A PROSPECTIVE, TWO-CENTER OBSERVATIONAL STUDY OF THE PREVALENCE AND DETERMINANTS OF MEDICATION ADMINISTRATION ERRORS IN CLINICAL WARDS

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Abstract

In order to ascertain the frequency and factors that contribute to medication administration errors (MAEs). Understanding the factors that influence MAEs is crucial in order to develop preventative interventions. A prospective observational investigation conducted in a teaching hospital and university hospital in the Netherlands. The data was gathered through the process of observation. Priority was given to determining what percentage of administrations contained one or more MAEs. As secondary outcomes, the nature, intensity, and causes of MAEs were evaluated. Determinant analysis was conducted utilising logistic regression analyses with mixed effects and variables. The reporting process conforms to the STROBE standard. In 352 out of 2576 medication administrations (13.7%), MAEs were observed. The forms of MAEs that occurred most frequently (n = 380) were omission (n = 87) and improper medication handling (n = 75). 11.8 percent or 45 MAEs were potentially hazardous. In comparison to oral solid, the following pharmaceutical forms were more susceptible to MAEs: oral liquid (odds ratio [OR] 3.22, 95% confidence interval [CI] 1.43–7.25), infusion (1.73, CI 1.02–2.94), injection (OR 3.52, CI 2.00–6.21), ointment (10.78, CI 2.10–55.26), suppository/enema (OR 6.39, CI 1.13–36.03), and miscellaneous (6.17, CI 1.90–20.04). Medication administration between 10 a.m. and 2 p.m. (OR 1.91, CI 1.06–3.46) and 6 p.m. and 7 a.m. (OR 1.88, CI 1.00–3.52) increased the likelihood of MAEs compared to 7 a.m. to 10

a.m., and when performed by personnel with a higher professional education increased the likelihood of MAEs (OR 1.68, CI 1.03–2.74). The teaching hospital had a reduced incidence of MAEs (OR 0.17, CI 0.08–0.33). MAEs were not associated with variables such as day of the week, patient-to-nurse ratio, interruptions, or other attributes of nurses (e.g., degree, experience, employment classification). This research revealed a significant prevalence of MAE. MAE reduction may be aided by concentrating interventions on complex pharmaceutical formulations and administration times prone to error, as suggested by the identified determinants.In order to ascertain the frequency and factors that contribute to medication administration errors (MAEs). Understanding the factors that influence MAEs is crucial in order to develop preventative interventions. A prospective observational investigation conducted in a teaching hospital and university hospital in the Netherlands. The data was gathered through the process of observation. Priority was given to determining what percentage of administrations contained one or more MAEs. As secondary outcomes, the nature, intensity, and causes of MAEs were evaluated. Determinant analysis was conducted utilising logistic regression analyses with mixed effects and variables. The reporting process conforms to the STROBE standard. In 352 out of 2576 medication administrations (13.7%), MAEs were observed. The forms of MAEs that occurred most frequently (n = 380) were omission (n = 87) and improper medication handling (n = 75). 11.8 percent or 45 MAEs were potentially hazardous. In comparison to oral solid, the following pharmaceutical forms were more susceptible to MAEs: oral liquid (odds ratio [OR] 3.22, 95% confidence interval [CI] 1.43–7.25), infusion (1.73, CI 1.02–2.94), injection (OR 3.52, CI 2.00–6.21), ointment (10.78, CI 2.10–55.26), suppository/enema (OR 6.39, CI 1.13–36.03), and miscellaneous (6.17, CI 1.90–20.04). Medication administration between 10 a.m. and 2 p.m. (OR 1.91, CI 1.06–3.46) and 6 p.m. and 7 a.m. (OR 1.88, CI 1.00–3.52) increased the likelihood of MAEs compared to 7 a.m. to 10 a.m., and when performed by personnel with a higher professional education increased the likelihood of MAEs (OR 1.68, CI 1.03–2.74). The teaching hospital had a reduced incidence of MAEs (OR 0.17, CI 0.08–0.33). MAEs were not associated with variables such as day of the week, patient-to-nurse ratio, interruptions, or other attributes of nurses (e.g., degree, experience, employment classification). This research revealed a significant prevalence of MAE. MAE reduction may be aided by concentrating interventions on complex pharmaceutical formulations and administration times prone to error, as suggested by the identified determinants.

Keywords: Prospective, Observational Study, Prevalence, Determinants, Medication Administration Errors, Clinical Wards

1 INTRODUCTION

Globally, improper medication administration is the primary cause of patient injury (Panagioti et al., 2019; World Health Organisation, 2017). Medication administration is in particular a critical phase, as an error at this juncture can result in direct harm to a patient and significant repercussions for the staff member involved. The multistep nature of the medication administration procedure renders it susceptible to errors. In addition to the multitude of services and individuals involved, the complexity of procedures, and the frequent introduction of new technologies and procedures are also contributing factors. Medication administration for hospitalised patients is entrusted to nurses, who are also entrusted with an extensive array of intricate duties pertaining to the direct provision of patient care. Over the past few decades, numerous hospitals across the globe, including those in the Netherlands, have adopted various interventions to aid nursing staff in their

daily tasks and mitigate medication administration errors (MAEs). These interventions include electronic medication administration record (eMAR) and computerised physician order entry (CPOE) (Keers et al., 2014; Manias et al., 2020; Westbrook et al., 2020). Although the rates of MAE remain consistently high (Kuitunen et al., 2021b; Manias et al., 2020; Westbrook et al., 2020), further preventive and supportive measures are necessary. Identifying determinants associated with MAEs in these settings is crucial, as they may form the basis for targeted interventions.

2 BACKGROUND

Medication errors are a prevalent occurrence in healthcare environments and have the potential to result in escalated costs of healthcare, patient morbidity, and mortality (Batel Marques et al., 2016; Berdot et al., 2013; Keers et al., 2013b; Panagioti et al., 2019). There are numerous types of errors that can occur during the medication administration procedure, including omission and incorrect dosage. Significant rates of MAEs are documented in systematic evaluations that investigate their prevalence or the efficacy of strategies aimed at mitigating their occurrence (Berdot et al., 2013; Keers et al., 2013b; Kuitunen et al., 2021b; Manias et al., 2020). Excluding incorrect time errors (WTEs), one systematic review documents a median error rate of 8.0% (interquartile range [IQR]: 5.1%–10.9%). Conversely, another review presents a median error rate of 10.5% (IQR: 7.3%–21.7%). Keers et al. (2013b); Bernardot et al. (2013).

Barcode-assisted medication administration; simulation-based training; electronic medical record (EMR), CPOE, and eMAR systems; and barcode-assisted medication administration are a few of the preventative measures that have been investigated (Berdot et al., 2016; Hutton et al., 2021; Keers et al., 2014; Kuitunen et al., 2021b; Manias et al., 2020; Shah et al., 2016). Many of these interventions are expensive and only affect a limited number of MAE varieties. Furthermore, the efficacy of these interventions may be compromised by technological challenges and human factors (e.g., the use of remedies) (Mulac et al., 2021; van der Veen et al., 2018).

Knowledge-related factors (e.g., ignorance of medication information), personal circumstances (e.g., fatigue and complacency), and environmental context (e.g., interruptions, heavy workload, and equipment design) are cited in numerous reviews based on qualitative and quantitative studies as potential causes of MAEs (Keers et al., 2013a, 2015; Kuitunen et al., 2021a; Parry et al., 2015; Schroers et al., 2020). Nevertheless, there is inconsistency in the findings of quantitative research regarding associated determinants such as time of administration, day of the week, and nursing staff characteristics. This can be attributed to the clinical and methodological diversity of these studies, including variations in country, setting, technology utilisation, data collection methods, and settings (Alemu et al., 2017; Baraki et al., 2018; Berdot et al., 2012; Blignaut et al., 2017; Feleke et al., 2015; Hammoudi et al., 2018; Harka Numerous of these studies were centred on particular categories of clinical wards, including intensive care units and paediatric units. Furthermore, a number of studies conducted in developing nations or at an earlier time period fail to account for contemporary clinical practice. In the interim, numerous hospitals, primarily located in high-income and middle-income nations, have adopted highly effective preventive measures such as electronic medical records (EMR), clinical practice order entry (CPOE), and electronic medical records (eMAR). There is a paucity of research on the determinants of MAEs in contemporary clinical practice, specifically with electronic medication systems providing support.

Furthermore, as far as our understanding goes, no investigation of this nature has been conducted in an environment that includes an EMR, CPOE, and eMAR system. Given the continued prevalence of MAEs in contemporary hospitals equipped with these systems, it is critical to identify targeted interventions that can reduce the occurrence of these errors. Therefore, we undertook a prospective observational study in two Dutch hospitals that utilise a variety of supportive electronic medication systems (e.g., EMR, CPOE, and eMAR) to determine the prevalence, nature, and potential severity of MAEs, in addition to the factors that contribute to their occurrence.

3 METHODS

This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies (Appendix S1).

3.1 Study design

This prospective observational study was performed in Erasmus MC, University Medical Center Rotterdam in Rotterdam, the Netherlands and in Amphia Hospital in Breda, the Netherlands, respectively, a university hospital and general teaching hospital. The Medical Ethics Review Committee of Erasmus MC waived approval for this study (reference number MEC-2018-1532) in accordance with the Dutch Medical Research involving human subjects Act. Verbal consent from nursing staff members was obtained for participation in this study, and data were handled confidentially according to the Dutch General Data Protection Regulation.

3.2 Study setting

Data collection took place from October 2018 through February 2019 in Erasmus MC and from June 2019 through August 2019 in Amphia Hospital. Both hospitals had an EMR, a CPOE system and an eMAR system in place. This study was performed several months before planned extensive operations to improve medication safety, such as barcode-assisted medication administration. Table 1 shows the setting characteristics.

TABLE 1. Setting characteristics

Characteristics	Erasmus MC, University Medical Center Rotterdam	Amphia Hospital
Hospital characteristics		
Hospital type	University hospital	Teaching hospital
Clinical wards	Internal oncology	Internal medicine
	Neurology	Neurology
	Pulmonary medicine	General surgery
	Haematology	Orthopaedic surgery one
	Neurosurgery	Orthopaedic surgery two

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Characteristics	Erasmus MC, University Medical Center Rotterdam	Amphia Hospital
	Hepatopancreatobiliary surgery	
System features		
EMR, eMAR, CPOE software[a]	HiX®	Epic®
Additional CPOE[a]	Practocol®	Not applicable
BCMA	No	For parenteral medication
Patient identification verification by scanning	Yes	Yes
Medication cart filling	Decentrally and manually by nursing staff in the clinical wards	Decentrally and manually by pharmacy staff in the clinical wards
Instructions on medication administration	Electronic protocols for oral and parenteral medication	Electronic protocols for oral and parenteral medication

- Abbreviations: BCMA, barcode-assisted medication administration; CPOE, computerised physician order entry; eMAR, electronic medication administration record; EMR, electronic medical record.
- [a] HiX® version 6.1 (ChipSoft B.V.; Amsterdam, the Netherlands); Epic® (Epic Systems Corporation; Verona, Wisconsin, United States); Practocol® version 2.0.9.3 and 2.1.5.1 (Practocol B.V.; Rotterdam, the Netherlands). Practocol® is the system for prescriptions of medication in chemotherapy protocols.

3.3 Definitions and classification of MAE

In our study, an MAE was defined as any error during the administration of medication by nursing staff, that is a deviation from medication orders used by the nursing staff to administer medication, a deviation from local medication administration protocols, or a deviation from the medication information sheets provided by the manufacturer if local protocols were not available. Procedural errors (e.g. hygiene errors and labelling errors) and WTEs were not within the scope of this study. WTEs were excluded because they are highly prevalent (Berdot et al., 2013; Keers et al., 2013b) and generally considered as minor errors by clinicians. MAEs were classified into the following categories (Allan & Barker, 1990; van den Bemt & Egberts, 2007): omission, wrong medication handling, wrong dose, wrong administration technique, unordered drug, wrong dosage form, wrong route of administration, expired medication and other. Regarding the category wrong dose, deviations of more than 10% of the declared dose were marked as an MAE, considering that a deviation of 10% or less for the declared dose of pharmaceutical products within the shelf-life is widely accepted (International Conference on Harmonisation, 1999). The potential severity of

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MAEs was categorised according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) severity index, which ranges from category A (circumstances or events that have the capacity to cause error) to I (an error occurred that may have contributed to or resulted in the patient's death) (National Coordinating Council for Medication Error Reporting & Prevention, 2001).

3.4 Data collection

We collected data on medication administration using the disguised observation method (Allan & Barker, 1990; Dean & Barber, 2001), meaning that nursing staff were not aware of the detailed purpose of the study to prevent a Hawthorne effect. They were informed that the study was performed to examine the medication process. Observers that had completed an extensive training programme of several days accompanied the nursing staff to observe and record every dose administration on data collection forms designed for this study. After having arrived at a ward, observers selected the nurses to be observed through convenience sampling. Observation rounds were planned in periods of 1–2 weeks for each clinical ward. For ethical reasons, observers were instructed to intervene right before the administration if they had noticed a severe MAE (i.e. a dose deviation of at least 20%, wrong patient or wrong medication). Observation data were compared with medication prescriptions and protocols after the observation and not during observation, which complies with the gold standard of methods to detect medication errors (Dean & Barber, 2001). For each hospital, two raters independently reviewed approximately 200 observations ($n = 405$ observations, i.e. 405 medication administrations, in total over the two hospitals) to assess the presence, type and severity of MAEs, and disagreement was resolved by consensus between the two raters. The raters were one pharmacist (JJ) and hospital pharmacist (NH) in Erasmus MC and one hospital pharmacy resident (MR) and pharmacy student in Amphia Hospital. After exclusion of 2 of the 405 observations because of missing reviewer data, the Cohen's kappa for the presence of one or more MAEs was 0.81, indicating high interrater reliability. Therefore, the remaining observations were reviewed by one reviewer (JJ or MR) to assess whether an MAE occurred. Subsequently, the type and severity of each MAE were assessed by JJ and NH in Erasmus MC and MR and one pharmacist in Amphia Hospital and disagreement between the two raters was resolved by consensus.

After completion of the observation period in a particular clinical ward, data on staff member characteristics were collected on forms by e-mail or in person. JJ or MR categorised the medication class by Anatomical Therapeutic Chemical class (WHO Collaborating Centre for Drug Statistics Methodology, 2020) and the day of the week of each observed medication administration. In Erasmus MC, patient-characteristic data (i.e. gender, birth date and number of prescribed medications per day) were collected by JJ from the EMR system HiX® (Chipsoft B.V.; Amsterdam, the Netherlands) and from the CPOE system Practocol® (Practocol B.V.; Rotterdam, the Netherlands) for medication in chemotherapy protocols. In Amphia Hospital, patient-characteristic data were collected by MR from the EMR system Epic® (Epic Systems Corporation; Verona, Wisconsin, United States). Collected data were processed in OpenClinica® version 2.1 (OpenClinica LLC; Waltham, Massachusetts, United States).

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3.5 Inclusion and exclusion criteria

Medication administrations to inpatients performed by nursing staff were included. Excluded were medication administrations that were 1. not completed during the observation, 2. were declined by patients for other reasons than being erroneous, or 3. medication administrations with the medication name missing on the data collection form.

3.6 Study outcomes

The primary outcome was the proportion of medication administrations with one or more MAEs. The secondary outcomes were the type and potential severity of MAEs and the association between determinants and the occurrence of one or more MAEs.

We considered the following potential determinants: pharmaceutical form; medication class; hospital type; clinical ward type; day of the week; time window; patient-to-nurse ratio (i.e. number of patients per nurse); interruptions; double check of parenteral medication administration; and nursing staff age, gender, educational level, degree type and employment type. Considered determinants were based on proposed associations in literature and on theoretical assumptions (Alemu et al., 2017; Baraki et al., 2018; Berdot et al., 2012; Feleke et al., 2015; Hammoudi et al., 2018; Harkanen et al., 2015; Keers et al., 2013a; Keers et al.; 2015; Kuitunen et al., 2021a; Nguyen et al., 2015; Ong & Subasyini, 2013; Parry et al., 2015; Prot et al., 2005; Rodriguez-Gonzalez et al., 2012; Sears & Goodman, 2012; Tissot et al., 2003; van den Bemt et al., 2002; Wondmieneh et al., 2020).

3.7 Sample size calculation

Assuming an MAE rate of 10% (Berdot et al., 2013; Hassink et al., 2012; Keers et al., 2013b; Shah et al., 2016), a sample size of at least 1700 administrations would be required to examine 17 variables, using the rule of thumb that only one variable should be studied for every ten events (Peduzzi et al., 1996). The aim was to include at least 2000 administrations because the number of repeated measurements on nurse and patient level could not be predicted with convenience sampling. A total of 136 observation rounds were planned in advance (based on the expected number of observations per round), distributed over different days of the week and time windows. An extension was not needed, but the number of rounds was planned to be extended if fewer than 2000 administrations were included.

3.8 Data analysis

Descriptive statistics were used for the prevalence, type and severity of MAEs. Both univariable and multivariable mixed-effects logistic regression analyses (i.e. generalised linear mixed models) were used to determine the association between the determinants and MAEs accounting for within-subject correlations due to repeated measurements within the nurse and patient level.

Because of data clustering and the quantified number of MAEs in our study, fewer variables were tested than planned. The following variables were examined in the mixed-effects logistic

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regression analyses: pharmaceutical form (categorised; oral solid, oral liquid, infusion, injection, nebulising solution, ointment, suppository/enema, miscellaneous); hospital type (categorised; university hospital, teaching hospital); day of the week (categorised; weekdays, weekend); time window (categorised; 7 a.m.–10 a.m., 10 a.m.–2 p.m., 2 p.m.–6 p.m., 6 p.m.–7 a.m.); patient-to-nurse ratio (continuous); interruptions during administration (categorised: yes, no); and nursing degree type (categorised; nurse, specialised nurse, other), educational level (categorised; secondary vocational education, higher professional education, other), employment type (categorised; temporary, non-temporary), and experience in healthcare settings (categorised; 0–1 year, 1–5 years, more than 5 years). Medication class was excluded from the analysis because of the high number of classes in addition to assumed limited added value. The variable hospital type was chosen instead of clinical ward type because of low power for including the latter in the analysis. Because of the low number of participating male nursing staff members (n = 8, 6.1%), gender was excluded. Nurses' age and experience since first nursing diploma registration were excluded because of multicollinearity with experience in healthcare settings.

Two main multivariable mixed-effects logistic regression analyses were performed, with and without nursing staff characteristics, because staff characteristic data were only available for 55.7% of observed nurses. For the univariable model and the multivariable model without staff characteristics, two random effects, that is a random intercept by staff member and a random intercept by patient, were included to account for repeated measurements and the within-subject correlations. For the multivariable model with staff characteristics, only a random effect by patient was included, because a random intercept by staff member had no significant effect in the model.

The variable ‘double check of parenteral medication administration’ was excluded from the main analysis because only a limited portion of our data concerned parenteral medication. We performed post hoc analyses for this variable, that is a univariable and multivariable mixed-effects logistic regression analysis, which included two random intercepts (by staff member and patient) and the following confounders that were categorised identically to the main model: hospital type, day of the week, time window and patient-to-nurse ratio. For all logistic regression models, complete case analyses were performed. Odds ratios with 95% confidence intervals are presented. Data analyses were performed with R Statistics® version 4.0.2. (The R Foundation; Vienna, Austria) for the mixed-effects logistic regression analyses and with SPSS Statistics® version 25 (IBM Corporation, Armonk, New York, United States) for other analyses.

4 RESULTS

A total of 2629 medication administrations administered by 235 nursing staff members to 416 patients were observed. A total of 53 observations (2.0%), particularly oral solids (n = 46), were excluded from MAE analyses because patients declined administration for other reasons than being erroneous. Observers intervened in nine administrations. The characteristics of the included 2576 medication administrations, nursing staff members and patients are shown in Table 2.

TABLE 2. Characteristics of observed medication administrations, nursing staff members and patients

Characteristics	
Observed medication administrations, *n*	2576
Medication characteristics	
Pharmaceutical form[a], *n* (%)	
Oral solid	1800 (69.9)
Oral liquid	92 (3.6)
Infusion	273 (10.6)
Injection	241 (9.4)
Nebulising solution	72 (2.8)
Ointment	30 (1.2)
Suppository/enema	19 (0.7)
Miscellaneous	48 (1.9)
Medication class (ATC code), *n* (%)	
Alimentary tract and metabolism (A)	612 (23.8)
Blood and blood forming organs (B)	230 (8.9)
Cardiovascular system (C)	226 (8.8)
Dermatologicals (D)	28 (1.1)
Genitourinary system and sex hormones (G)	13 (0.5)
Systemic hormonal preparations (H)	93 (3.6)
Anti-infectives for systemic use (J)	286 (11.1)
Antineoplastic and immunomodulating agents (L)	64 (2.5)
Musculoskeletal system (M)	46 (1.8)
Nervous system (N)	823 (31.9)
Antiparasitic products (P)	1 (0.0)
Respiratory system (R)	117 (4.5)
Sensory organs (S)	20 (0.8)

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Characteristics	
Other (V)	17 (0.7)
Ward characteristics	
Clinical ward, *n* (%)	
University hospital	
Internal oncology	252 (9.8)
Neurology	196 (7.6)
Pulmonary medicine	375 (14.6)
Haematology	234 (9.1)
Neurosurgery	281 (10.9)
Hepatopancreatobiliary surgery	152 (5.9)
Teaching hospital	
Internal Medicine	265 (10.3)
Neurology	236 (9.2)
General surgery	221 (8.6)
Orthopaedic surgery one	190 (7.4)
Orthopaedic surgery two	174 (6.8)
Time characteristics	
Day of the week, *n* (%)	
Monday	437 (17.0)
Tuesday	386 (15.0)
Wednesday	511 (19.8)
Thursday	471 (18.3)
Friday	266 (10.3)
Saturday	231 (9.0)
Sunday	274 (10.6)
Time window, *n* (%)	
7 a.m.–10 a.m.	961 (37.3)

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Characteristics	
10 a.m.–2 p.m.	408 (15.8)
2 p.m.–6 p.m.	551 (21.4)
6 p.m.–7 a.m.	656 (25.5)
Workload characteristics	
Patient-to-nurse ratio[b], median (IQR)	6 (4–8)
Interruptions[c], *n* (%)	
Yes	262 (10.2)
Staff characteristics	
Observed staff members[d], n	235
Staff members, personal data available, *n* (%)	131 (55.7)
Male, *n* (%)	8 (6.1)
Age, median (IQR)	28 (24–47)
Nursing degree type, *n* (%)	
Nurse	91 (69.5)
Specialised nurse	28 (21.4)
Student nurse	10 (7.6)
Other	2 (1.5)
Educational level[e], *n* (%)	
Secondary vocational education	56 (43.1)
Higher professional education	62 (47.7)
University education	2 (1.5)
Other	10 (7.7)
Experience since nursing diploma, *n* (%)	
0–1 year	20 (15.3)
1–5 years	33 (25.2)
More than 5 years	67 (51.1)
Not applicable	11 (8.4)

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Characteristics	
Experience in healthcare settings[e], *n* (%)	
0–1 year	1 (0.8)
1–5 years	43 (33.1)
More than 5 years	86 (66.2)
Employment type[e], *n* (%)	
Non-temporary	117 (90.0)
Temporary	7 (5.4)
Other	6 (4.6)
Patient characteristics	
Patients, *n*	416
Male, *n* (%)	214 (51.4)
Age, median (IQR)	65 (54–74)
Prescribed medications per day, median (IQR)	13 (9–16)

- Abbreviations: ATC, Anatomical Therapeutic Chemical; IQR, interquartile range.
- [a] Missing, *n* = 1. Miscellaneous: eye drops, eye gel, inhalation aerosol or powder, intestinal gel, nasal spray, patch.
- [b] Missing, *n* = 61.
- [c] Missing, *n* = 9.
- [d] Range of observed staff members in each clinical ward: university hospital 22–38, teaching hospital 7–16.
- [e] Missing, *n* = 1.

4.1 Prevalence, type and severity of MAEs

The prevalence, type and severity of MAEs are shown in Table 3. Of the 2576 included medication administrations, one or more MAEs occurred in 352 administrations (13.7%). Of the total number of MAEs (*n* = 380), the most common MAE types were omissions (*n* = 87, 22.9%), wrong medication handling (*n* = 75, 19.7%) and wrong dose (*n* = 73, 19.2%). Of all errors, 45 (11.8%) were potentially harmful MAEs, that is errors classified in NCC MERP category E or higher. Examples of potentially harmful MAEs are shown in Appendix S2.

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TABLE 3. Prevalence, type and potential severity of medication administration errors (MAEs) in two Dutch hospitals

Included medication administrations, *n*	2576
Administrations with one or more MAEs, *n* (%)	352 (13.7)
Total MAEs, *n*	380
Administrations with 1 MAE	325
Administrations with 2 MAEs	26
Administrations with 3 MAEs	1
Type of MAEs, *n* (%)	
Omission	87 (22.9)
Wrong medication handling	75 (19.7)
Wrong dose	73 (19.2)
Wrong administration technique	
Too fast administration	53 (13.9)
Incompatibility of parenteral medication	21 (5.5)
Other	6 (1.6)
Unordered drug	29 (7.6)
Wrong dosage form	28 (7.4)
Wrong route of administration	6 (1.6)
Expired medication	1 (0.3)
Other	1 (0.3)
Potential severity of MAEs[a], *n* (%)	
Error, no harm	
C	214 (56.3)
D	121 (31.8)
Error, harm	
E	36 (9.5)
F	7 (1.8)

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G	0
H	2 (0.5)

- [a] NCC MERP classification: no error (category A); error, no harm (category B–D); error, harm (category E–H); and error, death (category I). C: an error occurred that reached the patient but did not cause patient harm; D: an error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm; E: an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention; F: an error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation; G: An error occurred that may have contributed to or resulted in permanent patient harm; H: an error occurred that required intervention necessary to sustain life.

4.2 Determinants of MAEs

The associations between the potential determinants and MAEs are shown in Table 4. Compared to oral solids, the following forms were more prone to MAEs: oral liquid, infusion, injection, ointment, suppository/enema and miscellaneous (eye drops, eye gel, inhalation aerosol or powder, intestinal gel, nasal spray, patch). MAEs were more likely to occur between 10 a.m.–2 p.m. and 6 p.m.–7 a.m. compared to 7 a.m.–10 a.m. Furthermore, MAEs were more likely in the university hospital compared to the teaching hospital or when nursing staff with higher professional education administered medication compared to nursing staff with secondary vocational education. Associations were comparable in the multivariable analysis without staff characteristics, except for the time window 6 p.m.–7 a.m. In the multivariable analyses, no significant associations were found for the determinants day of the week, patient-to-nurse ratio, interruptions and staff characteristics other than educational level.

TABLE 4. Association between determinants and the occurrence of one or more medication administration errors (MAEs) without wrong time errors

Determinants	**Mixed-effects logistic regression analysis**			
	Univariable analysis[a]		**Multivariable analysis[b]**	**Multivariable analysis[a]**
	n	**OR (95% CI)**	***n* = 1253**	***n* = 2502**
			With staff characteristics	**Without staff characteristics**
			Adjusted OR (95% CI)	**Adjusted OR (95% CI)**
Medication characteristics				
Pharmaceutical form	2569			
Oral solid		Reference	Reference	Reference

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Determinants	Mixed-effects logistic regression analysis			
	Univariable analysis[a]		Multivariable analysis[b]	Multivariable analysis[a]
	n	OR (95% CI)	*n* = 1253	*n* = 2502
			With staff characteristics	Without staff characteristics
			Adjusted OR (95% CI)	Adjusted OR (95% CI)
Oral liquid		**5.52 (3.13–9.74)**	**3.22 (1.43–7.25)**	**4.73 (2.68–8.33)**
Infusion		**3.36 (2.25–5.02)**	**1.73 (1.02–2.94)**	**2.58 (1.71–3.89)**
Injection		**3.58 (2.38–5.39)**	**3.52 (2.00–6.21)**	**3.20 (2.08–4.92)**
Nebulising solution		1.89 (0.86–4.18)	1.49 (0.55–4.01)	1.69 (0.77–3.73)
Ointment		**12.08 (4.84–30.15)**	**10.78 (2.10–55.26)**	**14.01 (5.33–36.82)**
Suppository/enema		**3.77 (1.19–11.95)**	**6.39 (1.13–36.03)**	**3.62 (1.16–11.35)**
Miscellaneous[c]		**11.96 (5.65–25.33)**	**6.17 (1.90–20.04)**	**12.13 (5.68–25.88)**
Hospital characteristics				
Hospital type	2570			
University hospital		Reference	Reference	Reference
Teaching hospital		**0.20 (0.13–0.31)**	**0.17 (0.08–0.33)** [d]	**0.22 (0.13–0.36)** [d]
Time characteristics				
Day of the week	2570			
Weekdays		Reference	Reference	Reference
Weekend		**1.52 (1.03–2.25)**	0.84 (0.53–1.32)[e]	0.98 (0.67–1.45)[e]
Time window	2570			
7 a.m.–10 a.m.		Reference	Reference	Reference

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Determinants	Mixed-effects logistic regression analysis			
	Univariable analysis[a]		Multivariable analysis[b]	Multivariable analysis[a]
	n	OR (95% CI)	*n* = 1253	*n* = 2502
			With staff characteristics	Without staff characteristics
			Adjusted OR (95% CI)	Adjusted OR (95% CI)
10 a.m.–2 p.m.		**2.13 (1.40–3.25)**	**1.91 (1.06–3.46)**	**1.77 (1.14–2.74)**
2 p.m.–6 p.m.		1.53 (0.98–2.39)	1.31 (0.69–2.48)	1.13 (0.71–1.81)
6 p.m.–7 a.m.		**2.16 (1.40–3.31)**	**1.88 (1.00–3.52)**	1.33 (0.84–2.10)
Workload characteristics				
Patient-to-nurse ratio	2512	0.98 (0.90–1.06)	1.00 (0.89–1.12)	1.02 (0.95–1.11)
Interruptions	2561			
No		Reference	Reference	Reference
Yes		0.84 (0.52–1.36)	0.71 (0.32–1.57)	1.01 (0.61–1.66)
Staff characteristics				
Nursing degree type	1321			
Nurse		Reference	Reference	
Specialised nurse		**2.15 (1.07–4.34)**	1.74 (0.90–3.35)	
Other		1.76 (0.72–4.29)	1.62 (0.82–3.18)	
Educational level	1320			
Secondary vocational education		Reference	Reference	
Higher professional education		1.14 (0.65–2.01)	**1.68 (1.03–2.74)**	

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Determinants		Mixed-effects logistic regression analysis		
		Univariable analysis[a]	Multivariable analysis[b]	Multivariable analysis[a]
	n	OR (95% CI)	*n* = 1253	*n* = 2502
			With staff characteristics	Without staff characteristics
			Adjusted OR (95% CI)	Adjusted OR (95% CI)
Other		1.56 (0.62–3.90)	1.47 (0.67–3.22)	
Experience in healthcare settings	1315			
0–1 year		1.11 (0.11–11.04)	0.91 (0.20–4.17)	
1–5 years		0.83 (0.48–1.45)	0.84 (0.52–1.35)	
More than 5 years		Reference	Reference	
Employment type	1301			
Non-temporary		Reference	Reference	
Temporary		0.72 (0.30–1.74)	1.11 (0.55–2.25)	

Note

- Odds ratios in bold have a *p* value < .05.
- Abbreviations: CI, confidence interval; OR, odds ratio.
- [a] Mixed-effects logistic regression analyses were used to account for within-subject correlations due to repeated measurements by staff member and patient.
- [b] Mixed-effects logistic regression analyses were used to account for within-subject correlations due to repeated measurements by patient.
- [c] Miscellaneous: eye drops, eye gel, inhalation aerosol or powder, intestinal gel, nasal spray, patch.
- [d] Represents the OR during weekdays.
- [e] Represents the OR for the university hospital (the teaching hospital did not include weekend administrations).

4.3 Association between double checking of parenteral medication administration and MAEs

Parenteral medication administrations accounted for 24.8% (*n* = 248) of administrations in the university hospital and for 11.4% (*n* = 126) in the teaching hospital. For parenteral medication, one or more MAEs occurred in 123 of 488 administrations (25.2%) and the double check during

administration was performed in 135 out of 433 parenteral administrations (35.8%). The determinant double check of parenteral medication was not significantly associated with the occurrence of MAEs (odds ratio 1.51, 95% confidence interval 0.64–3.55; adjusted odds ratio 0.90, 95% confidence interval 0.25–3.25, n = 404).

5 DISCUSSION

MAEs were detected in one out of every seven medication administrations in this prospective observational study conducted in two Dutch hospitals equipped with supportive electronic medication systems; one out of every eight MAEs was potentially hazardous. Incorrect dosage, improper medication management, or omission comprised 62% of all MAEs. Several factors were identified in this study as being correlated with a higher likelihood of medication errors (MAEs). These factors included the use of complex pharmaceutical forms, time windows spanning from 10 a.m. to 2 p.m. and 6 p.m. to 7 a.m., and nurses who had obtained a higher professional education. Additionally, the incidence of MAEs was higher in the university hospital than in the teaching hospital.

MAEs were detected in 352 out of 2576 administrations (13.7 percent), a rate that is consistent with the findings reported in the literature. The median MAE rate reported in a systematic review of Berdot et al. (2013) is 10.5% (IQR 7.3%–21.7%) (Berdot et al., 2013). In contrast, Keers et al. (2013) demonstrate a median error rate of 8.0% (IQR 5.1%–10.9%) (Keers et al., 2013b). Our study's distribution of MAE categories and severity scores is consistent with that of these other studies as well. It is challenging, however, to compare the results of various MAE or MAE determinant studies due to the substantial clinical and methodological heterogeneity between research efforts (e.g., variations in ward types, administration procedures, electronic medication systems, data collection methods, and studied error types).

The likelihood of MAEs was found to be significantly higher with nearly all pharmaceutical forms in comparison to oral solids. The majority of these formulations necessitate supplementary procedures during administration, such as volume calculations, infusion pump adjustment, or suspension shaking. With each additional stage, the potential for error increases. A heightened likelihood of errors has been extensively linked to parenteral medication in particular (Keers et al., 2013b; Nguyen et al., 2015). An intriguing discovery revealed that numerous injections, including furosemide, granisetron, and dexamethasone, were administered significantly earlier than the suggested rate, frequently within a few seconds, despite the fact that the maximum administration rates were explicitly specified in the computer-accessible local electronic protocols. Additional research has examined this matter (Ong & Subasyini, 2013; Sutherland et al., 2020; Taxis & Barber, 2003; Westbrook et al., 2020). It appears that nurses might be unaware of the optimal administration rate or mistakenly believe that any deviation from it lacks clinical significance (Keers et al., 2013a; Schroers et al., 2020). Certain pharmaceutical formulations, including aerosols for inhalation and ointments, appeared to be more prone to omission. One possible explanation is that these medications are not typically regarded as critical necessities while hospitalised. Support from pharmacy staff to perform medication handling tasks using standard protocols, increased use of ready-to-administer medication (Kuitunen et al., 2021b), smart infusion pumps (Kuitunen et al., 2021b), and educational programmes for nurses, such as simulation-based training, are examples of interventions that target relatively complex, error-prone pharmaceutical

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forms (Kuitunen et al., 2021b). The initial two approaches possess the potential to diminish the occurrence of errors associated with medication handling, incorrect dosage, incorrect dosage form, and rapid administration (specifically, when providing infusions as opposed to concentrated solutions). When utilised appropriately, intelligent infusion pumps equipped with a drug library have been demonstrated to decrease the occurrence of incorrect infusion rates and doses (Kuitunen et al., 2021b).

In contrast to the university hospital, the teaching hospital exhibited a reduced likelihood of MAEs. There are several potential contributing factors, including local workplace elements such as technology, culture, medication supply and dispensing, and local training programmes. However, it is worth noting that the teaching hospital's comparatively simpler patient and medication systems may also contribute to this observation (Keers et al., 2013a). This explanation is supported by the higher percentages of included parenteral medication (11.3% vs. 25.2%) and anti-infective medication (5.8% vs. 15.0%) at the university hospital. An alternative rationale is that the teaching hospital had previously instituted barcode verification for parenteral medication, a practice that has demonstrated efficacy in averting certain categories of errors (Hutton et al., 2021). Additional distinctions between hospitals encompass the medication management system types (HiX® versus Epic®) and the staff responsible for loading medication carts (pharmacy personnel in the teaching hospital as opposed to nursing staff in the university hospital). May 2018 saw the university hospital's relocation to an entirely new facility, which required the nursing staff to learn numerous new protocols. Furthermore, despite the implementation of rigorous review protocols to mitigate discrepancies in assessor evaluations, it is impossible to rule out divergences between the reviewing teams of the two institutions.

Compared to the early morning, MAEs were more likely to occur between 6 p.m. and 7 a.m. and between 10 a.m. and 2 p.m. This may be attributable to variables including nursing staff fatigue or vigour, an irregular distribution of tasks throughout the day, or workload. It has been reported that night shift administration is particularly prone to error (Feleke et al., 2015; Wondmieneh et al., 2020), as the absence of circadian adaptation to night work can result in decreased alertness and performance (Ganesan et al., 2019). A critical examination of the daily routines in regards to the distribution of labour and standard medication administration rounds is warranted in light of these time-related factors. This may provide information regarding the optimal periods for administering standard medications that are specific to a given clinical ward. Assistance provided by pharmacy personnel, such as dispensing medications in patient medication cabinets or handling medications themselves, could potentially reduce the time and effort required by nursing staff. These aspects have been found to be significantly correlated with medication administration errors (Schroers et al., 2020; Kuitunen et al., 2021a; Parry et al., 2015). Overall, there may be further advantages to involving nurses in the process of customising interventions to suit their own practice (Alomari et al., 2020).

Unexpectedly, a greater professional education was associated significantly with a greater probability of MAE. The potential correlation between this discovery and an individual's level of assurance or propensity for supposition (Schroers et al., 2020) is a subject that warrants further investigation. Data on nursing staff characteristics were unavailable in approximately 45% of observations; therefore, this finding should be interpreted with caution. Earlier studies on

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determinants related to nursing staff characteristics have shown conflicting results (Feleke et al., 2015; Nguyen et al., 2015; Prot et al., 2005; Rodriguez-Gonzalez et al., 2012).

In contrast to several previous studies, no significant associations were found for the determinants day of the week (Harkanen et al., 2015, Nguyen et al., 2015, van den Bemt et al., 2002), patient-to-nurse ratio (Berdot et al., 2012; Feleke et al., 2015) and interruptions (Blignaut et al., 2017; Feleke et al., 2015; Harkanen et al., 2015; Westbrook et al., 2010; Wondmieneh et al., 2020). However, a study conducted in a similar environment as ours, Berdot et al. (2012), also failed to identify significant correlations between interruptions and day of the week. A significant number of MAEs identified in our study were not deemed accidental errors, but rather recurrent deviations in which identical mistakes were made repeatedly. Notable examples include administering intravenous medications too quickly or combining all oral medications for feeding tube administration. In this context, the absence of a correlation between interruptions and MAEs may be explained by this result. Our study is not the first to demonstrate that there is no correlation between the nurse-to-patient ratio and MAEs (Rodriguez-Gonzalez et al., 2012). While the patient-to-nurse ratio is frequently employed as an indicator of workload, it fails to consider various pertinent workload-related elements, including the severity of the patient's condition and non-patient-related responsibilities (Carayon & Gurses, 2008; Griffiths et al., 2020).

The discovery that multiple MAEs transpired repeatedly underscores the necessity for supplementary and customised systemic safeguards, particularly technological barriers, in order to avert MAEs. For instance, intelligent infusion pumps equipped with hard limits that are immutable will prevent the administration of intravenous medication at an excessively rapid rate. Additionally, barcode-assisted medication administration with hard stops will prevent errors involving the wrong drug, dosage, and dosage form (Hutton et al., 2021). This is in the event that the incorrect medication or patient is scanned. It is crucial to avoid the use of workarounds, as they have the potential to undermine the advantageous outcomes of scanning (Mulac et al., 2021; van der Veen et al., 2018). Further measures to mitigate the associated risks include enhancing the knowledge of nurses (e.g., incorporating supplementary medication education into nursing undergraduate and postgraduate curricula) and improving the accessibility of essential information (e.g., through direct inclusion in the eMAR). This study was performed before the scheduled comprehensive operations to improve medication safety in both hospitals. Thus after conducting this study, both hospitals optimised their medication process by implementing several interventions, including automated unit-dose dispensing and barcode-assisted medication administration (Jessurun et al., 2021).

5.1 Strengths and limitations

A strength of this study is that, to our knowledge, this is the first study on the determinants of MAEs in a setting with an EMR, a CPOE and an eMAR system in place. Also, we investigated medication administrations to inpatients in 11 clinical wards in two hospitals and examined many types of medication administrations performed by more than 200 nursing staff members, supporting the generalisability of the results of this study to similar hospitals. Additionally, we used a robust method to assess MAEs and analyse determinants of MAEs.

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This study has several limitations. First, observer and reviewer bias may have occurred, even though the disguised observation method is the gold standard to detect MAEs (Allan & Barker, 1990; Dean & Barber, 2001). Several measures have been taken to limit observer and reviewer bias, such as comprehensive training programmes for observers and protocols for reviewers. Second, timing errors were excluded because these errors occur frequently (Berdot et al., 2013; Keers et al., 2013b), while being considered not clinically relevant in many cases. This could be debated because these errors may be clinically relevant for time-sensitive medication and important from a system-failure perspective (Allan & Barker, 1990). However, the possibility of an exceptionally high error rate may hamper determinant analysis. Third, we measured potential harm instead of the actual harm to patients. Fourth, fewer determinants were tested than initially planned to prevent overfitting of the multivariable mixed-effects model. For instance, hospital type was chosen instead of clinical ward type in order to decrease the number of variables to be tested and because MAE rates were comparable for the clinical wards in the same hospital. Last, we may have addressed several determinants insufficiently, such as personal factors (e.g. stress levels and job satisfaction), patient factors (e.g. clinical condition) and environmental factors (e.g. noisy environment) (Carayon & Gurses, 2008; Keers et al., 2013a, 2015; Kuitunen et al., 2021a; Parry et al., 2015; Schroers et al., 2020).

5.2 Further research

Future studies should focus on the determinants insufficiently addressed in our study and should include measurement of clinically relevant outcomes.

6 CONCLUSION

In the two hospitals with supportive electronic medication systems (i.e. EMR, CPOE and eMAR), MAEs occurred in 352 of 2576 administrations (13.7%), with one out of eight having the potential to lead to patient harm. The determinants identified in this study indicate that the complexity of pharmaceutical forms, working conditions and complex patient populations are contributing factors. Strategies to reduce the occurrence of MAEs and therefore to optimise patient care should target the identified determinants and focus on systemic defences to prevent structural errors.

7 RELEVANCE TO CLINICAL PRACTICE

Medication errors are major contributors of preventable patient harm globally. In this study, we showed that MAEs, including harmful errors, are prevalent in modern care, even with several supportive electronic medication systems in place. Additional preventive strategies are needed to tackle this issue. The determinants identified in our study can be used to develop targeted strategies and interventions to improve patient safety across similar hospital settings.

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