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Anticoagulant medication errors in hospitals and primary care: a cross-sectional study

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Abstract

Objective: To assess the proportion of all medication error reports in hospitals and primary care that involved an anticoagulant. Secondary objectives were the anticoagulant involved, phase of the medication process in which the error occurred, causes and consequences of 1000 anticoagulant medication errors. Additional secondary objectives were the total number of anticoagulant medication error reports per month, divided by the total number of medication error reports per month and the proportion of causes of 1000 anticoagulant medication errors (comparing the pre- and post-guideline phase).
Design: A cross-sectional study.
Setting: Medication errors reported to the Central Medication incidents Registration reporting system.
Participants: Between December 2012 and May 2015, 42 962 medication errors were reported to the CMR.
Intervention: N/A.
Main outcome measure: Proportion of all medication error reports that involved an anticoagulant. Phase of the medication process in which the error occurred, causes and consequences of 1000 anticoagulant medication errors. The total number of anticoagulant medication error reports per month, divided by the total number of medication error reports per month (comparing the pre- and post-guideline phase) and the total number of causes of 1000 anticoagulant medication errors before and after introduction of the LSKA 2.0 guideline.
Results: Anticoagulants were involved in 8.3% of the medication error reports. A random selection of 1000 anticoagulant medication error reports revealed that low-molecular weight heparins were most often involved in the error reports (56.2%). Most reports concerned the prescribing phase of the medication process (37.1%) and human factors were the leading cause of medication errors mentioned in the reports (53.4%). Publication of the national guideline on integrated antithrombotic care had no effect on the proportion of anticoagulant medication error reports. Human factors were the leading cause of medication errors before and after publication of the guideline.
Conclusions: Anticoagulant medication errors occurred in 8.3% of all medication errors. Most error reports concerned the prescribing phase of the medication process. Leading cause was

human factors. The publication of the guideline had no effect on the proportion of anticoagulant medication errors.

Key words: medical errors, patient safety, guidelines, appropriate health care

Introduction

Medication errors are one of the most common types of medical errors and cause significant morbidity and mortality [1–4]. A medication error is defined as any preventable event that may cause or lead to inappropriate medication usage or patient harm while the medication is in the control of the healthcare professional, patient or consumer [5]. The 1999 Institute of Medicine report, 'To Err is Human,' stated that 44 000–98 000 hospitalized patients in the USA die each year because of medical errors [6]. In the Netherlands, the Hospital Admissions Related to Medication (HARM) study showed that 5.6% of all unplanned hospitalizations were drug-related and that 6.3% of these drug-related hospitalizations were attributable to anticoagulants [7].

A few studies characterized anticoagulant medication errors. Desai *et al.* described the characteristics, causes and outcomes of reported anticoagulant medication errors in nursing homes. They found that the documentation and monitoring phases of medication use were disproportionately involved in anticoagulation errors compared with other types of errors [8]. Fanikos and colleagues outlined characteristics and causes of reported anticoagulant medication errors in a hospital setting. Dosing errors accounted for nearly 68% of the 130 anticoagulant medication errors [9].

Given the fact that anticoagulants carry high risk for patient safety and are among the most frequently prescribed drugs involved in harmful medication errors [9–12], a multidisciplinary guideline was drafted in the Netherlands to provide a standard for antithrombotic therapy to provide optimal care to patients on antithrombotic therapy: the 'Landelijke Standaard Ketenzorg Antistolling' (LSKA; Dutch guideline on integrated antithrombotic care) [13].

Despite anticoagulants frequently being involved in medication errors, little is known about the characteristics of anticoagulation-related medication errors reported in hospitals and primary care.

Moreover, most studies focused on medication errors associated with warfarin or low-molecular weight heparin (LMWH) and do not concern patients using other vitamin K antagonists (VKAs) or direct oral anticoagulants (DOACs) [8, 9].

Finally, the consequences of implementation of a guideline on the proportion of medication errors has not been investigated yet. The hypothesis is that interventions, such as introducing a new guideline lead to a short-term increase in medication error reports but will lead to fewer medication error reports in the long term. The immediate increase in error reports may be due to the rising attention and higher awareness after publication of the guideline. This effect was also shown in an intervention study in the USA. Weant *et al.* described an increase in the number of medication errors reported during the initial transition period after implementation of computerized prescriber order entry [14].

The primary aim of our study was to determine the proportion of medication error reports in hospitals and primary care in which anticoagulants are involved. Secondary goals were to describe the involved anticoagulant, phase of the medication process in which the error occurred, causes and consequences within a subsample of 1000 anticoagulant medication errors and to analyse the influence of the publication of the national guideline on integrated antithrombotic care on the proportion and causes of reported anticoagulant medication errors.

Methods

Design and setting

This study is designed as a retrospective cross-sectional study. The Central Medication incidents Registration (CMR) is a Dutch nationwide online registration system for medication error reports. The system is based on anonymous self-reports of medication errors by caregivers. Medication errors derived from internal reporting systems in hospitals and community pharmacies in the Netherlands are reported through a web-based CMR reporting form. The reporting form consists of three sections: administrative information, patient data and information about the medication error. The description of the medication error starts with an open question to describe the medication error. The remaining questions are multiple-choice questions with predefined answers in dropdown menus. The CMR screens, analyses and evaluates the reported medication errors. The support staff at the CMR organization consists of a clinical pharmacologist, a physician, a pharmacy technician and a nurse [15]. The data for our study were collected from the CMR reports in an aggregated way. Access to the original error reports was not possible due

Table 1 Included drugs

Group of anticoagulants (ATC code)	Anticoagulants (ATC code)
VKA (B01AA)	Acenocoumarol (B01AA07)
	Phenprocoumon (B01AA04)
LMWH (B01AB)	Dalteparin (B01AB04)
	Enoxaparin (B01AB05)
	Nadoparin (B01AB06)
	Tinzaparin (B01AB10)
Heparin (B01AB)	Heparin (B01AB01)
Direct thrombin inhibitor (B01AE)	Bivalirudin (B01AE06)
	Dabigatran etexilate (B01AE07)
Direct factor Xa inhibitor (B01AF)	Rivaroxaban (B01AF01)
	Apixaban (B01AF02)
Other anticoagulants (B01AX)	Fondaparinux (B01AX05)
Group of haemostatic agents (ATC code)	**Haemostatic agents (ATC code)**
Antihemorrhagics (B02)	Tranexamic acid (B02AA02)
	Phytomenadione (B02BA01)
	Human fibrinogen (B02BB01)
	Coagulation factor IX, II, VII and X in combination (B02BD01)
	Eptacog alfa (B02BD08)
	Protamin (V03AB14)

ATC, anatomical therapeutic chemical.

to privacy constraints. Anticoagulant medication errors of the drugs listed in Table 1 reported to the CMR reporting system between December 2012 and May 2015 were collected. Haemostatic agents play a crucial role in anticoagulation therapy by reversing the anticoagulant effect when bleeding occurs. Therefore, we also included medication errors involving haemostatic agents.

To determine the proportion of medication error reports that involved an anticoagulant; all CMR reports from December 2012 to May 2015 were included as denominator. The numerator consisted of the reports that involved an anticoagulant or haemostatic agent. The anticoagulant medication error reports were stratified on the origin of the report (hospital or primary care). Medication errors in primary care are mainly from community pharmacies since they have been reporting since March 2010, while general practitioners have been participating since 2015.

A random number generator in SPSS was used to select 1000 anticoagulant medication errors, for detailed analysis. With 1000 anticoagulant medication errors, we expect to have a representative sample of the total number of anticoagulant medication errors between December 2012 and May 2015. Within this subsample, we analysed the involved anticoagulant, phase of the medication process in which the error occurred, causes and consequences of anticoagulant medication errors.

An antithrombotic guideline was drafted to provide a standard for antithrombotic therapy and to stress the importance of providing optimal care to patients on antithrombotic therapy: the 'Landelijke Standaard Ketenzorg Antistolling' (LSKA; Dutch guideline on integrated antithrombotic care). The first version of the LSKA guideline was published in 2012 focusing on the collaboration between healthcare providers at the local level of patients using VKAs. In July 2014, the second version of the LSKA guideline appeared. In addition to the collaboration at the local level, the LSKA 2.0 guideline focuses on the individual caregiver and the organization in the hospital and primary care. The LSKA 2.0 describes the tasks and responsibilities and how the communication and coordination take place between healthcare providers at a regional level (thrombotic service, general practitioner, community pharmacist and hospital care) and the patient. Furthermore, the DOACs and platelet aggregation inhibitors were integrated in LSKA 2.0 guideline. As the LSKA 2.0 guideline covers the entire process of anticoagulant use, this may have caused an increase in anticoagulant medication error reports due to the raised awareness. This hypothesis was tested in the secondary objectives of this study.

Data collection

The following data of each error report, filled in by caregivers, were collected: date of error, origin of report (hospital or primary care), phase of the medication process in which the error occurred, cause of error and consequences.

The phase of the medication process in which the error occurred was divided into five categories: prescribing, transcribing and verifying, dispensing, administering and monitoring [16]. The medication surveillance type of error was incorporated into the prescribing category and the order entry of the prescription into the prescribing and transcribing/verifying categories. The classification of causes of error was based on the Eindhoven classification method, which discriminates between technical, organizational, communication and human factors [17, 18]. The Dutch coding system for patient safety was used to classify the consequences of the error, divided into five classes: no harm, minimal/mild harm, serious temporary harm, serious permanent harm and death [19].

For the analysis of the effect of the LSKA 2.0 guideline on the proportion of medication errors, the total number of medication errors per month and the number of anticoagulant medication errors per month reported to the CMR were collected, both in the period before introduction of the LSKA 2.0 guideline (December 2012 until July 2014) and in the period after the guideline introduction (July 2014–May 2015). To assess the effect of LSKA 2.0 guideline on the proportion of causes of medication errors, the total number of causes of 1000 anticoagulant medication errors reported to the CMR were collected, both in the period before introduction of the LSKA 2.0 guideline and in the period after the introduction of LSKA 2.0 guideline.

Outcomes

Primary outcome was the proportion of all medication error reports in hospitals and primary care that involved an anticoagulant. Secondary outcomes were the anticoagulant involved, phase of the medication process in which the error occurred, causes and consequences of 1000 anticoagulant medication errors. Additional secondary outcomes were the total number of anticoagulant medication error reports per month, divided by the total number of medication error reports per month (comparing the pre- and post-guideline phase) and the total number of causes of 1000 anticoagulant medication errors before and after introduction of the LSKA 2.0 guideline.

Data analysis

All data were processed with MS Excel 2010 and analysed with SPSS version 21.0. Descriptive statistics were used to determine the proportion of anticoagulant medication reports and the involved anticoagulant, phase of the medication process in which the error occurred, causes, consequences of 1000 anticoagulant medication errors and the influence of the publication of the LSKA 2.0 guideline on the proportion of causes of 1000 anticoagulant medication errors.

For the analysis of the influence of the publication of the LSKA 2.0 guideline on the proportion of anticoagulant medication errors, we used segmented regression analysis for the interrupted time series (ITS) data. The anticoagulant medication errors were analysed using months as data points (i.e. 19 data points before and 10 data points after the intervention of the time series). The interruption was the introduction of the guideline (July 2014). Durbin–Watson statistics was used to check for possible autocorrelation [20]. To estimate the level and trend of the percentage of anticoagulant errors before the publication of the antithrombotic guideline and to estimate the changes in level and trend after the publication of the antithrombotic guideline, the following linear regression model was used: [21]

$$Y_t = ß_0 + ß_1 * \text{time}_t + ß_2 * \text{intervention}_t + ß_3 * \text{time after intervention}_t + e_t$$

Y_0 = mean percentage at time is $0 = ß_0$
$ß_1$ = baseline trend
$ß_2$ = immediate change after intervention
$ß_3$ = change in trend

Results

From December 2012 to May 2015, 42 962 medication errors were reported to the CMR. Of these errors, 37 325 (87%) originated

Table 2 Phases of the medication process in which the anticoagulant medication error occurred

Phase of medication process	Reported errors of the phase of the medication process ($n = 1000$) N (%)
Prescribing	**371 (37.1)**
Incomplete prescription	161 (16.1)
Wrong dose	33 (3.3)
Drug omitted from prescription	28 (2.8)
Wrong duration	24 (2.4)
Wrong time	18 (1.8)
Other	106 (10.6)
Transcribing and verifying	**216 (21.6)**
No prescription	37 (3.7)
No or incomplete medical information of the patient	34 (3.4)
Prescription has not been processed	28 (2.8)
Wrong duration	13 (1.3)
Wrong dose or frequency	13 (1.3)
Other	90 (9.0)
Dispensing	**81 (8.1)**
Ordered drug not dispensed	25 (2.5)
Wrong dose or frequency	12 (1.2)
Wrong strength	11 (1.1)
Wrong drug	10 (1.0)
Expired product	4 (0.4)
Other	19 (1.9)
Administering	**298 (29.8)**
Ordered drug not given	111 (11.1)
Given drug not ordered	40 (4.0)
Wrong dose or frequency	34 (3.4)
Wrong time	33 (3.3)
Wrong duration	11 (1.1)
Other	68 (6.8)
Monitoring	**32 (3.2)**
Insufficient monitoring	18 (1.8)
Incorrect actions based on monitoring results	12 (1.2)
Other	1 (0.1)
Unknown	**2 (0.2)**

The bold values are the percentages of the overall categories.

Table 3 Causes of anticoagulant medication errors

Cause of medication error	Reported cause of errors ($n = 1300$) N (%)
Technical	**70 (5.4)**
Errors in the electronic prescribing system	44 (3.4)
Medication name confusion	15 (1.2)
Other	11 (0.8)
Organizational	**111 (8.5)**
Unclear protocols or guidelines	30 (2.3)
High work pressure and short-staffed	21 (1.6)
No protocol or guidelines	12 (0.9)
Protocol or guideline not implemented	12 (0.9)
Other	24 (1.8)
Communication	**124 (9.5)**
Unclear communication between caregivers	33 (3.2)
Wrong transfer of information between caregivers	33 (3.2)
No transfer of information between caregivers	28 (2.2)
Wrong communication to the patient	21 (1.6)
Other	9 (0.7)
Human factors	**694 (53.4)**
Performance deficit[a]	305 (23.5)
Protocols or guidelines not followed	162 (12.5)
No double-checking performed	159 (12.2)
Insufficient expertise	63 (4.8)
Other	5 (0.4)
Unknown	**301 (23.2)**

[a]Failure to do what is known to be right.

The bold values are the percentages of the overall categories.

from hospitals and 5637 (13%) from primary care. Anticoagulant medication errors were seen in 3557 reports out of 42 962 (8.3%), of which 96% were reported by hospitals.

A random selection of 1000 anticoagulant medication error reports was analysed in more detail. 933 out of 1000 (93.3%) anticoagulant medication errors were from the hospital. The most frequently reported medication classes were LMWHs (56.2%) and VKAs (27.7%). Heparins accounted for 6.8%, followed by haemostatic agents (4.3%). DOACs were the least frequently type of anticoagulant involved in the reports (3%).

Most anticoagulant medication errors were reported as prescribing errors (37.1%), followed by administering errors (29.8%). Detailed analysis identified incomplete prescription (16.1%) and ordered drug not given (11.1%) as the most commonly reported errors in these categories (Table 2).

Table 3 shows the causes of anticoagulant medication errors. Human factors are the most common causes mentioned in the medication error reports (53.4%). In this category, human performance deficit (failure to do what is known to be right), not following protocols and guidelines, and not performing the double-checking procedures are the most common reported errors.

In 982 (98.2%) medication error reports, the consequences for the patient of the error were not reported. Twelve errors were reported to be associated with patient harm. Two of these errors resulted in death; one in serious permanent harm, six in serious temporary harm, three in minimal/mild harm and six in no harm.

Figure 1 shows the percentage of anticoagulant errors reported to the CMR during the study period. Anticoagulant medication errors were seen in 2538 reports out of a total of 26 891 (9.4%) reports before the introduction of the LSKA 2.0 guideline (December 2012–July 2014) and in 1019 reports out of 16 071 (6.3%) reports after the guideline introduction (July 2014–May 2015).

The publication of the LSKA 2.0 guideline was associated with an immediate increase in level of 2.57% (95% CI: −3.97, 9.10%) of anticoagulant errors ($ß_2$), and a change in trend of −0.64% (95% CI: −1.51, 0.23) per month ($ß_3$). A trend of −0.19% (95% CI: −0.54, 0.16%) of anticoagulant errors was observed at baseline. The change in level and change in trend were not statistically significant.

No significant autocorrelation was detected for any of the outcome parameters presented (Durbin–Watson value of 1.7).

Table 4 shows the proportion of causes of 1000 anticoagulant medication errors before and after the introduction of the LSKA 2.0

guideline. Both before (55.7%) and after (47.9%) the publication of the LSKA 2.0 guideline, human factors were the leading cause of medication errors.

Discussion

This study revealed that anticoagulants were found to be frequently involved in medication error reports, 1 of every 12 reported errors (8.3%). This is comparable to anticoagulant-related medication errors in previous studies [8, 9]. Fanikos *et al.* reported that 7.2% of all medication errors in the hospitalized patient were caused by anticoagulants and Rishi *et al.* found that in 1 in 20 medication errors in nursing homes an anticoagulant was involved. The hospital is more active in reporting of medication errors to the CMR than primary care. This is shown by the fact that 87% of the errors were reported by hospitals. The small number of reported errors from primary care (community pharmacies and general practitioners) is comparable with two studies where 8.5 and 6% of the errors came from primary care [22, 23]. A possible explanation for the larger number of reported errors by hospitals is the reporting culture. Contrary to primary care, in hospitals there are more staff members to report and there is a dedicated person for medication safety. Moreover, hospitals can report to the CMR reporting system since 2006, while community pharmacies participated since 2010 and general practitioners since 2015. Therefore, hospitals have more experience with the reporting of errors to the CMR reporting system. In addition, because treatment with anticoagulants is often initiated in the hospital, the majority of anticoagulant medication errors will come from hospitals. Another possible reason for the small number of reported errors from primary care may be due to the influence of the thrombosis services. In the Netherlands, treatment with VKAs in primary care is mostly carried out by medical doctors in well-organized thrombosis services. These medical doctors are specialized in this task and have a lot experience with this patient population, which could result in less medication errors.

VKAs were the most commonly used anticoagulants in the Netherlands at the time of this study [24]. Nevertheless, the LMWHs were most often associated with reported medication errors. LMWHs are frequently used for bridging during perioperative interruption of VKA treatment in the hospital. Bridging anticoagulation therapy is a complex procedure with a high risk of errors [25]. Henriksen *et al.* found that admission to or discharge from hospital, or undergoing surgery was associated with the highest number of serious and fatal adverse medication incidents. This was supported by medication incidents related to prescribing situations such as bridging. During surgery, prescribing excess anticoagulant was the most frequent problem.

In our study, we found that DOACs were least often associated with reported anticoagulant medication errors. A possible explanation is the greater ease of use (no need for laboratory monitoring and administering of fixed dose) [26], fewer drug and food interactions and wider therapeutic window of DOACs compared with VKAs. The use of DOACs, however, was substantially less than the other anticoagulants, as only 10% of the patients in the Netherlands used DOACs at the time of our study [27]. This low use in itself can also be an explanation for the low number of errors related to DOACs.

This study showed that anticoagulant medication errors were most often reported during the prescribing phase and administering phase of the medication process. These results are in line with prior studies that found the majority of reported medication errors in the prescribing and administering phase [9, 28–32]. Fanikos *et al.* found that errors

	γ_0 (95% CI) (mean percentage at time = 0)	β_1 (95% CI) (baseline trend)	β_2 (95% CI) (immediate change)	β_3 (95% CI) (change in trend)
Anticoagulant errors	**12.78*** **(8.79; 16.77)**	–0.19 (–0.54; 0.16)	2.57 (–3.97; 9.10)	–0.64 (–1.51; 0.23)

*Significant values are in bold type face

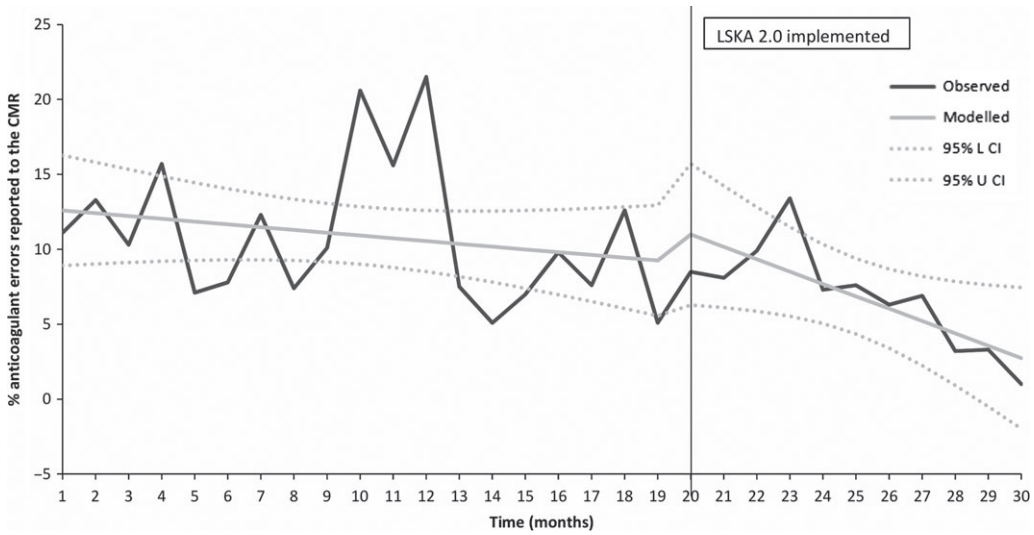

Figure 1 Impact of Landelijke Standaard Ketenzorg Antistolling, version 2 (LSKA; Dutch guideline on integrated antithrombotic care) on percentage of anticoagulant errors reported to the CMR.

Table 4 Impact of Landelijke Standaard Ketenzorg Antistolling, version 2 (LSKA; Dutch guideline on integrated antithrombotic care) on percentage of causes of 1000 anticoagulant errors reported to the CMR

Cause of medication error	Reported cause of errors before LSKA 2.0 guideline: December 2012–July 2014 ($n = 918$[a]) *N* (%)	Reported cause of errors after LSKA 2.0 guideline: July 2014–May 2015 ($n = 382$[a]) *N* (%)
Technical	51 (5.6)	19 (5.0)
Organizational	81 (8.8)	30 (7.9)
Communication	87 (9.5)	37 (9.7)
Human factors	511 (55.7)	183 (47.9)
Unknown	188 (20.5)	113 (29.6)

[a]A medication error may result from multiple causes.

with anticoagulant therapy were most often seen during drug administration, whereas Winterstein *et al.* and Samsiah *et al.* reported the most medication errors during the prescribing phase [9, 28, 32].

In our study, human factors were most often mentioned as a cause of the reported anticoagulant medication errors (53.4%). The most frequent types of human factors were as follows: human performance deficit (23.5%), not following protocols and guidelines (12.5%) and not performing double-checking of medication (12.2%). This corresponds with previous results of Zhan *et al.* who showed that human performance deficit and not following procedures and protocols were among the most common causes of warfarin errors in hospitals and outpatient facilities [33]. The same causes of errors were seen in the study of Pham *et al.*, who reported that 29% of the medication errors in emergency departments were caused by human performance deficit and 17% by not following procedures and protocols [29].

Our study showed no statistical significant effect on the proportion of reported anticoagulant medication errors after publication of the national guideline on integrated antithrombotic care. Circumstances other than the implementation of a guideline (i.e. introduction of the DOACs) could have affected the number of reported anticoagulant medication errors. Another reason for not finding a significant effect may be that the publication of the second version of the LSKA guideline had less impact than the first version of the LSKA guideline published in 2012. The lack of effect may be explained by the limited number of monthly data points after the publication of the guideline of the time series. Because implementation of a guideline takes time and does not improve care itself, active methods, such as education are needed to improve the awareness of the guideline. A change in trend after the publication of the LSKA 2.0 guideline may be suggested in Fig. 1, although it did not reach statistical significance.

This study showed that human factors were the leading cause of anticoagulant medication errors before and after publication of the LSKA 2.0 guideline.

Our study has several limitations. First, reporting of medication errors to the CMR reporting system is voluntary. Underreporting, selective reporting and incomplete reporting of medication errors are widely seen in voluntarily self-reporting systems [34]. A second limitation is that we did not analyse the total number of anticoagulant medication errors reported to the CMR in detail, but a random selection of 1000 errors to describe the anticoagulant involved, phase of the medication process in which the error occurred, causes and consequences. Third, in 982 (98.2%) medication error reports, the consequences for the patient were unknown. Due to the large number of missing values for anticoagulant medication errors leading to harm, definite conclusions cannot be drawn.

Finally, because implementation of a guideline takes time, it is possible that the influence of the LSKA 2.0 guideline on the frequency of anticoagulant medication errors in our study is limited and its influence after implementation may become apparent only after some time. Despite these limitations, our study is the first study describing the influence of a national guideline on integrated antithrombotic care on the proportion of anticoagulant medication errors using an ITS approach.

To conclude, anticoagulant medication errors are frequently reported. LMWHs were most often reported as a causative agent. Especially the prescribing and administering phases were involved in anticoagulant errors. The majority of errors made in the prescribing phase arose from incomplete prescriptions. Omission errors (ordered drug not given) were responsible for the highest percentage of errors in the administering phase. Human factors such as performance deficit and not following protocols and guidelines were the most common causes of reported anticoagulant medication errors, before and after the introduction of the LSKA 2.0 guideline. Interventions should focus on these causes, for example, by introducing computerized physician order entry in which incomplete prescriptions are impossible. Future research is needed to determine the impact of such interventions on the number of anticoagulant medication errors. These future studies should also take into account the presence of bias in voluntarily self-reporting systems.

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Contributors

ARD wrote the manuscript; all other co-authors commented on previous versions of the manuscript and agreed with the final content. ARD coordinated the study start-up and data collection. PMLAvdB designed the study. PGMM performed the ITS analysis. MJHAK, JD, VEB and FWGL participated in the study design. All authors read and approved the final manuscript.

Competing interest

None.

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