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RESEARCH ARTICLE

# Voluntarily reported prescribing, monitoring and medication transfer errors in intensive care units in The Netherlands

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## Abstract

*Background* Medication errors occur frequently in intensive care units (ICU). Voluntarily reported medication errors form an easily available source of information. *Objective* This study aimed to characterize prescribing, monitoring and medication transfer errors that were voluntarily reported in the ICU, in order to reveal medication safety issues. *Setting* This retrospective data analysis study included reports of medication errors from eleven Dutch ICU's from January 2016 to December 2017. *Method* We used data extractions from the incident reporting systems of the participating ICU's. The reports were transferred into one database and categorized into type of error, cause, medication (groups), and patient harm. Descriptive statistics were used to calculate the proportion of medication errors and the distribution of subcategories. Based on the analysis, ICU medication safety issues were revealed. *Main outcome measure* The main outcome measure was the proportion of prescribing, monitoring and medication transfer error reports. *Results* Prescribing errors were reported most frequently ($n = 233$, 33%), followed by medication transfer errors ($n = 85$, 12%) and monitoring errors ($n = 27$, 4%). Other findings were: medication transfer errors frequently caused serious harm, especially the omission of home medication involving the central nervous system and proton pump inhibitors; omissions and dosing errors occurred most frequently; protocol problems caused a quarter of the medication errors; and medications needing blood level monitoring (e.g. tacrolimus, vancomycin, heparin and insulin) were frequently involved. *Conclusion* This analysis of voluntarily reported prescribing, monitoring and medication transfer errors warrants several improvement measures in these processes, which may help to increase medication safety in the ICU.

**Keywords** Incident reporting system · Intensive care unit · Medication error · Medication safety · Patient safety · The Netherlands · Voluntarily reports

## Abbreviations

| | |
|---|---|
| APTT | Activated Partial Thromboplastin Time |
| ATC | Anatomical Therapeutic Chemical (a medication classification system) |

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| | |
|---|---|
| CPOE | Computerized provider order entry |
| CNS | Central nervous system |
| ICU | Intensive care unit |
| INR | International normalized ratio |
| IRS | Incident reporting system |
| IT | Information technology |
| LMWH | Low molecule weight heparin |
| ME | Medication errors |
| MoE | Monitoring errors |
| MTE | Medication transfer errors |
| PE | Prescribing errors |
| PIS | Patient Information System |
| TDM | Therapeutic drug monitoring |

## Impacts on practice

- The frequently reported prescribing errors can be prevented by introducing or improving medication safety practices like decision support in electronic prescribing, and the daily attendance of a pharmacist during patient rounds.
- Medication reconciliation at ICU admission should be part of standard ICU care; this service should be combined with the early continuation of high-risk home medication, like medication involving the central nervous system and proton pump inhibitors.
- Medication needing blood level monitoring (e.g. tacrolimus, vancomycin, heparin and insulin) are prone to medication errors in the ICU.

## Introduction

Medical errors occur frequently in intensive care units (ICU's) [1, 2]. This can be attributed to complex patient conditions, acute life-sustaining treatments and a considerable workload fluctuation [1–4]. Medication errors (ME) account for most of the medical errors in the ICU [2, 4] and seem to occur at a higher frequency and with a greater likelihood for harm in ICU patients compared to non-ICU patients [5–7]. An ME can be defined as an unintended failure in the medication process that leads to, or has the potential to lead to harm to the patient [8]. The frequency of ME is estimated to be 106 per 1000 patient days in adult ICU's [6].

Kane-Gill et al. [6] found that the types of voluntarily reported ME, contributing factors, drug classes and outcomes were different in ICU's compared to the general care units. They concluded that there is a need for ICU specific surveillance systems for ME, so that systematic improvements specific to the ICU environment can be implemented.

There are a few studies on voluntarily reported ME in the ICU available [6, 9–12], giving insight into the specific epidemiology of ME in the ICU. However, since medication administration errors in general dominate the reports, other important ME like prescribing errors (PE), monitoring errors (MoE) and medication transfer errors (MTE) may be overlooked in these studies, although these errors are known as common and important causes of adverse events [13–15].

Notwithstanding the known limitations of voluntarily reported ME, such as under- and selective reporting [16, 17], analyzing voluntarily reported PE, MoE and MTE in the ICU in a multi-center sample provides a valuable insight into high-risk situations and may help to identify opportunities for improvement [18].

## Aim of study

This study aimed to characterize and analyze prescribing errors, monitoring errors and medication transfer errors that were voluntarily reported in the ICU, in order to reveal ICU medication safety issues related to prescribing, monitoring and ICU medication transfer.

## Ethics approval

Since data used in this study neither contained patient information nor reporter information, a waiver from the Zuid Holland Medical Ethics committee (METC, nr: 18-098) was obtained.

## Method

### Design and setting

We designed a retrospective data analysis study of incidents reported in 11 of the 83 (13%) Dutch adult ICU's. For this purpose, we used datasets derived from seven different web-based, voluntary IRS systems from the first of January 2016 until the 31th of December of 2017.

Data were obtained from two university hospitals (Erasmus University Medical Center Rotterdam and University Medical Centre Groningen) and five general teaching hospitals (HMC general teaching hospital Den Haag (location Bronovo, location Westeinde and location Antoniushove), Haga general teaching hospital Den Haag, Franciscus Gasthuis and Vlietland Rotterdam, Reinier de Graaf Hospital Delft and Jeroen Bosch Hospital Den Bosch. Data were collected without identifiers of patients and staff members.

## Description of the IRS systems

The involved hospitals all participated in the nationwide patient safety program which aims to minimize patient harm through reducing medical errors. Part of this program is the presence of a local incident reporting system (IRS) for voluntarily reporting of medical errors (including ME) by the hospital staff [19]. These IRS systems are characterized by their decentralized management. All included hospitals used a web-based intranet reporting tool (Iprova version 4.8, Infoland, Veldhoven, The Netherlands) [20], which was locally available and was easily accessible for hospital staff. After registration of the incidents by the healthcare provider, the incidents were periodically reviewed, analyzed and managed by a local multidisciplinary incident report committee in the ICU, consisting of ICU nurses, ICU doctors and quality officers. The reviews of the incidents were also documented in the IRS systems.

All IRS reports contained a combination of structured and non-structured data. However, since there was no obligatory Dutch standardization regarding the registration of incidents, every IRS system had a different structure.

## Data collection

### Hospital data

We collected the following information:

*Organization related information* type of hospital (university hospital, general teaching hospital), type of ICU (general versus specialized, and medical versus surgical), number of ICU beds.

*Information technology (IT) related information*: availability of CPOE (computerized provider order entry) (yes/no), one CPOE for the entire hospital including the ICU (yes/no).

*Clinical pharmacy related information* pharmacist attendance in the ICU (number of times a week), dedicated ICU pharmacist (yes/no), medication reconciliation at ICU admission (yes/no), how pharmacists provide medication surveillance (electronic medication surveillance in the pharmacy, patient round attendance, after consultation).

Based on the pharmacist attendance we defined three levels: level 0: no pharmacist attendance, level 1: some pharmacist attendance at the ICU and level 2: a dedicated pharmacist, five days a week.

Based on the medication reconciliation group we defined two groups: level 0: no medication reconciliation at the ICU and level 1: medication reconciliation at the ICU.

### ME data screening process and inclusion in final data set

All reported ME in 2016 and 2017 occurring in the ICU were extracted from the hospital IRS databases. The following data of an ME-report were collected: date of error, origin of report (hospital type, ICU type), description of the incident, preventive measures as suggested by the reporter (whenever available), hospital ME analysis and follow up (whenever available), drug name and route of administration (whenever available), potential causes, potential consequences (whether the error reached the patient, whether harm occurred, estimated risk of severity and estimated risk of reoccurrence of the error). The data frequently contained timelines and perspectives and it included (whenever performed) a root cause analysis, improvement measures and recommendations for improving medication safety by the ICU incident report committee.

All ME reports were thoroughly reviewed and checked to ensure that no duplicates or medical events without medication involvement were included. Since the structure and categorization of the databases were different, we made a new standardized database structure and transferred the data into this new database. This new structure was based on the Dutch standard [21], and can be found in "Appendix 1".

After categorizing we selected the PE, MoE and MTE for inclusion in the study.

For most reports our classifications were more or less available in the primary datasets or easy to detect from the available written non-structured information in the reports. The first author double-checked all available classifications and corrected several inconsistencies made by the reporters. Whenever a classification was missing, the first author categorized the report, based on the abundant non-structured available information. However, whenever a classification was not available nor traceable based on the non-structured data, a "not known" classification was given to the report. All original information was saved in the final database, this made extra checks for correctness possible during the analyzation process. Figure 1 shows the study flow.

## Data analysis

All data were processed and classified in MS Excel 2016 (Microsoft Corp., Redmond, USA) and analyzed with IBM SPSS Statistics version 24.0 (IBM Corp., Armonk, New York, USA). Descriptive statistics were used to determine the proportion of PE, MoE and MTE in the ICU, as well as the subtypes, the type of medication involved, the route of administration, the causes and patient harm. Through reviewing all ME, we revealed some ICU medication safety issues. These were used to discuss suitable ICU medication safety practices which could be introduced (when not available) or improved (when available).

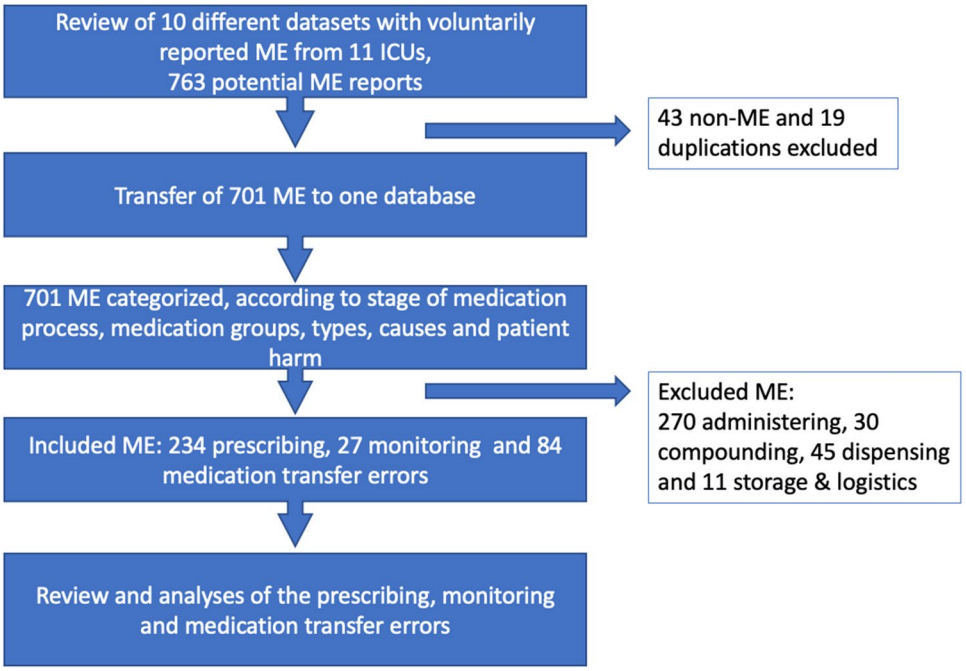


**Fig. 1** Study flow. ICU = intensive care unit, ME = medication errors

To be able to give an indication of the differences between ICU's in reporting, we divided the total number of reports per ICU by the number of beds and the number of years.

For the comparison of reporting rates between ICU's with different pharmacy services (pharmacist attendance level 0,1 and 2 and medication reconciliation level 0 and 1), we divided the total number of ME of a group of ICU's with the same level of pharmacy service by the number of beds in the ICU's of that level.

## Results

### Setting

Relevant characteristics of the ICU's are summarized in Table 1.

### Characteristics of included ME reports

The number of voluntarily reported ME was 701, which amounts to 2–6 reports per bed per participating ICU.

We included 345 (49%) ME reports, among which most were PE ($n = 233$, 33%), followed by MTE ($n = 85$, 12%) and MoE ($n = 27$, 3.9%).

ME involving a single medication occurred in 277 (80%) cases, 43 (12%) two or more medications and 25 (7%) did not specify the medication.

Compared to nursing staff, the medical staff tended to report more serious errors (12% vs. 4%).

ICU's with pharmacist attendance had higher report rates and percentages of reported PE. Likewise, ICU's with a medication reconciliation service had a higher report rate and percentage of reported MTE.

The following subgroups were only reported in ICU's with attending pharmacists: wrong frequency, contraindication, wrong time, incorrect actions based on monitoring results, allergies and wrong strength.

MTE were most frequently associated with serious harm (MTE = 11, 13%, PE = 5, 2% and MoE = 4, 15%), most frequently omissions during the ICU admission process ($n = 9$, 3%). Other error types leading to serious harm were monitoring problems ($n = 5$, 1%) and wrong dose ($n = 4$, 1%).

Table 2 summarizes the main characteristics of the PE, MoE and MTE reports.

### Medication involved

Figure 2 shows the medication groups involved in the ME.

Within the anti-infectives group (J = 64, 19%), cephalosporins ($n = 17$, 5%) and vancomycin ($n = 11$, 3%) accounted for almost half of the reported ME. The vancomycin reports were mostly related to problems with therapeutic drug monitoring (TDM).

The antithrombotic agents (B05 = 58, 17%) most frequently leading to a report were the low molecule weight heparins (LMWHs = 31, 69%). Noteworthy, besides the common types of error (i.e. wrong dose ($n = 11$, 24%) and omissions ($n = 10$, 22%), "duplicate medication" errors ($n = 7$, 16%) were frequently reported errors in the antithrombotic agents. For example, 3 reports described

**Table 1** Characteristics of participating ICU's

| ICU characteristics | $n = 11$ ICU's in 7 hospitals |
|---|---|
| *Type of patients, n (%)* | |
| Mixed (surgical and medical) | 10 (91%) |
| Cardiothoracic | 1 (9%) |
| *Type of hospital, n (%)* | |
| University Hospital | 2 (29%) |
| General teaching Hospital | 5 (71%) |
| Beds per ICU, median (range) | 14 (6–44) |
| CPOE available, *n* (%) | 11(100%) |
| Same CPOE on general ward and ICU, *n* (%) | 9 (82%) |
| *Attendance of pharmacist in the ICU (days/week)*, n (%)* | |
| 0 | 3 (27%) |
| 1–2 | 3 (27%) |
| 4–5 | 5(45%) |
| *ICU specialized or dedicated pharmacists, n (%)* | |
| Specialized ICU pharmacist | 3 (27%) |
| Group of pharmacists dedicated to ICU | 3 (27%) |
| Not specialized nor dedicated | 5 (45%) |
| *How do pharmacists address interventions, n (%)* | |
| Electronic medication surveillance | 11 (100%) |
| Patient rounds/ in the ICU | 8 (73%) |
| After consultation/on request | 11 (100%) |
| *Pharmacist attending patient rounds, n (%)* | |
| Level 0 | 3 (27%) |
| Level 1* | 5 (45%) |
| Level 2 | 3 (27%) |
| *Medication reconciliation service, n (%)* | |
| No service available | 5 (45%) |
| Service available | 6 (55%) |

CPOE = computerized provider order entry, ICU = Intensive Care Unit, ME = Mediation Error

*Level 1 contained different forms of pharmacy service; some ICU's had pharmacists working in groups dedicated to the ICU and attended the ICU 1–3 times a week, where others had no dedicated/specialized pharmacist, these ICU's had the pharmacists on duty attending the ICU patient round on a daily basis

starting a therapeutic dose of LMWH, without noticing that the patient still had an INR (international normalized ratio, based on vitamin K antagonist use) within the target range.

Besides frequently occurring, CNS medications ($n = 57$, 17%; opioids = 25, 44%), were also most often associated with serious harm ($n = 7$, 2%), primarily omissions of home medication at ICU admission. The induced harm was, for example, inadequate pain regulation, or patient agitation.

Twenty-five ME with insulin were reported (7%), most of them being MoE ($n = 18$, 72%), five insulin cases led to serious temporary harm.

Hypoglycemia due to erroneous continuation of insulin infusion after stopping or reducing enteral feeding was reported ten times (3%) in 6 of the 7 hospitals, leading to serious harm in two cases. Moreover, the omission of insulin treatment after ICU discharge of patients with DM type I was another type of ME occurring several times, leading to serious harm in one case.

The three serious harm errors involving proton pump inhibitors were all omissions of home medication at ICU admission leading to a gastro-intestinal bleeding.

Fifteen ME with tacrolimus were reported in the university hospitals, accounting for 10% of the reported ME in the 2 university hospitals, predominantly occurring in the first days of the post-transplantation period. Like vancomycin, these errors were in general caused during the TDM process, such as forgetting to measure blood levels or forgetting to adjust the dose after the results of TDM became available.

"Appendix 2" shows examples of the reported ME.

### Causes

Figure 3 shows the primary causes of error related to patient harm.

Noteworthy, 90 (26%) of the primary causes of error were related to problems with protocols, especially "protocol or guideline not followed" ($n = 67$, 19%), followed by "unclear protocol" ($n = 17$, 5%), "protocol or guideline not implemented" ($n = 5$, 1%) and "no protocol or guideline" ($n = 1$, 0.3%).

The errors made while using CPOE ($n = 83$, 24%) were reported in all hospitals, regardless of the type of CPOE used.

Four PE were due to sound-alike medication names: nitroprusside confused with nitroglycerine, dipyridamole confused with dipidolor, ketanserine confused with Ketanest® (esketamine) and finally calcium with citrate which are both used in continuous renal replacement therapy systems.

As was expected, half of the MTE were due to communication factors, especially unclear or no communication between health care providers (both 16 reports, 19%).

## Discussion

This study is the first to systematically explore voluntarily reported prescribing, monitoring and medication transfer errors in a representative group of Dutch ICU's, enabling us to identify ICU medication safety issues. The prescribing (PE = 233, 33%), monitoring (MoE = 27, 4%) and medication transfer errors (MTE = 85, 12%) accounted for half of the ME reports and were further analyzed.

The percentage of reported ME associated with harm was higher as compared to literature [6, 12], which may be explained by cultural or organizational differences [22] and the fact that a relatively large number of reports were made

**Table 2** Characteristics of voluntarily reported ME

| | PE | MoE | MTE | Total |
|---|---|---|---|---|
| | 233 (68%) | 27 (8%) | 84 (25%) | 345 (49%) |
| **Type of error, *n* (%)** | | | | |
| *Errors related to the choice of medicine* | | | | |
| Omission | 43 (18%) | – | 44 (52%) | 87 (25%) |
| Wrong medication | 17 (7%) | – | 2 (2%) | 19 (6%) |
| Wrong route of administration | 4 (2%) | – | 0 (0%) | 4 (1%) |
| Wrong dosage form | 2 (1%) | – | 1 (1%) | 3 (1%) |
| *Errors related to dosing, frequency and duration of therapy* | | | | |
| Wrong dose | 41 (18%) | – | 11 (13%) | 52 (15%) |
| Wrong infusion rate | 11 (5%) | – | 1 (1%) | 12 (3%) |
| Wrong frequency/duration | 22 (9%) | – | 2 (2%) | 24 (7%) |
| Wrong strength | 4 (2%) | – | 1 (1%) | 5 (1%) |
| Wrong time of administration | 10 (4%) | – | 1 (1%) | 11 (3%) |
| *Errors related to medication surveillance* | | | | |
| Allergy/intolerance | 3 (1%) | – | 1 (1%) | 4 (1%) |
| Contraindication | 12 (5%) | – | 2 (2%) | 14 (4%) |
| Double medication | 18 (8%) | – | 3 (4%) | 21 (6%) |
| No indication | 5 (2%) | – | 3 (4%) | 8 (2%) |
| *Patient monitoring errors* | | | | |
| Incorrect actions based on monitoring results | 1 (0.4%) | 4 (15%) | 4 (5%) | 9 (3%) |
| Insufficient monitoring | 8 (3%) | 23 (85%) | 0 (0%) | 31 (9%) |
| *Others* | | | | |
| Dose change or start not correctly communicated | 11 (4%) | – | 3 (4%) | 14 (4%) |
| Error with CPOE | 18 (8%) | – | 0 (0%) | 18 (5%) |
| Wrong patient | 3 (1%) | – | 0 (0%) | 3 (1%) |
| Non-specified | 0 (0%) | – | 6 (7%) | 6 (2%) |
| **Cause of Error, *n* (%)** | | | | |
| Technical factors | 86 (37%) | 3 (11%) | 2 (2%) | 91 (26%) |
| Organizational factors | 16 (7%) | 5 (19%) | 8 (10%) | 29 (8%) |
| Communication factors | 40 (17%) | 4 (15%) | 42 (50%) | 86 (25%) |
| Human performance factors | 90 (39%) | 14 (52%) | 30 (35%) | 134 (39%) |
| Unknown | 1 (0%) | 1 (4%) | 3 (4%) | 5 (1%) |
| **Did ME reach patient, *n* (%)** | | | | |
| Yes | 165 (71%) | 26 (96%) | 68 (81%) | 259 (75%) |
| No | 52 (22%) | 1 (4%) | 12 (14%) | 65 (19%) |
| Unknown | 17 (7%) | 0 (0%) | 4 (5%) | 21 (6%) |
| **Patient harm, *n* (%)** | | | | |
| Serious permanent harm | 1 (0%) | 0 (0%) | 0 (0%) | 1 (0%) |
| Serious temporary harm | 4 (2%) | 4 (15%) | 11 (13%) | 19 (6%) |
| Minimal/mild harm | 33 (14%) | 14 (52%) | 14 (16%) | 61 (18%) |
| No harm | 164 (70%) | 8 (30%) | 48 (57%) | 220 (64%) |
| Unknown | 31 (13%) | 1 (4%) | 12 (14%) | 44 (13%) |
| **Pharmacist attending patient rounds, *n*(%[a]/PE/bed)** | | | | |
| Level 0 | 12 (23%/0.32) | – | – | – |
| Level 1 | 96 (30%/0.81) | – | – | – |
| Level 2 | 125 (39%/0.59) | – | – | – |
| **Medication reconciliation service, *n* (%[#] / MTE/bed)** | | | | |
| No service available | – | – | 27 (10%/0.18) | – |
| Service available | – | - | 58 (14%/0.27) | – |

[a]Percentage of all reported ME

ME = medication errors, MoE = monitoring errors, MTE = medication transfer errors, PE = Prescribing errors, PE/bed = number of prescribing errors per ICU bed, per year, MTE/bed = number of medication transfer errors per ICU bed, per year

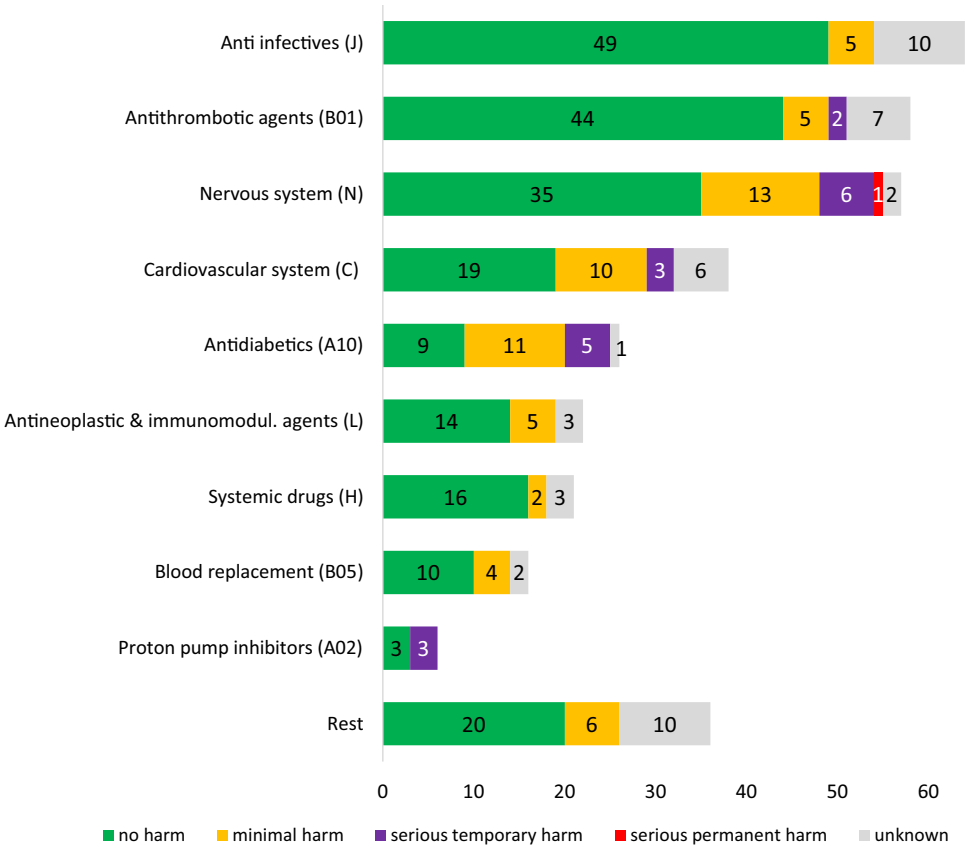


**Fig. 2** Medication groups involved in the reported medication errors, related to consequences (harm)

by physicians, who are known for reporting more severe errors [23].

## Prescribing errors

The PE percentage was in line with data from self-reporting studies in the UK and the USA [11, 12] but lower compared to Kane-Gill et al. [6]. The higher number of PE found by Kane-Gill et al.could be attributed to the absence of an ICU CPOE at the time of study, while in our study all ICU's had a CPOE. Other reasons for this difference may be due to cultural or organizational differences [22].

Most frequently reported PE were wrong dosages and omissions, which is in line with literature [6, 12]. These PE can be prevented by introducing or improving medication safety practices, like decision support software in the CPOE [24, 25] and the attendance of an ICU pharmacist during patient rounds [26–34]. Clearly, one should understand that none of these suggested medication safety practices will eliminate the occurrence of PE, so additional improvement measures remain needed [35–37].

Noteworthy, we found higher numbers and percentages of PE in the ICU's with a pharmacist attending patient rounds. This increase makes sense, since IRS data always suffer from important underreporting. Therefore, reporting rates probably relate more to organization and safety culture than to the actual number of ME. In other words, the positive association between pharmacist attendance and higher reporting rates might be explained by a higher awareness of medication safety issues. Contrarily, the highest level of pharmacist attendance was associated with less PE. Noteworthy these ICU's were all academic, so organization differences might have caused this lower rate.

## Medication transfer errors

MTE were not previously documented as such in literature, but their proportion was in line with "transcribing and documenting" ME in other studies, which varied from 11–22% of all reported ME [6, 12]. Surprisingly we found relatively more MTE associated with serious harm, compared to PE. Two thirds of the serious harm MTE were omissions of PPI and CNS home medication, suggesting that these groups are home medications needing early restart at ICU admission. Interestingly, the consequence of omission at ICU admission of home CNS medication was recently studied [38]. Early restart of CNS medication proved to be optimal for the patient, as it was associated with maintaining lower levels of sedation, less delirium and potentially fewer ventilation days. Since it is known that MTE can be prevented by medication reconciliation [13], we emphasize that medication reconciliation at ICU admission, with an early restart of


Human performance
Protocols or guidelines not followed
48
10
4
5
Performance deficit
22
9
3
6
Insufficient expertise
12
9
1
1
No double checking performed
1
1
Other
1
Equipment and software
Errors in the CPOE or PIS
65
7
1
10
Medication name confusion
5
1
Dosageform confusion
1
1
Communication
Unclear communication between caregivers
17
8
2
9
No transfer of information between caregivers
19
4
3
3
Wrong transfer of information between caregivers
13
4
3
Wrong communication caregiver and patient
1
Organization
Unclear protocols or guidelines
9
3
4
1
Protocol or guideline not implemented
3
1
1
High work pressure or short-staffed
1
3
1
Other
1
No protocol or guidelines
1
Staffing problems other
1
Unknown
Unknown
2
2
0
10
20
30
40
50
60
70
80
90
no harm
minimal harm
serious temporary harm
serious permanent harm
unknown

◂**Fig. 3** Primary causes of reported medication errors, in the medication errors, related to consequences (harm) CPOE = computerized provider order entry, PIS = Patient Information System

relevant home medication, should be part of ICU standard care. Notably, as with the other medication safety practices, the introduction of medication reconciliation will never be able to eliminate all MTE, indeed for this practice the effectiveness must be evaluated and improved on a regular basis [35–37]. Just like ICU's with a pharmacist attending service, ICU's with a medication reconciliation service had a higher percentage and reporting rate of MTE.

Half of the MTE were caused by communication problems. Once more this finding underlines the importance of good face to face handover, combined with written information [39].

### Protocol adherence problems and blood level monitoring medications

Non-adherence to protocol and guidelines was a frequent cause of the reports, which is in line with literature [6, 12]. Making protocols will not result in better adherence or improved outcomes [40], therefor efforts should be paid to first improve protocols and processes, followed by thorough implementation, including strategies for education and adherence [41]. We think that especially medications requiring additional blood level monitoring will benefit from such a multi-faced, system-based approach, since the complexity of their monitoring process makes these medications prone to ME [42]. A good example of such an approach is the Six Sigma, a process performance improvement approach described by Egan et al. [43].

Our high number of insulin monitoring errors leading to hypoglycemia are in line with a previous review on severe incidents reports in England [11]. Clinical guidelines recommend target blood glucose between 7.8 and 10 mmol/L (140 and 180 mg/dL) for most patients in the intensive care unit (ICU) in order to reduce the potentially harmful effect of stress hyperglycemia on morbidity and mortality [44]. However tight glycemic control using intermittent blood glucose measurements is associated with a risk of hypoglycemia [44], as was seen in our study. The prevention of severe hyperglycemia and hypoglycemia, i.e. effective glucose management should be considered an objective of ICU's [45]. A relatively new medication safety practice is the continuous glucose monitoring combined with a validated insulin infusion protocol (including an algorithm), which may improve patient outcomes and reduce workload [45, 46].

Finally, antithrombotic ME were frequently reported in our study, this was also noticed in a study in the UK [11]. In this UK study many PE with heparin were found, whereas in our study nadroparin was most often involved. Based on the high number of reports, the potential risk of ME with antithrombotic agents and our review of the ME reports, we suggest that ICU's should develop a protocol, that is process based, focusing on safe (dis)continuation of therapeutic anticoagulants during ICU admission and discharge, the prevention of unintended duplicate ME, as well as safe dosing of heparin during the ICU stay.

### Strengths

A strength of this study on voluntary reported ME was that it concerned 11 ICU's, including university hospitals and general teaching hospitals from different regions of the Netherlands, making the results of this study generalizable to different types of ICU's.

Moreover, thorough review of the non-structured written information as well as thorough categorization of the ME by our team, made the categorization more precise and consequent, as compared to similar research where this was only performed by the reporting healthcare providers [6, 12].

Another strength of this study was that we were able to point out several medication safety issues, that in our opinion need further attention.

### Limitations

An important limitation of our study was the fact that voluntarily reported ME are always underreported [11, 18, 22], making sound conclusions or statistics based on the number of errors reported not feasible. Second, like all studies on voluntarily reported ME, our study suffered from "self-report bias", with the consequence that different types of ME were not equally reported [47]. The consequence of this "self-report bias" was that a statistics-based comparison between the different error groups or different settings could not be performed. Third, the MTE from the ICU to the general ward were underreported, since they were not present in most datasets, most probably because they were reported on the general ward instead of in the ICU, with the consequence that they were not part of the selection of our ICU datasets.

Future research should focus on developing, validating and assessing the impact of proposed medication safety practices in ICU quality improvement studies.

## Conclusion

This analysis of voluntarily reported prescribing, monitoring and medication transfer errors revealed several medication safety issues that warrants improvement measures in the ICU.

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## References

1. Garrouste-Orgeas M, Philippart F, Bruel C, Max A, Lau N, Misset B. Overview of medical errors and adverse events. Ann Intensive Care. 2012;2(1):2.
2. Rothschild JM, Landrigan CP, Cronin JW, Kaushal R, Lockley SW, Burdick E, et al. The critical care safety study: the incidence and nature of adverse events and serious medical errors in intensive care. Crit Care Med. 2005;33(8):1694–700.
3. Kane-Gill SL, Jacobi J, Rothschild JM. Adverse drug events in intensive care units: risk factors, impact, and the role of team care. Crit Care Med. 2010;38(6 Suppl):S83–S8989.
4. Garrouste-Orgeas M, Timsit JF, Vesin A, Schwebel C, Arnodo P, Lefrant JY, et al. Selected medical errors in the intensive care unit: results of the IATROREF study: parts I and II. Am J Respir Crit Care Med. 2010;181(2):134–42.
5. Cullen DJ, Sweitzer BJ, Bates DW, Burdick E, Edmondson A, Leape LL. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. Crit Care Med. 1997;25(8):1289–97.
6. Kane-Gill SL, Kowiatek JG, Weber RJ. A comparison of voluntarily reported medication errors in intensive care and general care units. Qual Saf Health Care. 2010;19(1):55–9.
7. Heselmans A, van Krieken J, Cootjans S, Nagels K, Filliers D, Dillen K, et al. Medication review by a clinical pharmacist at the transfer point from ICU to ward: a randomized controlled trial. J Clin Pharm Ther. 2015;40(5):578–83.
8. Agency EM. Medication errors [cited 2019 26 Nov]. Available from: https://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000570.jsp&mid=WC0b01ac0580659655.
9. Thomas AN, MacDonald JJ. A review of patient safety incidents reported as 'severe' or 'death' from critical care units in England and Wales between 2004 and 2014. Anaesthesia. 2016;71(9):1013–23.
10. Thomas AN, Panchagnula U. Medication-related patient safety incidents in critical care: a review of reports to the UK national patient safety agency. Anaesthesia. 2008;63(7):726–33.
11. Thomas AN, Taylor RJ. An analysis of patient safety incidents associated with medications reported from critical care units in the North West of England between 2009 and 2012. Anaesthesia. 2014;69(7):735–45.
12. Latif A, Rawat N, Pustavoitau A, Pronovost PJ, Pham JC. National study on the distribution, causes, and consequences of voluntarily reported medication errors between the ICU and non-ICU settings. Crit Care Med. 2013;41(2):389–98.
13. Bosma LBE, Hunfeld NGM, Quax RAM, Meuwese E, Melief P, van Bommel J, et al. The effect of a medication reconciliation program in two intensive care units in the Netherlands: a prospective intervention study with a before and after design. Ann Intensive Care. 2018;8(1):19.
14. Ridley SA, Booth SA, Thompson CM. Intensive care society's working group on adverse I. Prescription errors in UK critical care units. Anaesthesia. 2004;59(12):1193–200.
15. Kopp BJ, Erstad BL, Allen ME, Theodorou AA, Priestley G. Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection. Crit Care Med. 2006;34(2):415–25.
16. Montesi G, Lechi A. Prevention of medication errors: detection and audit. Br J Clin Pharmacol. 2009;67(6):651–5.
17. Mahajan RP. Critical incident reporting and learning. Br J Anaesth. 2010;105(1):69–75.
18. Kiekkas P, Aretha D, Stefanopoulos N, Baltopoulos GI. Knowledge is power: studying critical incidents in intensive care. Crit Care. 2012;16(1):102.
19. VMS. The Dutch patient safety programme [cited 2019 26 Nov]. Available from: https://www.medicalfacts.nl/2014/12/11/engelstalige-film-over-vms-veiligheidsprogramma/.
20. Infoland. Risk management software: change risks into opportunities! [cited 2019 26 Nov]. Available from: https://www.infoland.eu/software/risk-management/.
21. Cheung KC, van den Bemt PM, Bouvy ML, Wensing M, De Smet PA. A nationwide medication incidents reporting system in The Netherlands. J Am Med Inform Assoc. 2011;18(6):799–804.
22. Arabi YM, Al Owais SM, Al-Attas K, Alamry A, AlZahrani K, Baig B, et al. Learning from defects using a comprehensive management system for incident reports in critical care. Anaesth Intensive Care. 2016;44(2):210–20.
23. Brunsveld-Reinders AH, Arbous MS, De Vos R, De Jonge E. Incident and error reporting systems in intensive care: a systematic review of the literature. Int J Qual Health Care. 2016;28(1):2–13.
24. Kuperman GJ, Bobb A, Payne TH, Avery AJ, Gandhi TK, Burns G, et al. Medication-related clinical decision support in computerized provider order entry systems: a review. J Am Med Inform Assoc. 2007;14(1):29–40.
25. Z-index. Dutch drug database G-Standaard Medication Surveillance [cited 2019 26 Nov]. Available from: https://www.z-index.nl/english.
26. Horn E, Jacobi J. The critical care clinical pharmacist: evolution of an essential team member. Crit Care Med. 2006;34(3 Suppl):S46–51.
27. Kane SL, Weber RJ, Dasta JF. The impact of critical care pharmacists on enhancing patient outcomes. Intensive Care Med. 2003;29(5):691–8.
28. MacLaren R, Bond CA. Effects of pharmacist participation in intensive care units on clinical and economic outcomes of critically ill patients with thromboembolic or infarction-related events. Pharmacotherapy. 2009;29(7):761–8.
29. MacLaren R, Bond CA, Martin SJ, Fike D. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. Crit Care Med. 2008;36(12):3184–9.
30. Papadopoulos J, Rebuck JA, Lober C, Pass SE, Seidl EC, Shah RA, et al. The critical care pharmacist: an essential intensive care practitioner. Pharmacotherapy. 2002;22(11):1484–8.
31. Bosma BE, van den Bemt P, Melief P, van Bommel J, Tan SS, Hunfeld NGM. Pharmacist interventions during patient rounds in two intensive care units: clinical and financial impact. Neth J Med. 2018;76(3):115–24.
32. Chisholm-Burns MA, Kim Lee J, Spivey CA, Slack M, Herrier RN, Hall-Lipsy E, et al. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. Med Care. 2010;48(10):923–33.
33. Montazeri M, Cook DJ. Impact of a clinical pharmacist in a multidisciplinary intensive care unit. Crit Care Med. 1994;22(6):1044–8.
34. Bond CA, Raehl CL. Clinical pharmacy services, pharmacy staffing, and hospital mortality rates. Pharmacotherapy. 2007;27(4):481–93.

35. Provost LP. Analytical studies: a framework for quality improvement design and analysis. BMJ Qual Saf. 2011;20(Suppl 1):i92–i9696.
36. Vo TH, Charpiat B, Catoire C, Juste M, Roubille R, Rose FX, et al. Tools for assessing potential significance of pharmacist interventions: a systematic review. Drug Saf. 2016;39(2):131–46.
37. Shulman R, McKenzie CA, Landa J, Bourne RS, Jones A, Borthwick M, et al. Pharmacist's review and outcomes: treatment-enhancing contributions tallied, evaluated, and documented (PROTECTED-UK). J Crit Care. 2015;30(4):808–13.
38. La MK, Thompson Bastin ML, Gisewhite JT, Johnson CA, Flannery AH. Impact of restarting home neuropsychiatric medications on sedation outcomes in medical intensive care unit patients. J Crit Care. 2018;43:102–7.
39. van Sluisveld N, Oerlemans A, Westert G, van der Hoeven JG, Wollersheim H, Zegers M. Barriers and facilitators to improve safety and efficiency of the ICU discharge process: a mixed methods study. BMC Health Serv Res. 2017;17(1):251.
40. Sevransky JE, Checkley W, Herrera P, Pickering BW, Barr J, Brown SM, et al. Protocols and hospital mortality in critically Ill patients: the united states critical illness and injury trials group critical illness outcomes study. Crit Care Med. 2015;43(10):2076–84.
41. Corwin GS, Mills PD, Shanawani H, Hemphill RR. Root cause analysis of ICU adverse events in the veterans health administration. Jt Comm J Qual Patient Saf. 2017;43(11):580–90.
42. Nolan TW. System changes to improve patient safety. BMJ. 2000;320(7237):771–3.
43. Egan S, Murphy PG, Fennell JP, Kelly S, Hickey M, McLean C, et al. Using six sigma to improve once daily gentamicin dosing and therapeutic drug monitoring performance. BMJ Qual Saf. 2012;21(12):1042–51.
44. Umpierrez GE, Pasquel FJ. Management of inpatient hyperglycemia and diabetes in older adults. Diabetes Care. 2017;40(4):509–17.
45. Krinsley JS, Chase JG, Gunst J, Martensson J, Schultz MJ, Taccone FS, et al. Continuous glucose monitoring in the ICU: clinical considerations and consensus. Crit Care. 2017;21(1):197.
46. Preiser JC, Lheureux O, Thooft A, Brimioulle S, Goldstein J, Vincent JL. Near-continuous glucose monitoring makes glycemic control safer in ICU patients. Crit Care Med. 2018;46(8):1224–9.
47. Kiekkas P, Aretha D, Karga M, Karanikolas M. Self report may lead to underestimation of 'wrong dose' medication errors. Br J Clin Pharmacol. 2009;68(6):963–4.