

Medication-related adverse events during hospitalization: a retrospective patient record review study in The Netherlands

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ABSTRACT

Purpose Medication-related adverse events (MRAEs) are an important priority for patient safety. Results from Dutch AE studies showed that—despite various improvement initiatives—the incidence of preventable MRAEs did not decline. The aim of this study is to describe the characteristics of MRAEs during hospitalizations using national patient data from records of patients admitted to Dutch hospitals in 2008 and 2011/2012.

Methods Trained nurses and physicians reviewed the randomly selected records of 8071 patients admitted to one of 20 hospitals in 2008 or 2011/2012 during a two-stage review process. Patient and admission characteristics were collected. After identification of a MRAE, physicians determined their potential preventability, drug type, related prescribing factors, and potential consequences.

Results The physicians identified 928 adverse events (AEs) in 857 admissions, of which 218 (15.2%) were medication-related. They judged 55 (18.4%) of these as preventable. Preventability of MRAEs was high in anticoagulant treatment (42.5%). Haematoma (39.0%) and intra-cerebral haemorrhage (25.5%) were common types of anticoagulant-related AEs. Anticoagulant-related AEs were often related to dosage factors (46.9%) and often resulted in an intervention (80.2%), of which 40.2% was judged as preventable.

Conclusions This study provided detailed information on MRAEs during hospital admissions in The Netherlands. A substantial proportion of AEs was medication-related (15.2%), of which 18.4% was judged to be preventable. As preventability in MRAEs was especially high in anticoagulant treatment (42.5%), those medications are a threat to patient safety. Future research and new safety programs should focus on prevention of AEs related to this medication group. Copyright © 2016 John Wiley & Sons, Ltd.

KEY WORDS—adverse events; anticoagulant treatment; hospitals; medication errors; patient safety; retrospective studies; pharmacoepidemiology

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INTRODUCTION

Patient safety continues to be a major challenge and a high priority in hospitals worldwide. Healthcare-related adverse events (AEs) are common and can be defined as unintended injuries that result in temporary or permanent disability, death, or prolonged hospitalization, caused by healthcare management rather than patients' underlying disease.^{1–4}

Medication-related adverse events (MRAEs) occur as a consequence of medication errors or adverse drug reactions and are one of the most common types of healthcare-related AEs.^{4–6} In The Netherlands, the first

national AE study took place in 2004, in which the extent and nature of AEs and their preventability were evaluated in 21 Dutch hospitals.⁷ The results from this study indicated that MRAEs comprise around 15% of all AEs, with almost 30% of them being preventable.^{8–10} In addition, MRAEs were associated with considerable longer hospital stays and higher healthcare costs,⁹ imposing a high burden on patients, caregivers, and the healthcare system. These results were in line with findings from other AE studies^{11–14} and also confirmed in systematic reviews and meta-analyses.^{5,6}

Over the last years, the prevention of AEs has become an important priority for patient safety in The Netherlands. In 2008, the national program 'Prevent Harm, Work Safely' was launched. The overall goal of this safety program was to reduce the number of preventable AEs in Dutch hospitals by 50% through

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the implementation of a Safety Management System in all hospitals and through improvement modules on 10 clinical themes, including medication processes such as medication reconciliation and high-risk medication.¹⁵

To keep track of changes in patient safety on a national level, a second and third measurement of the national AE study was conducted in 2008 and 2011/2012. In recent publications, general trends in AEs over time and main categories of preventable AEs have been assessed.^{16,17} These studies showed that—despite various safety improvement initiatives such as the safety program—the incidence of preventable MRAEs did not decline over the years. Hence, the aim of the current study is to describe the characteristics of (potential preventable) MRAEs during hospitalizations, using national patient data from records of patients admitted to Dutch hospitals in 2008 and 2011/2012. This information could contribute to the design of future medication safety initiatives.

METHODS

Study design and population

We used the data from two of our previous AE studies,^{16,17} in which patient records of hospital admissions in 2008 and 2011/2012 were assessed. Review of these admissions records took place in 2009/2010 and 2012/2013, respectively. In both studies, the same 20 hospitals of the in total 93 Dutch hospitals were included. The hospital samples were both stratified by hospital type: university, tertiary teaching, and general hospitals. Within these strata, hospitals were randomly selected, and a proper representation of urban and rural settings in the sample was verified. Per hospital, for each measurement year, about 200 patient admissions were randomly selected: half of these consisted of admissions of patients discharged alive from the hospital after a stay of at least 24 h. The other half consisted of inpatient deaths regardless of the length of hospital stay. In both studies, only one admission per patient was included. As was also common in other AE studies, records from patients admitted to the psychiatry or obstetrics department, and records of children younger than 1 year of age were excluded. Detailed information on the design of the studies was published previously.^{7,17} Both study protocols were approved a priori by the medical ethics committee of the VU University Medical Center, Amsterdam, The Netherlands.

Patient record review

Trained external nurses and external physicians reviewed the nursing and medical records of included

admissions. The method of determining AEs, which was comparable to those of other international studies^{18,19} and based on the Canadian AE study,¹ comprised two phases: first, a nurse screened the records by using triggers indicating potential AEs. In the second phase, a physician further reviewed admissions positive for at least one trigger. These physicians belonged to the specialty surgery, internal medicine, or neurology, and AE reviews were assigned based on their specialty. If needed, they could consult with specialties other than their own. Patient records of the index-hospital admission were reviewed, as were the patient records of patient admissions a year before and after the index-admission. Presence of AEs was determined by the physicians based on a standardized procedure.

An AE was defined by three criteria:

- (1) An unintended physical or mental injury;
- (2) The injury resulted in prolongation of hospital stay, temporary or permanent disability or death;
- (3) The injury was caused by healthcare management rather than the patient's underlying disease.

To determine whether the injury was caused by healthcare management or the disease process, a six-point Likert scale was used:

- (1) (Virtually) no evidence of management causation;
- (2) Slight to modest evidence of management causation;
- (3) Management causation not likely (<50/50, but borderline);
- (4) Management causation more likely (>50/50, but borderline);
- (5) Moderate to strong evidence of management causation;
- (6) (Virtually) certain evidence of management causation.

The cause of an AE was counted as caused by healthcare if the score was 4–6.

If an AE was identified, questions about the clinical process during which the AE occurred were asked. Physicians were able to choose from the following clinical processes: diagnostics, surgery, drug, medical procedure, other clinical management, discharge, and others. All AEs in which a drug was chosen to be the main clinical process during which the AE had occurred were marked as MRAEs.

A MRAE was considered to be preventable when the care given fell below the current level of expected performance of practitioners or systems. In accordance with our previous studies,^{7,9,16} preventability was assessed on the following six-point Likert scale:

- (1) Almost no evidence of preventability;
- (2) Slight to modest evidence of preventability;
- (3) Modest preventability (<50/50, but borderline);
- (4) Modest to strong evidence of preventability (>50/50, but borderline);
- (5) Strong evidence of preventability;
- (6) Almost certain evidence of preventability.

A score of 4–6 indicated that the reviewer regarded the MRAE as having a greater than 50% chance of being potentially preventable.

To add more structure to the implicit review process, the causation and preventability scores were each preceded by 13 questions to facilitate the final reviewers' judgment. In addition, physicians were trained in assessing the causation and preventability prior to reviewing patient admissions, and frequent reflection meetings were organized to uphold a high quality of the review process.

After identification of a MRAE, the physician reviewers determined among others drug type, related prescribing factors, and potential consequences associated with the MRAE.¹ As for the timing of MRAEs, MRAEs that occurred during the patient's index-hospital admission and were detected during either the index-admission ($n=147$) or subsequent admissions over the following 12-month period ($n=13$) were counted. Also counted were MRAEs related to patient admissions in the same hospital within the 12 months preceding the index-admission but which were not detected until the index-admission ($n=58$). Exceptions were made for MRAEs related to hair loss as a result of cytostatic treatment and neutropenia without fever, as these were common side effects of cancer chemotherapy, and therefore, not counted as AEs in this study.

Statistical methods

Weighting procedure. In accordance with our previous studies,^{8,9,16} during analyses, all proportions were corrected for the oversampling of deceased patients and university hospitals. In our sample, 50% of the patients were inpatient deaths, whereas in reality, this is 3%. In the results, we weighted our 50% back to the actual 3%. We followed the same procedure for the distribution of hospital types: In our sample, 20% of the hospitals were university hospitals, whereas in reality, this is 10%. Therefore, in the results, we weighted our 20% back to the actual 10%. After weighting for this sample frame, the total study sample—that is, both discharged and deceased patients—was representative of the total Dutch population of

hospitalized patients. Detailed information on the weighting procedure was published previously.⁷ As a consequence of the weighting process, proportions were not directly comparable to the accompanying crude numbers.

Conducted analyses. Summary and descriptive statistics for patient and admission characteristics were calculated for all reviewed patients and for all patients who were assessed to have experienced an MRAE. SPSS complex samples were used to calculate weighted rates of patients who had experienced at least one MRAE during the admission and their preventability (referred to as 'MRAEs—admission level' in the accompanying tables). As it was possible for patients to experience more than one MRAE during a hospital admission, we also assessed the total number of MRAEs and preventable MRAEs (referred to as 'MRAEs—adverse event level' in the accompanying tables). We further analysed medication type. For the drug type most frequently related to a preventable MRAE, we further analysed possible related prescribing factors as well as consequences. All statistical analyses were performed in SPSS 20.0 and STATA 13.

RESULTS

In total, records of 8071 patient admissions were included in the study, of which 4023 of 2008 and 4048 of 2011/2012. Patient and hospital characteristics of the study sample are described in Table 1.

Medication-related adverse events

The hospital admissions were assessed for the presence of AEs and MRAEs and their preventability. In the second stage, the physicians identified 928 AEs in 857 admissions, of which 218 (15.2%) in 204 admissions were medication-related. They judged 55 (18.4%) of these MRAEs in 53 admissions as preventable. MRAEs often occurred in patients aged 66–79 years. The preventability of MRAEs was high in patients who died in-hospital, urgently admitted patients, patients admitted to a urology or neurology department, and patients admitted to tertiary teaching hospitals (Table 2).

Table 3 shows that the majority of MRAEs were adverse drug reactions related to cancer chemotherapy ($n=58$, 22.0%), anticoagulant treatment ($n=43$, 17.1%), and antibiotics ($n=22$, 13.6%). Preventability in MRAEs was especially high in anticoagulant treatment ($n=17$, 42.5%) and insulin/oral diabetics ($n=7$,

Table 1. Patient and hospital characteristics of the study sample

	Total population		
	<i>n</i>	Unweighted %	Weighted %*
Inpatient admissions	8071		
<i>Hospital admission year</i>			
2008	4023	49.9	49.8
2011/2012	4048	50.1	50.2
Age in years, mean (median/SD)			60.2 (64.0/20.8)
<i>Age categories</i>			
1–18	286	3.5	5.8
19–40	533	6.6	10.8
41–65	2365	29.3	37.6
66–79	2665	33.0	29.0
80 and older	2222	27.5	16.8
<i>Discharge status</i>			
Alive	4039	50.0	95.3
Inpatient death	4032	50.0	4.7
<i>Gender</i>			
Male	4155	51.5	50.0
Female	3916	48.5	50.0
<i>Patient admissions</i>			
University hospital	1593	19.7	13.9
Tertiary teaching	2843	35.2	44.1
General	3635	45.0	41.9
Length of hospital stay, days (median/SD)			6.5 (4.0/12.1)
<i>Urgent admission</i>			
No	2496	30.9	45.6
Yes	5575	69.1	54.4
<i>Department to which patient was admitted</i>			
Cardiology	814	10.1	11.1
Surgery	1410	17.5	21.7
Geriatrics	163	2.0	1.1
Coronary Care Unit	286	3.5	3.3
Intensive Care	543	6.7	1.9
Paediatrics	172	21.3	3.4
Internal medicine	1720	2.1	16.2
Orthopaedics	510	2.2	11.1
Neurology	695	9.9	7.2
Pulmonology	802	8.6	6.5
Ear, nose, and throat	178	6.3	3.7
Urology	251	3.1	5.0*
Other	527	6.5	7.8*

*Weighted for overrepresentation of deceased patients and hospital type.

34.8%). MRAEs related to chemotherapy were seldom considered preventable: 0.7% ($n=3$) of all chemotherapy-related MRAEs.

Anticoagulant-related adverse events

As MRAEs related to anticoagulant treatment were common and often preventable, we further analysed this type of medication. Although preventability in insulin/oral diabetic-related MRAEs was also found to be high, they only comprised 5.0% ($n=12$) of total MRAEs (Table 3). Therefore, because of power constraints, we did not perform further analyses on this medication type.

Most anticoagulant-related AEs were related to coumarins ($n=24$, 55.8%) and heparins ($n=13$,

Table 2. Patient and hospital characteristics of medication-related adverse events

	MRAEs	Preventable MRAEs
	($n=204$)*	($n=53$)*
	<i>n</i> (column %, weighted) [†]	<i>n</i> (row %, weighted) ^{‡‡}
<i>Age categories</i>		
1–18	5 (4.2)	0 (0.0)
19–40	9 (4.0)	1 (22.6)
41–65	47 (25.1)	7 (17.4)
66–79	88 (41.3)	24 (17.9)
80 and older	55 (25.5)	21 (22.7)
<i>Discharge status</i>		
Alive	67 (90.9)	11 (17.2)
Inpatient death	137 (9.1)	42 (30.7)
<i>Gender</i>		
Male	104 (46.8)	26 (18.1)
Female	100 (53.2)	27 (18.7)
<i>Patient admissions</i>		
University hospital	41 (14.5)	8 (14.5)
Tertiary teaching	57 (36.9)	13 (21.2)
General	106 (48.7)	32 (17.5)
<i>Urgent admission</i>		
No	44 (26.1)	8 (14.0)
Yes	160 (73.9)	45 (20.0)
<i>Department to which patient was admitted</i>		
Cardiology	19 (8.5)	9 (7.2)
Surgery	11 (2.2)	3 (9.0)
Geriatrics	5 (1.4)	2 (9.6)
Coronary Care Unit	5 (3.1)	3 (7.6)
Intensive Care	15 (5.8)	4 (29.2)
Internal medicine	75 (33.4)	13(6.9)
Paediatrics	2 (2.0)	–
Ear, nose, and throat	2 (1.1)	–
Pulmonology	28 (15.1)	8 (25.9)
Neurology	15 (6.9)	4 (34.1)
Orthopaedics	8 (5.5)	2 (29.0)
Urology	6 (7.1)	3 (50.1)
Other	13 (7.8)	2 (23.1)

MRAE, medication-related adverse event.

*MRAEs—admission level.

[†]Weighted for overrepresentation of deceased patients and hospital type.

^{‡‡}No preventability was shown if numbers of MRAEs were smaller than 5.

30.2%) (results not shown in table). Although numbers were small, most of the anticoagulant-related AEs were among patients of 66 years or older and in patients urgently admitted. The preventability of anticoagulant-related AEs was high in urgently admitted patients and patients admitted to tertiary teaching hospitals (Table 4).

Haematoma ($n=5$, 39.0%), intra-cerebral haemorrhage ($n=8$, 25.5%), and gastrointestinal bleeding ($n=9$, 12.6%) were common types of anticoagulant-related AEs. Anticoagulant-related AEs were often related to dosage factors ($n=14$, 46.9%), of which 66.2% ($n=7$) was judged as preventable. Although therapeutic factors were less often related to anticoagulant-related AEs, their preventability was high ($n=4$, 90.6%). Anticoagulant-related AEs often resulted in an intervention ($n=26$, 80.2%), of which

Table 3. Drug type of medication-related adverse events

	MRAEs (<i>n</i> = 218)*	Preventable MRAEs (<i>n</i> = 55)*
	<i>n</i> (column %, weighted) [†]	<i>n</i> (row %, weighted) ^{†‡}
Antiasthmatic	1 (0.0)	–
Antibiotic	22 (13.6)	3 (11.2)
Anticoagulant	43 (17.1)	17 (42.5)
Antidepressant	1 (1.8)	–
Antiepileptic	2 (1.1)	–
Antihypertensive	4 (2.9)	–
Antiplatelet	7 (6.3)	1 (1.6)
Antipsychotic	2 (0.1)	–
Chemotherapy	58 (22.0)	3 (0.7)
Cardiovascular	11 (6.9)	5 (4.4)
Diuretic	5 (3.1)	0 (0.0)
Insulin/Oral diabetic	12 (5.0)	7 (34.8)
Potassium	1 (0.0)	–
Morphine/Opioid	9 (3.0)	2 (5.3)
NSAID	1 (0.0)	–
Sedative	9 (1.4)	4 (15.5)
Other	30 (15.5)	7 (27.8)
Total	218 (100)	55 (18.4)

MRAE, medication-related adverse event; NSAID, non-steroidal anti-inflammatory drug.

*MRAEs—adverse event level.

[†]Weighted for overrepresentation of deceased patients and hospital type.

[‡]No preventability was shown if numbers of MRAEs were smaller than 5.

40.2% (*n* = 10) was judged as preventable. In 18.9% (*n* = 2), anticoagulant-related AEs resulted in readmission (Table 5).

DISCUSSION

In the current study, a substantial proportion of all healthcare-related AEs were medication-related (*n* = 218, 15.2%). Of all 218 identified MRAEs, 55 (18.4%) were deemed to be preventable. Preventability of MRAEs was especially high in anticoagulant treatment (*n* = 17, 42.5%). Haematoma (*n* = 5, 39.0%) and intra-cerebral haemorrhage (*n* = 8, 25.5%) were common types of anticoagulant-related AEs. Anticoagulant-related AEs were often related to dosage factors (*n* = 14, 46.9%), and they often resulted in an intervention (*n* = 26, 80.2%), of which 40.2% (*n* = 10) was judged as preventable.

The results of this study corroborate the findings of previous studies, demonstrating that MRAEs were responsible for 12–37% of all AEs,^{2,4,9,11–14,17} which was also confirmed in systematic reviews and meta-analyses.^{5,6,20–22} In these earlier studies, 30–50% of MRAEs was judged to be preventable, whereas in our study, this number was considerably lower (18.4%). The finding that anticoagulant treatment accounted for a substantial proportion of preventable MRAEs was also in line with previous

Table 4. Patient and hospital characteristics of anticoagulant-related adverse events

	Anticoagulant-related AE (<i>n</i> = 41)*	Preventable anticoagulant-related AE (<i>n</i> = 17)*
	<i>n</i> (column %, weighted) [†]	<i>n</i> (row %, weighted) ^{†‡}
<i>Age categories</i>		
1–18	0 (0.0)	–
19–40	1 (0.3)	–
41–65	5 (14.0)	2 (60.8)
66–79	17 (33.0)	7 (39.0)
80 and older	18 (52.7)	8 (40.6)
<i>Gender</i>		
Male	22 (38.6)	10 (57.0)
Female	19 (61.4)	7 (33.8)
<i>Discharge status</i>		
Alive	11 (89.3)	4 (42.6)
Inpatient death	30 (10.7)	13 (44.1)
<i>Urgent admission</i>		
No	10 (15.9)	3 (6.5)
Yes	31 (84.1)	14 (49.6)
<i>Patient admissions</i>		
University hospital	6 (10.7)	0 (0.0)
Tertiary teaching	9 (51.2)	4 (59.7)
General	26 (38.2)	13 (32.1)
<i>Department to which patient was admitted</i>		
Cardiology	6 (2.1)	4 (65.8)
Surgery	4 (1.4)	–
Geriatrics	1 (0.4)	–
Coronary Care Unit	3 (16.1)	–
Intensive Care	1 (0.3)	–
Internal medicine	13 (25.9)	5 (37.0)
Paediatrics	0 (0.0)	–
Ear, nose, and throat	1 (0.3)	–
Pulmonology	3 (19.6)	–
Neurology	3 (1.2)	–
Orthopaedics	2 (0.7)	–
Urology	4 (32.1)	–
Other	0 (0.0)	–

AE, adverse event.

*MRAEs—admission level.

[†]Weighted for overrepresentation of deceased patients and hospital type.

[‡]No preventability was shown if numbers of MRAEs were smaller than 5.

research.^{11,13,23–25} As compared with the results of the first measurement of the national AE study,⁹ no visible differences were found in the occurrence of anticoagulant-related MRAEs (18.0% in 2004 vs. 17.1% in this study, respectively), but their preventability slightly decreased from 54.0% in 2004 to 42.5% in our study.

Over the past decades, several interventions have been developed to reduce MRAEs and improve medication safety. In The Netherlands, the national program 'Prevent Harm, Work Safely' was launched in 2008 and aimed to reduce the number of preventable AEs in Dutch hospitals by 50%. The program included two improvement modules on medication processes: reducing events that involve high-risk medication and reducing medication errors on admission and discharge.¹⁵ Baines et al. (2015)¹⁶ concluded that during the safety

Table 5. Factors and consequences of anticoagulant-related adverse events

	Anticoagulant-related AEs (<i>n</i> = 43)*	Preventable anticoagulant-related AEs (<i>n</i> = 17)*
	<i>n</i> (column%, weighted) [†]	<i>n</i> (row %, weighted) ^{‡‡}
<i>Prescribing factors</i>		
Administrative/Procedure	0 (0.0)	–
Dosage	14 (46.9)	7 (66.3)
Therapeutic	6 (10.1)	4 (90.6)
Delivery	0 (0.0)	–
Administering	0 (0.0)	–
Other	22 (20.0)	11 (20.0)
<i>Type of adverse event</i>		
Shock	1 (0.4)	–
Heart failure	1 (0.4)	–
Pulmonary embolism	2 (0.7)	–
Renal insufficiency	1 (6.8)	–
Other renal failure	1 (0.4)	–
Intra-cerebral haemorrhage	8 (25.5)	3 (38.6)
Thromboembolism	1 (0.4)	–
Haematoma	5 (39.0)	1 (31.0)
Gastro-intestinal bleeding	9 (12.6)	4 (14.2)
Cerebrovascular accident	7 (3.0)	0 (0.0)
Catheter-related blood infection	1 (0.3)	–
Pulmonary infection	1 (0.4)	–
Postsurgical haemorrhage	1 (0.4)	–
Other	1 (9.9)	–
<i>Consequences[§]</i>		
Intervention	26 (80.2)	10 (40.3)
Impairment at moment of discharge	1 (4.9)	–
Extended length of stay	4 (5.9)	–
Readmission	2 (18.9)	–
Death	18 (12.1)	4 (11.3)
Outpatient visit	1 (10.8)	–
Other	2 (11.1)	–

AE, adverse event.

*MRAEs—adverse event level.

[†]Weighted for overrepresentation of deceased patients and hospital type.

[‡]No preventability was shown if numbers of MRAEs were smaller than 5.

[§]More than one answer was possible. Therefore, the total percentage sums up to more than 100.

program, no visible improvements in medication safety were established. MRAEs are therefore still a threat to patient safety, and our results indicate that especially on certain high-risk medications, such as anticoagulant treatment, many preventable MRAEs still occur.

Other intervention methods and tools to prevent MRAEs have also been proposed. The most commonly implemented interventions are ‘computerized physician order entry systems (CPOEs)’, a form of patient management software allowing healthcare providers to electronically enter patient treatment instructions.^{26,27} While CPOE systems are well implemented in most hospitals, a considerable amount of MRAEs was still reported, and CPOE systems introduced new types MRAE as well.^{28,29} Clinical pharmacy interventions have also been investigated, with a

hospital pharmacist interacting and advising the healthcare team.^{30,31} Although these interventions contributed to the reduction of (preventable) MRAEs, most of them are costly and time consuming and difficult to provide continuously.³¹ Recent research showed that evidence-based drug rules seem promising in preventing MRAEs, but their clinical efficacy is yet to be tested.³²

Although in the current study, anticoagulant-related AEs were the most common types of preventable MRAEs, none of the aforementioned interventions specifically targeted this medication group. Anticoagulant care is considered complex, and potential risks of bleeding and thrombosis should always be taken into account. In addition, various healthcare professionals are involved in the treatment of patients, including medical specialists, pharmacists, general practitioners, dentists, and the anticoagulation services. These different healthcare providers need to collectively coordinate anticoagulant care. It was previously argued that suboptimal communication and coordination within this ‘chain’ of healthcare providers is common and associated with adverse patient outcomes.³³ In The Netherlands, several guidelines have been developed addressing these integrated care problems, but one of our recent studies showed that adherence to these guidelines is still trivial.³⁴ Future research is needed to further examine the complex nature of MRAEs, hereby focusing on hospital-related factors as well as suboptimal integrated care. This knowledge could contribute to the design of future medication safety initiatives, which should especially target the areas with the highest risk of preventable MRAEs, such as anticoagulant treatment.

Strengths and limitations

One of the strengths of the current study is that we reviewed 8071 patient records over two periods in time based on an international method for standardized assessment method of patient admissions. Although assessing patient records on AEs is a difficult process, retrospective chart studies currently offer the best method available to assess their incidence and are considered as the ‘golden standard’.³⁵ This more implicit method also allows us to focus on a broad range of MRAEs instead of an explicit range of MRAEs and gives a good insight in the general state of medication safety in hospitals.

Retrospective review studies also have disadvantages. The incidence of preventable MRAEs may be underestimated because not all information is available or written down in the patient records.³⁶ However, due to hindsight bias the incidence of MRAEs may have been overestimated.³⁷ As knowing the outcome of an

admission may influence the judgement of the causality and preventability of MRAEs. We found that anticoagulants still account for a large proportion of the total amount of preventable MRAEs. Unfortunately, we did not register the use of anticoagulants and other medications for *all* included patients. Therefore, a numerator was not available, and the incidence of anticoagulant-related AEs could not be calculated.

CONCLUSION

The current study provided detailed information on MRAEs during hospital admissions in The Netherlands. A substantial proportion of AEs was medication-related ($n=218$, 15.2%), of which 18.4% ($n=55$) was judged to be preventable. As preventability in MRAEs was especially high in anticoagulant treatment ($n=17$, 42.5%), those medications are a threat to patient safety. It is therefore recommended that future research and new safety programs focus on the prevention of AEs related to this high-risk medication group.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Key Points:

- Medication-related adverse events (MRAEs) are common types of healthcare-related adverse events (AEs) and an important priority for patient safety.
- Recent AE studies indicated that their incidence did not decline over the past years despite various improvement initiatives.
- Characterization of MRAEs in hospitals is lacking.
- The results of this study show that preventability in MRAEs is especially high in anticoagulant treatment.
- Anticoagulant-related AEs often result in an intervention, of which a substantial proportion is preventable.
- Future research and new safety programs should focus on the prevention of anticoagulant-related AEs, as they are a threat to patient safety.

COMPETING INTERESTS

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.

pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work.

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