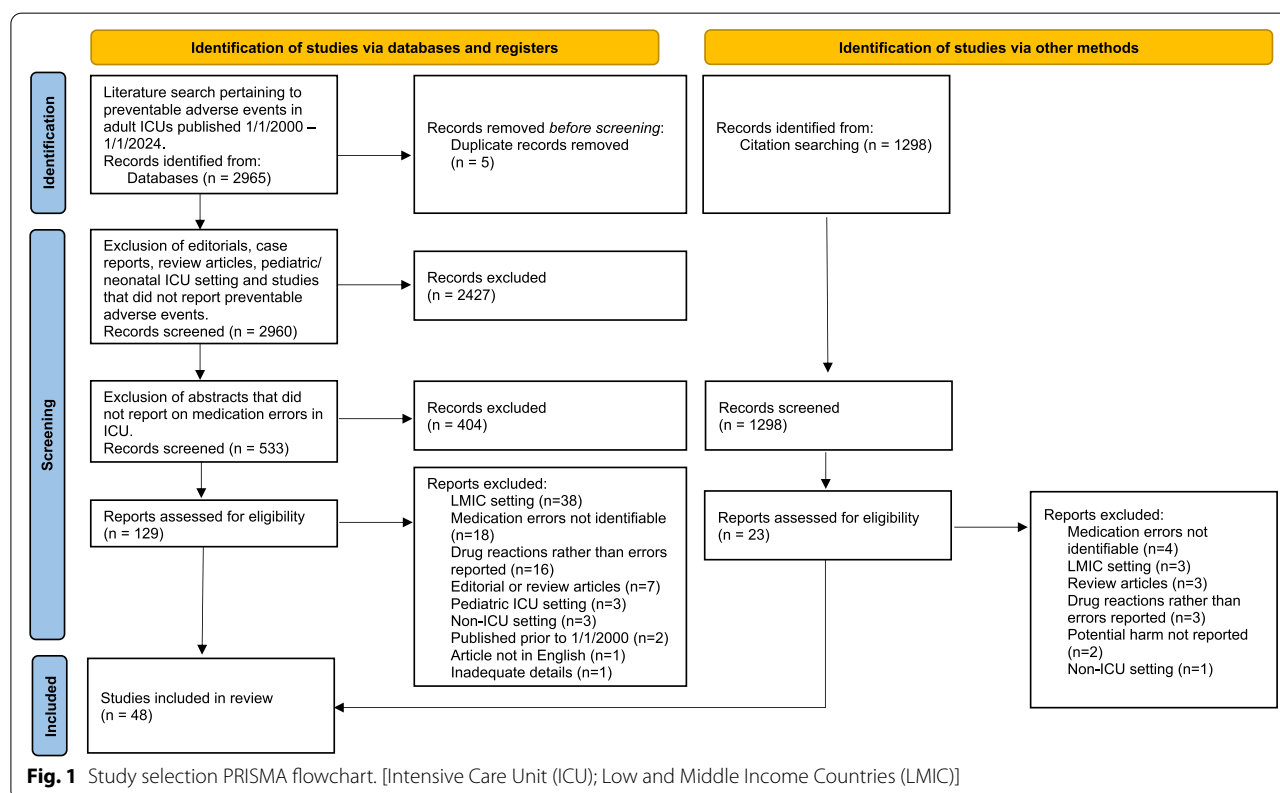
that specifically included MEs or preventable ADEs. This excluded 404 references and left 129 for full text reading to evaluate them against the eligibility criteria. Full text papers were obtained (EK, MvM) and distributed amongst the research team, resulting in 40 full papers to be included. Finally, backwards citation analysis of included reports [20], a previous systematic review [12] and the recent European Association of Hospital Pharmacists Investigation of Medication Errors in ICUs [21], was undertaken (KP, MvM, RB), identifying 8 additional reports which met inclusion criteria resulting in 48 included reports (Fig. 1).

Data charting

A data extraction form was developed and data extracted onto the form by all team members before secondary review by KP, MvM, and RB to ensure completeness. Disagreements were resolved by discussion between experts.

Data items

The following was collected from each eligible study: published year, country of setting, research aim, study design, setting, population included and limitations of the study design/ execution. Outcomes of interest included reported incidence rates, categories of error,



risk factors, mitigating factors, interventions evaluated and any other pertinent outcomes.

Synthesis of results

We grouped the studies by whether they reported prevalence/incidence/epidemiology, impact, and/or mitigation measures. We summarized the type of settings, populations and study designs for each group, along with the broad findings. We described the prevalence of medication error where proportion as a percentage of the included population affected at any time point during their ICU stay is available. Additionally, where incidence rates were reported, these were described in terms of rate per 1000 patient days and/ or rate per 100 prescriptions.

Themes were identified (KP, MvM, RB) and discussed with the wider research team. These themes were then developed through team discussions upon reviewing the preliminary results.

Future research priorities areas not yet addressed by the literature were determined by the research group following review of the overall results.

Results

Data from the 48 included reports are summarised in Table 1 and described in more detail in Supplemental File 2 [1, 9, 22–67].

Prevalence and incidence of MEs in the ICU

The literature search identified 34 papers that reported on incidence of MEs, categories and risk factors (Supplemental File 3) [1, 9, 22–41, 43–53, 58].

MEs were the most commonly identified patient safety incidents in an ICU setting accounting for 57–61% of reported errors [1, 22–26]. Compared to a non-ICU environment the rate of ME was found to be approximately five-times higher in ICU [27].

Three studies reported the prevalence of MEs in adult ICU patients with a wide range of reported rates. A retrospective study of self-reported incidents identified errors affecting 5.5% [27], whereas a study that utilized retrospective external review of records described medication errors in 92% [29]. The only prospective study used pharmacists to observe the prescription and administration of 20 high-risk medications and observed a rate of errors affecting 22% of the patients observed [28].

The reported incidence rates varied, with MEs, ranging from 6.8 to 4995 per 1000 patient days [1, 9, 22, 29–37]. The corresponding rate per 100 prescriptions was 3.4 to 27 [31, 35–39]. The rate of ADEs was 1 to 150 per 1000 patient days, and 0.15 to 1.0 per 100 prescriptions [1, 9, 22, 26, 36–38, 40–42].

Categorisation by medication stage and class

MEs can happen at any point during the medication use process (Fig. 2) with errors in prescription, dispensing, and administration being the most commonly reported phases when an error was likely to occur [1, 9, 27–29, 31, 32, 35–39, 43–47]. Inadequate therapeutic drug monitoring and dosing can also result in error and is more common in the setting of renal or liver dysfunction [32]. Drug classes frequently associated with MEs include sedatives, antimicrobials, vasopressors, anticoagulants and insulin [1, 22, 25, 28, 31, 32, 36, 38, 40, 43, 46–50].

Risk factors and causal analysis

Figure 3 demonstrates factors that contribute to the risk of MEs and ADEs. Patient factors associated with a higher risk of MEs are higher severity of illness, emergency ICU admission, older age and prolonged ICU stay [29, 32, 41, 51, 52]. Of note, renal dysfunction seems to be associated with an increase in ME risk [29, 51, 52].

Several articles explored the staff (human) factors associated with MEs. Limitations in education and training [31, 43, 45, 50], clinician inexperience [41, 46] and staff fatigue and stress have all been demonstrated to contribute towards MEs [43, 45, 46]. Improving clinician working pattern and sleep deprivation has been demonstrated to result in a 21% reduction in ME rate [30]. Organizational failures such as work overload, time pressures, interruptions, inappropriate staff allocation and inappropriate documentation have been deemed to contribute to 40% of MEs [43]. A survey of ICU nursing staff on perceived risk factors for MEs and reported high patient–nurse ratio, poor interdisciplinary communication, frequent staff changes, transfer of care and lack of medication labels as important factors that contributed to administration MEs [53].

Contact isolation has been demonstrated to lead to an increased number of ADEs associated with anticoagulant prescriptions and insulin administration [49].

Transfer of the patient for a diagnostic or surgical intervention has also been identified as an at-risk period associated with a 74% increased likelihood of an ADE [51]. Additionally, 46% of patients at the point of transfer from an ICU to a non-ICU location were found to have a ME [52]. The most common type of ME was inappropriate continuation of ICU-specific medications such as stress ulcer prophylaxis and antipsychotics without an ongoing indication.

Impact on patient and organizational outcomes

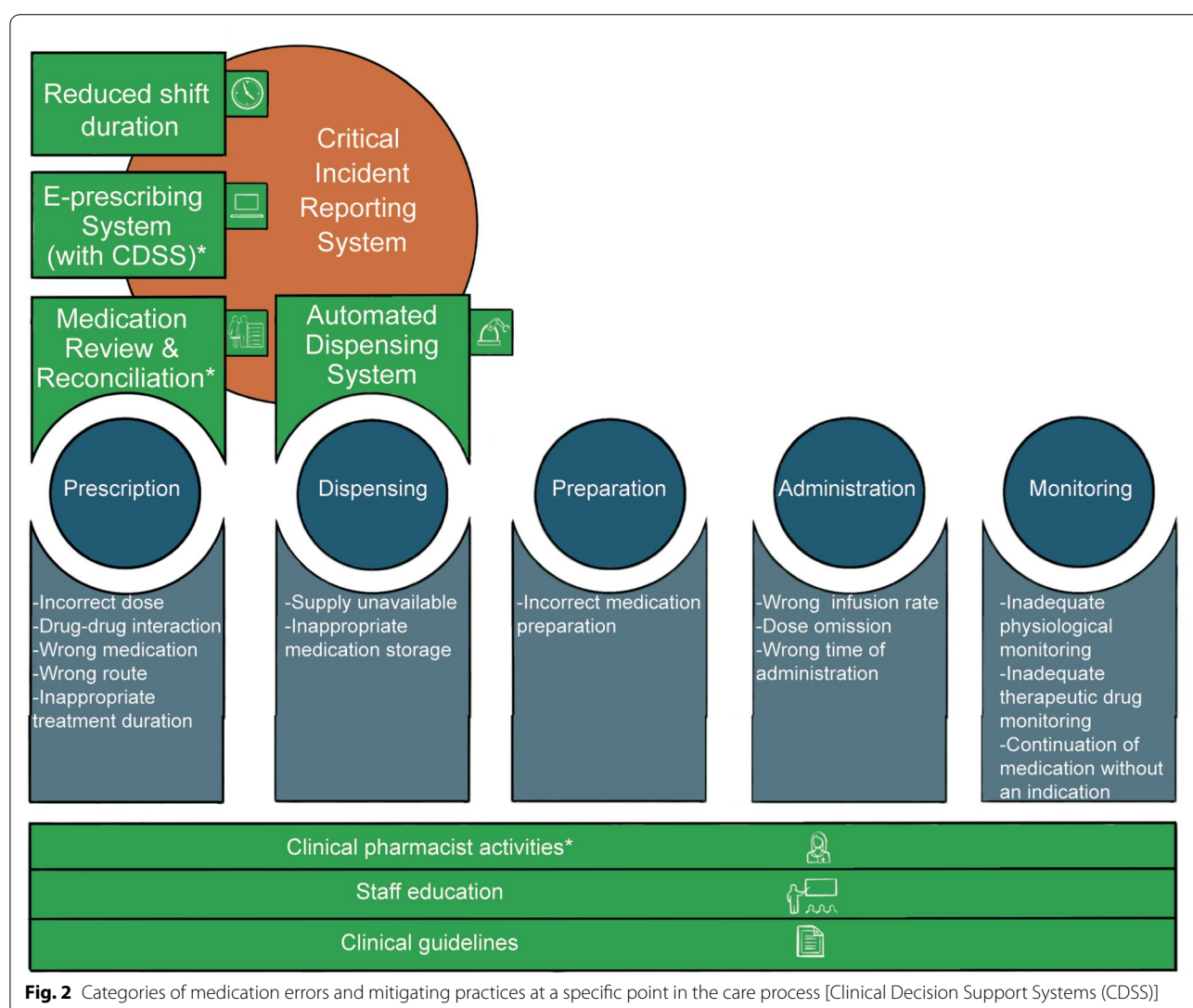
Eleven of the included studies reported on the impact of MEs and ADEs on diverse patient outcomes (Table 2 and Fig. 4) [24, 29, 32, 37, 41, 44, 50, 54–57]. Some studies utilised the National Coordinating Council for

Table 1 Studies meeting inclusion criteria for scoping review

Author, year	Sample	Outcome of interest
Prospective study, independent verification of error		
Aljadhey (2013) [37]	977 patients/5 ICUs	Adverse drug events
Calabrese (2001) [28]	851 patients/5 ICUs	Medication errors associated with specific error-prone drugs
Carayon (2014) [9]	630 patients/single center	Medication safety and medication errors
Chase (2023) [64]	150 patients/single center	Medication regimen complexity score and medication errors
Colpaert (2006) [36]	90 patients/single center	Prescribing errors with computer vs. paper prescribing units
Forster (2008) [54]	207 patients/single center	Mortality and length of stay related to any ICU adverse event
Forster (2011) [23]	211 patients/single center	Impact of an adverse events surveillance program
Garrouste (2010) [48]	1369 patients/70 ICUs	Mortality related to specific medical errors in ICU
Garrouste (2012) [62]	2117 patients/3 ICUs	Impact of interventions on reducing specific errors in ICU
Herout (2004) [34]	71 patients/1 surgical ICU	Medication errors for continuous infusion medications
Kopp (2006) [31]	33 nursing shifts/single ICU	Medication errors and adverse drug events
Landrigan (2004) [30]	634 patients/single center	The impact of sleep deprivation on serious medical errors
Ohta (2014) [41]	459 patients/3 ICUs	Morbidity and mortality related to adverse drug events
Rothschild (2005a) [1]	198 patients/single center	All adverse events and serious errors in ICU
Rothschild (2005b) [57]	735 patients/1 cardiac ICU	Impact of smart infusion pump on serious medication error rates
Tully (2019) [52]	985 patients/58 ICUs	Medication errors at the time of transition of care from ICU
Valentin (2006) [39]	1913 patients/205 ICUs	All patient safety incidents in ICU
Van den Bemt (2002) [58]	24 patients/2 ICUs	Drug administration errors in the ICU
Prospective study, self-reporting of error		
Graf (2005) [24]	216 patients/single center	All errors and incidents in a medical intensive care unit
Merino (2012) [26]	1017 patients/79 ICUs	Any adverse or no-harm events
Ridley (2004) [38]	21,589 prescriptions/24 ICUs	Prescription errors and resulting adverse drug events
Valentin (2009) [46]	1328 patients/113 ICUs	Errors in parenteral medication in ICU
Retrospective study, independent verification of error		
Anthes (2013) [40]	254 patients/single center	Medication errors detected in ICU transfer summaries
Chen (2021) [22]	1018 patients/single center	Impact of blue-enriched light on all medical errors
Escriba Gracia (2021) [35]	87 patients/single center	Medication errors
Klopotowska (2024) [59]	84,422 patients/10 ICUs	Adverse drug events due to drug-drug interactions
Kucukarslan (2013) [42]	126 patients/single center	Adverse drug events and impact of ICU pharmacist
Nuckols (2007) [66]	4604 patients/2 centers	Adverse drug event rate between smart infusion pumps and conventional pumps
Seynaeve (2011) [51]	1009 ICU days/Single center	Adverse drug events related to nursing workload
Wong (2017) [65]	4776 patients/single center	Adverse drug events related to overrides of a clinical decision support system
Yoon (2022) [29]	293 patients/single center	Medication errors
Zahar (2013) [49]	1150 patients/single center	Medication errors/adverse drug events in isolated patients
Retrospective study, self-reporting of error		
Alharbi (2016) [27]	1966 patients/single center	Medication errors in ICU and non-ICU settings
Kane-Gill (2010) [50]	541 reports/single center	Medication errors in ICU and non-ICU settings
Ottosen (2023) [43]	150 reports/single center	Medication errors
Thomas (2008) [44]	12,084 reports/151 centers	Medication-related safety incidents
Thomas (2014) [25]	2238 reports/29 ICUs	Medication-related safety incidents
Thompson (2005) [45]	55 reports/3 ICUs	Medication errors related to computer prescribing
Wahr (2014) [47]	59,205 reports/641 ICUs	Medication errors
Weant (2007) [67]	88 reports/single center	Medication errors and impact of an e-prescribing system
Before: after intervention study		
Bosma (2018) [60]	476 patients/2 ICUs	Medication errors at the time of transfer and impact of medication reconciliation
Chapuis (2010) [61]	115 patients/single center	Impact of automated dispensing systems on medication errors

Table 1 (continued)

Author, year	Sample	Outcome of interest
Kessemeier (2019) [33]	336 patients/single center	Impact of clinical pharmacists on the prescribing error rate
Klopotowska (2010) [32]	1173 patients/single center	Impact of ICU pharmacist on the medication safety
Pagnamenta (2012) [63]	6404 patients/4 ICUs	Impact of a multifaceted intervention on adverse drug events
Shulman (2005) [55]	2465 prescriptions/1 ICU	Medication errors with hand-written vs electronic prescribing
Quality improvement study		
Tainter (2018) [56]	347 patients/1 cardiac ICU	Impact of a daily team-based medication review on errors
Cross-sectional survey		
Beaudart (2023) [53]	91 nurses	Staff perception of causes of errors in continuous infusion drug therapies

**Fig. 2** Categories of medication errors and mitigating practices at a specific point in the care process [Clinical Decision Support Systems (CDSS)]

Medication Error Reporting and Prevention Taxonomy of Medication Errors (NCC-MERP), providing an indication of whether the ME reached the patient and then categorisation of harm ranging from no harm (category

C) to patient death (category I) [32, 50, 57]. Others used categories based on the perceived clinical impact on the patient (e.g. organ damage, increased costs >100 €/day)

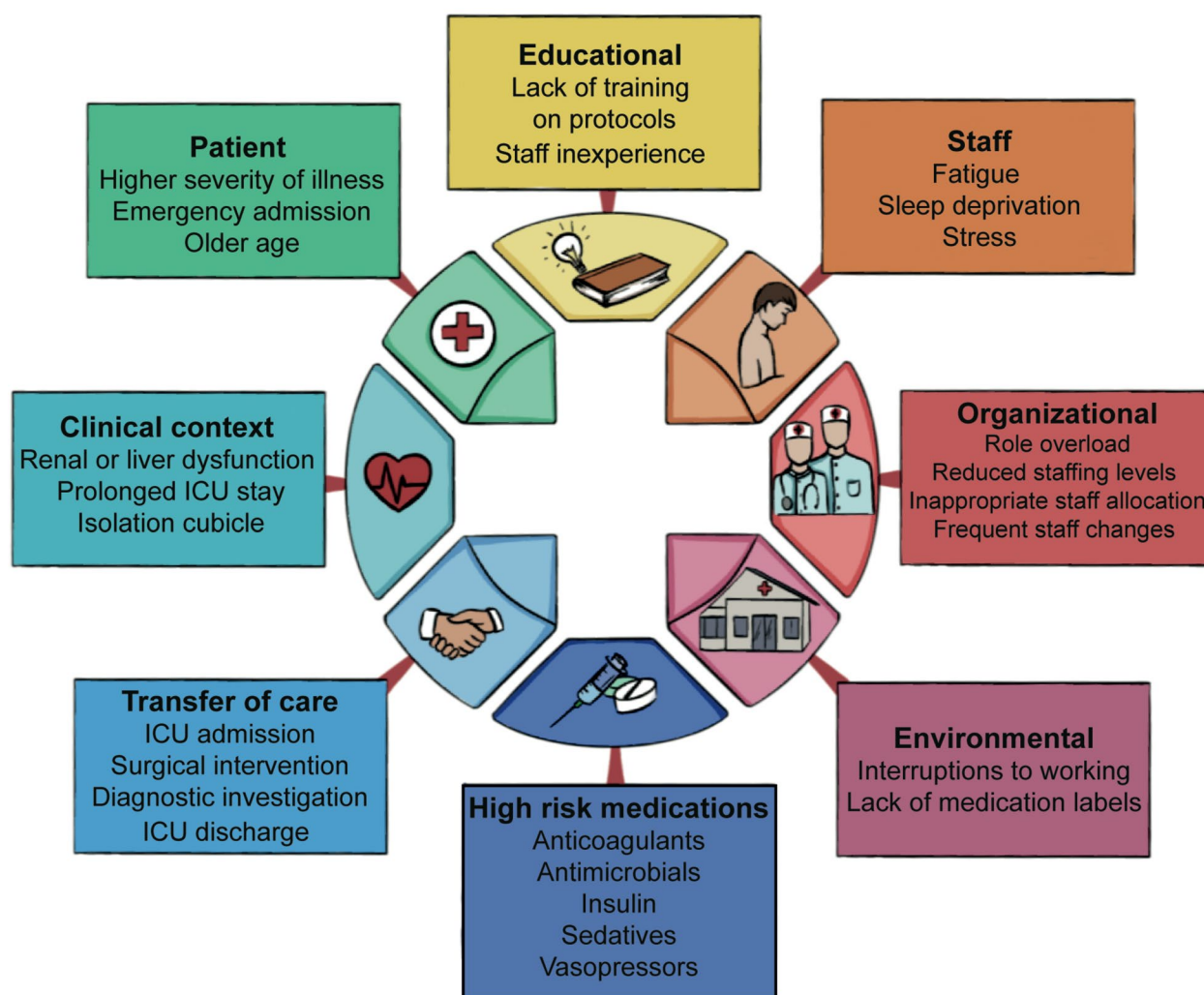


Fig. 3 Contributing factors to medication errors and adverse drug events

[33]; perceived severity (e.g. significant to fatal) [37]; and medication changes as trivial to major [56].

For most MEs and ADEs, human factors related to staff involvement seemed to contribute significantly to risks [24]. No studies were found describing the impact on emotional distress among ICU staff.

Degree of patient harm

The majority of MEs are reported as causing no actual harm with many being identified or intercepted before reaching the patient [28, 29, 31, 37, 43, 47, 55]. Shulman et al. reported that clinical pharmacists and nurses intercepted most prescribing MEs with the potential for moderate or major patient harm; nearly all MEs were classified as causing no or minor patient harm (95%) [55].

The rate of serious or life-threatening harm of all MEs was 1–5% [9, 27, 43] although higher rates were observed

in studies that specifically reported using patient harm incident reporting systems [25, 31, 38, 40, 58]. Severe MEs can potentially result in death of the patient, although, this was mostly reported as 0% [29, 32, 37, 44, 50, 54]. Only one study [41] reported 7% mortality for patients that experience an ADE, although after adjusting for age and organ dysfunction, ADEs were not associated with increased ICU mortality [41].

Organizational loss

Most of the studies (73%) reported on an association between MEs and ADEs with an increased ICU or hospital stay [29, 32, 33, 41, 44, 50, 54, 55], however, no studies reported on measured healthcare costs.

Table 2 Studies reporting on impact of medication errors and adverse drug events in ICU

Author, year	Relevant results reported on impact
Prospective study, independent verification of error	
Aljadhey (2013) [37]	Based on all patients (ICU and non-ICU) medication errors caused: 30% no harm 59% potential to cause harm 11% resulted in harm Mortality 0%
Forster (2008) [54]	ICU-based adverse events (all types) were associated with increased hospital length of stay of 31 days but no impact on mortality
Ohta (2014) [41]	Seven fatal or life-threatening ADEs occurred in 7 patients, which accounted for 7% of the 99 ADEs Mortality of patients with ADE 17% and without ADE 16% After adjusting for age and organ dysfunction, ADEs did not increase mortality
Rothschild (2005b) [57]	72% preventable ADEs were serious or life-threatening
Prospective study, self-reporting of error	
Graf (2005) [24]	14% of all errors and incidents may have been associated with harmful consequences for the patients
Retrospective study, independent verification of error	
Yoon (2022) [29]	MEs resulted in no harm in 30% Harmful events including temporary harm, permanent harm, life-threatening, and fatal events occurred in 70% Most patients with ME-related harmful events experienced temporary harm events (87%), which were resolved upon patient discharge from the hospital Clinically significant harmful events occurred in 8%
Retrospective study, self-reporting of error	
Kane-Gill (2010) [50]	Medication errors were associated with any harm in 12%; prolonged hospitalization 1%; and mortality 0%
Thomas (2008) [44]	Among self-reported incidents, 11.8% caused temporary harm and 1.8% permanent harm
Before–after intervention study	
Klopotowska (2023) [32]	In ICU patients with a potential drug–drug interaction, 65.4% experienced an actual ADE Among those with an ADE, 52.9% had severity level of serious or higher, and 19.3% contributed to a longer ICU length of stay
Shulman (2005) [55]	22% of medication errors considered moderate/ major severity 1.1% of medication errors led to increased length of stay
Quality improvement study	
Tainter (2018) [56]	Prescription changes required were described as trivial (40.4%), minor (50.5%) and major (9%)

ADE adverse drug event, ICU intensive care unit

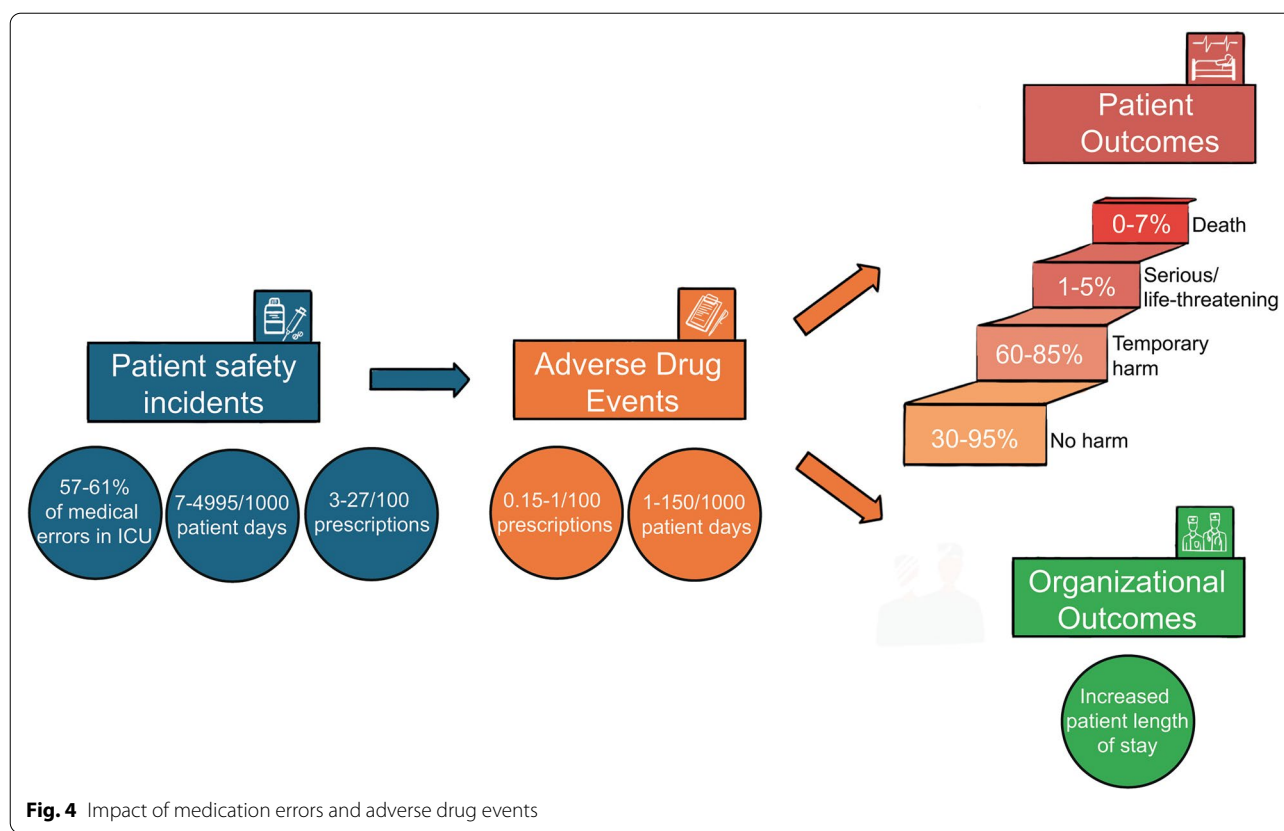
Interventions to mitigate medication errors

Of the 48 original articles included in the search strategy, 20 included interventions evaluated to reduce MEs and ADEs ($n=15$) or identified existing practices or systems that mitigated these errors and consequences ($n=5$), Supplemental File 4 [22, 30, 32, 33, 36, 42, 46, 52, 55–57, 59–67].

The intervention studies were heterogeneous in terms of the methodology used, although most of them ($n=9$) were observational or quasi-experimental, six before and after studies [32, 33, 55, 60, 61, 63]; two retrospective medical chart reviews [22, 66]; and one prospective controlled cross-sectional trial [36]. Only three randomized

studies were found, of which one was a randomized controlled trial [30], one a randomized time-series trial [57], and one was a multicenter cluster randomized study [62]. Most studies that reported ME reporting mitigation practices were prospective observational prevalence studies [46, 64] and retrospective observational studies [52, 59, 65].

Interventions that have been shown to reduce MEs include: pharmacist clinical activities (e.g. medication reconciliation and review, participation in multiprofessional ward rounds) [32, 33]; automated medication dispensing system [61]; reduced medical staff work hours [30]; electronic (e–) prescribing [36, 55]; medication



reconciliation [60] and medication review tasks [56] and multifaceted implementation programs described by Gorrouste (staff education; care guidelines; audit and feedback) [62] and Pagnamenta (e-prescribing; standardized infusion labeling; standardized infusion pumps) [63]. However, only e-prescribing [67] with clinical decision support [36, 55], pharmacist clinical activities [32, 33, 42], including medication reconciliation tasks [60] and medication review timeout [56], reported a reduction in potential or actual patient harm. Studies with factors reported to mitigate MEs also included clinical pharmacist activities [52, 64]; e-prescribing system [46] (including clinical decision support system alerts) [59, 65]; and critical incident reporting systems [46].

Most ($n=11$, 55%) interventions or mitigation strategies are focused on the medication prescription phase [30, 32, 33, 36, 52, 55, 56, 59, 60, 64, 65], although some studies addressed other phases of the process such as administering parenteral medication [46, 57]; dispensing of medication [61]; or more holistically over the wider medication use process [42, 63, 66, 67]. Some focused on a specific point in the care process, such as the transitions of care into ICU or from an ICU to non-ICU location [52, 60] (Fig. 2).

Discussion

Our findings provide an overview of MEs and potential or preventable ADEs in ICU patients. Medication errors are common and affect a high proportion of patients in the ICU. We identified the highest risk steps within the medication use process, the frequency and negative impact on patient and organizational outcomes and interventions reported to reduce MEs and ADEs. As such, we provide a basis for ICUs to evaluate their current medication systems and processes when considering priorities for making further improvements in medication safety within their local practice and context.

We found a high variation in the reported incidence of MEs and ADEs, reflecting the heterogeneity in study designs, surveillance methods and preventability assessments; with prospective, direct observational studies appearing as the most sensitive [5]. The degree of heterogeneity described in studies reporting incidences prevented calculation of any meaningful measure of central tendency and spread. As such, understanding the true rate of MEs and ADEs in an ICU setting remains challenging and while future meta-analyses of pooled reports may be possible, the current variation in methodological

approach and studied population across published literature, makes any such output challenging.

The low frequency of serious preventable ADEs may be due to underreporting [44] or under recognition in the context of complex critically ill patients with multiorgan failure. Adverse consequences of preventable ADEs have been identified at a patient level. Although most MEs appear to be intercepted by safety systems and ICU professionals' alertness and actions, many can still reach the patient and cause patient harm. ICU patients are exposed to several ME and ADE risk factors. Some of these simply reflect increased patient exposure to medications, many of which are high-risk (e.g., narrow therapeutic index, complicated administration, severe ADE potential and require monitoring and dose adjustment). This is in the context of increased biological vulnerability related to reduced clearance secondary to organ dysfunction (most notably renal). The net result is increased ME risk, and the requirement for alterations in medication dosing and/or monitoring to minimize toxicity and ADEs. This highlights the importance of having robust medication safety and reporting systems in place, supported by a continuous learning culture [68]. MEs lead to an increase in ICU and hospital length of stay and may impact mortality. From an organizational level, mitigating strategies for MEs could reduce length of stay, thus, potentially reducing healthcare costs.

Multiple interventions have been demonstrated to reduce MEs in an ICU setting with e-prescribing (with clinical decision support systems), medication reconciliation and review processes and clinical pharmacist activities reducing patient harm. These specific interventions are all regarded as high priorities for ICU medication safety systems. However, consensus-based recommendations identified many other interventions and mitigations as high priority for ICU medication safety policies [21], with a multitude of potential combinations. The priorities for intervention implementation will depend on local context and resources, accounting for patient safety incidents and trends. Similarly, implementation of priority interventions will require multi-faceted approaches, including staff education, process improvements and technological and or human-factors specific considerations with tailoring to the local clinical ICU context. When introducing new technological interventions, it is important to acknowledge these can be associated with new types (e.g., prescription mis-selection) and/ or increased numbers of MEs [55, 67, 69], highlighting the importance of effective implementation, and integration into the way staff work within ICUs. This requires acknowledgement of the key role human factors have in managing the complexity of medication systems and processes in ICUs [8, 12, 70]. Consideration of the degree of

clinical assessment required by healthcare professionals interacting with the technological system and the complexity of effective implementation is also required for medication safety benefits to be realised [71]. Clinical pharmacists embedded within the wider multiprofessional ICU team undertake medication-related activities that improve patient outcomes, including mortality and preventable ADEs [72], with healthcare cost-benefits [73].

Remaining areas of uncertainty

Further high-quality prospective studies using direct observation of medication errors, reporting robust measures of preventable or potential patient harm and patient outcomes are required. Interventions that target vulnerable populations, such as those with renal dysfunction and patients in isolation, should be evaluated as a means of providing a high-value impact on incidence of MEs. Transition of care has been identified as an at-risk period with established interventions potentially less reliable or underdeveloped. MEs can occur on any transition in care, although the ICU to ward transfer present particular challenges related to the complexity of process performance and interactions (patient and care teams), time pressures, communication challenges and variation in prescribing method or systems (such as digital to written, or differing prescribing systems) [74]. The requirement for discontinuation of ICU-specific medication and the re-introduction of pre-existing medications, with potential information loss due to changes in care teams. As such, future work should specifically aim to evaluate interventions aimed at reducing medication errors and patient harm at the point of transition of care [75].

We identified limited evidence of the potential impact of MEs and ADEs on some patient and organizational outcome measures e.g., unplanned readmission rates and emotional impact on staff. The impact on ICU professionals involved in a ME was not reported in the included studies. It could be expected that being involved in a ME, in particular with high-risk medication, causes emotional distress [76]. In turn, an unsafe work environment and being at risk for burnout, could increase the prevalence of MEs [77]. There is a responsibility for institutional policies addressing workflows and staffing ratios not burdening the already high workload. Integration of digital solutions contributing to reducing ME might be supportive, however, still underexplored. It should be noted that adequate coaching or psychological consulting should be available in case of a severe ME occurrence. Additionally, the impact of MEs on the environment has rarely been studied or is underreported, perhaps because of a lack of recognition or association.

There are opportunities to develop clinical decision support systems (CDS) and artificial intelligence (AI) to identify and help prevent ADEs [59]. Integration of AI into CDS has the potential to enhance timely and targeted interventions to improve medication safety [78]. Here, AI can work with humans to augment situational awareness, minimizing the negative potential impact of lapses on medication safety risks [78]. Prediction of medication treatment response and personalised medication dosing can be AI assisted [79]. Technology offers further closed-loop medication safety opportunities with integration of smart infusion pumps (incorporating drug error reduction software) with e-prescribing systems and barcode-assisted medication administration systems [21]. Such closed-loop technological approaches have been reported to reduce MEs in hospital settings [80]. However, human-technology interactions in routine clinical practice introduce risks of bypassing, workarounds and over-rides of technological safety systems [21, 57, 66]. Developments in AI can create opportunities for more autonomous CDS systems linked to closed-loop systems. As with other healthcare applications of AI, these come with the necessary requirements of data quality, validation, regulation and trust and transparency for staff, patients and family members [79]. The reduced ME rate and its relationship with potential patient harm has not yet been fully explored. Further understanding is needed on the optimal system, process and human interactions required for the patient safety benefits of such technological solutions to be realised when implementing and changing practice in ICUs.

The lack of high-grade evidence in this field is noteworthy. When mitigating strategies for MEs and ADEs are implemented and evaluated, multicentre randomized cluster/stepped wedge-controlled trials are needed [81]. These should include better intervention descriptions [82], process evaluations [83], and appropriate economic evaluations [84, 85], to inform practice change priorities. The importance of ICU and other healthcare staff in routinely identifying and addressing MEs and mitigating preventable ADEs was highlighted in our findings.

Strengths and limitations

Our scoping review is based on a clear and structured methodology, addressing a broad range of outcomes related to MEs and ADEs and could guide future mitigating strategies and new research avenues. However, some limitations should be acknowledged. First, the restricted bibliographic search and eligibility criteria might have excluded studies that showed interventions to reduce MEs and ADEs. To minimize this risk, the search was expanded with review of the reference lists of included studies and essential documents.

Second, the results apply to high-income countries and cannot be generalized beyond these. We excluded studies from low- and middle-income countries (LMICs) as medication errors tend to have a more severe impact due to more limited healthcare resources, inadequate infrastructure, and less robust healthcare systems [86]. The World Health Organization report on preventable medication-related harm in health care, while not limited to ICU settings, did demonstrate higher rates of ADEs in LMICs along with differences in the timing of error (ADEs as a result of prescribing error more common in LMICs where monitoring errors are more common in high-income countries). While some learning from this scoping review may be applicable to LMICs, the generalizability may not be fully applicable in this setting.

Third, uncertainty regarding prevalence and consequences arising from the heterogeneity of definition and tested methods should be underlined. The results might underreport the true impact of MEs and ADEs. This emphasizes the needs for adequately performed multicentre multinational assessment using external audit to more clearly assess prevalence, severity and consequences.

Conclusion

Despite an increasing focus on patient safety over recent years, MEs and preventable ADEs are extremely common in the ICU setting. While they rarely lead to serious patient harm, they are associated with increased length of stay. At risk populations and time periods exist, providing potential targets for future interventions. Whilst staff vigilance and activities ensure that the majority of MEs are intercepted prior to reaching the patient there is an inherent system limitation related to human factors. Technological solutions such as e-prescribing (with clinical decision support systems) have an important role in reducing MEs in the ICU setting. Medication reconciliation and review processes reduce MEs and related patient harm. Ultimately, these solutions are still dependent on the ICU clinical staff interactions, including clinical pharmacist activities, to provide the greatest impact on patient safety.

Supplementary Information

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Author contributions

Conceptualization: KP; MvM; RB. Methodology: MvM; KP; MD; MO; RB. Data curation: KP; MvM; AG; ES; MCMD; MO; RF; RB. Formal analysis and investigation: MvM; KP; RB. Writing—original draft preparation: KP; MvM; RB. Writing—review and editing: AG; EA; ES; MCMD; MD; MO; RF. Funding acquisition: EA. Resources: EK; MvM. Supervision: EA; RB. Project management: EK. Visualization: EK; RB.

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Data availability

Not applicable.

Declarations

Conflicts of interest

No conflicts of interests: AG; ES; KP; MCMD; MD; MO; MvM; RB; R. Elie Azoulay has received fees for lectures from Alexion, Sanofi, Pfizer and Gilead.

Ethical approval

Not applicable for this scoping review.

Patient consent

Not applicable for this scoping review.

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