Impact of electronic reminders on venous thromboprophylaxis after admissions and transfers

Beeler, P E ; Eschmann, E ; Schumacher, A ; Studt, J-D ; Amann-Vesti, B ; Blaser, J

Abstract: OBJECTIVE: Clinical decision support has the potential to improve prevention of venous thromboembolism (VTE). The purpose of this prospective study was to analyze the effect of electronic reminders on thromboprophylaxis rates in wards to which patients were admitted and transferred. The latter was of particular interest since patient handoffs are considered to be critical safety issues. METHODS: The trial involved two study periods in the six departments of a university hospital, three of which were randomly assigned to the intervention group displaying reminders during the second period. At 6 h after admission or transfer, the algorithm checked for prophylaxis orders within 0-30 h of the patient's arrival, increasing the specificity of the displayed reminders. RESULTS: The significant impact of the reminders could be seen by prophylaxis orders placed 6-24 h after admission (increasing from 8.6% (223/2579) to 12% (307/2555); p<0.0001) and transfer (increasing from 2.4% (39/1616) to 3.7% (63/1682); p=0.034). In admission wards, the rate of thromboprophylaxis increased from 62.4% to 67.7% (p<0.0001), and in transfer wards it increased from 80.2% to 84.3% (p=0.0022). Overall, the rate of prophylaxis significantly increased in the intervention group from 69.2% to 74.3% (p<0.0001). No significant changes were observed in the control group. Postponing prophylaxis checks to 6 h after admissions and transfers reduced the number of reminders by 62% and thereby minimized the risk of alert fatigue. CONCLUSIONS: The reminders improved awareness of VTE prevention in both admission and transfer wards. This approach may contribute to better quality of care and safer patient handoffs.

DOI: https://doi.org/10.1136/amiajnl-2013-002225

Impact of Electronic Reminders on Venous Thromboprophylaxis after Admissions and Transfers

Authorship Details

PE Beeler [1]	(Patrick Emanuel Beeler)	patrick.beeler@usz.ch
E Eschmann [1]	(Emmanuel Eschmann)	emmanuel.eschmann@usz.ch
A Schumacher [2]	(Anette Schumacher)	anette.schumacher@spitaeler-sh.ch
JD Studt [3]	(Jan-Dirk Studt)	jan-dirk.studt@usz.ch
B Amann-Vesti [4]	(Beatrice Amann-Vesti)	beatrice.amann@usz.ch
J Blaser [1]	(Jürg Blaser)	juerg.blaser@usz.ch

[1] Research Center for Medical Informatics, University Hospital Zurich, Switzerland
[2] Division of Angiology, Cantonal Hospital Schaffhausen, Switzerland
[3] Division of Hematology, University Hospital Zurich, Switzerland
[4] Division of Angiology, University Hospital Zurich, Switzerland

Site the work has been carried out: University Hospital Zurich.

Correspondence

Prof. Dr. Jürg Blaser
Research Center for Medical Informatics
Directorate of Research & Education
University Hospital Zurich
Sonneggstrasse 6, D5
CH-8091 Zurich
Switzerland
Phone: +41 44 255 3618
Fax: +41 44 634 5503

Keywords

Decision Support Systems, Clinical
Patient Handoff
Patient Transfer
Reminder Systems
Venous Thromboembolism

Word count

Abstract:	242
Text:	4,033

Abstract

Objective Clinical decision support has the potential to improve the prevention of venous thromboembolism (VTE). The purpose of this prospective study was to analyze the impact of electronic reminders on thromboprophylaxis rates in wards patients were admitted and transferred to. The latter was of particular interest since patient handoffs are considered to be critical safety issues.

Methods The trial involved two study periods in the departments of a university hospital, 3 out of 6 randomly assigned to the intervention group displaying reminders during the second period. 6h after admission or transfer, the algorithm checked for prophylaxis orders within 0-30h following the patient's arrival, increasing the specificity of the displayed reminders.

Results The significant impact of the reminders could be shown by prophylaxis orders placed 6-24h after admissions (increasing from 8.6% [223/2579] to 12% [307/2555]; $p<0.0001$) and transfers (from 2.4% [39/1616] to 3.7% [63/1682]; $p=0.034$). In admission wards the thromboprophylaxis rate increased from 62.4% to 67.7% ($p<0.0001$) and in transfer wards from 80.2% to 84.3% ($p=0.0022$). Overall, the rate of prophylaxis significantly increased in the intervention group from 69.2% to 74.3% ($p<0.0001$). No significant changes were observed in the control group. Postponing prophylaxis checks to 6h after admissions and transfers reduced the number of reminders by 62% and thereby minimized the risk of alert fatigue.

Conclusions The reminders improved the awareness of VTE prevention in both, admission and transfer wards. This approach may contribute to better quality of care and safer patient handoffs.

Background

Appropriate use of prophylaxis to prevent venous thromboembolism (VTE) is an important strategy for improving safety among hospitalized patients (1, 2). The American College of Chest Physicians has established evidence-based guidelines for the prevention of VTE, including recommendations for the use of both pharmacological and mechanical thromboprophylaxis (3). Nevertheless, insufficient guideline adherence is a recognized problem impeding appropriate prophylaxis regimens, and large clinical studies demonstrated that many patients at risk do not receive prophylaxis (4-6).

Clinical decision support (CDS) systems have the potential to improve guideline adherence and increase the rate of prophylaxis against VTE (7-10). The impact of electronic VTE alerting concepts has been shown to be sustainable (11, 12). Fiumara et al. investigated serial three-screen alerts which improved the use of prophylaxis (13). However, immediately consecutive alerts increase the risk of 'alert fatigue' (14). Despite studies that demonstrated CDS algorithms to increase the use of thromboprophylaxis, there is still potential regarding patients at risk for VTE (7, 11, 13, 15, 16).

Since an anticipated order of VTE prophylaxis may be forgotten after a patient's transfer to another unit, the question rises whether CDS could further improve quality of care after such a 'handoff'. Cohen and Hilligoss define handoff as "the exchange between health professionals of information about a patient accompanying either a transfer of control over, or of responsibility for, the patient" (17). The procedure when a patient is transferred from one unit to another and thereby a different team of providers gets instructed to take care, is referred to as 'patient handoff' (18). Disruptions in the continuity of care are considered to be critical safety issues because individuals of different teams may inadequately communicate to each other and important information may get lost (19, 20).

Some authors demonstrated improvements in patient handoff communication using software tools (21-23). Nevertheless, these tools pursue a comprehensive handoff procedure and demand additional user input entered either into the electronic health record (EHR) or directly into the respective tool. Consequently, the stored information may be erroneous or incomplete.

The clinical information system of the University Hospital Zurich provides automated VTE reminders, previously described elsewhere (8, 12). This algorithm has been upgraded to generate reminders again after transfers of patients, which is a novel approach to support patient handoffs. Only if no VTE prophylaxis has

been ordered within the first six hours following admission or transfer, does the VTE reminder show up in order to minimize the risk of alert fatigue (14).

The purpose of this hospital-wide trial was to determine the impact of electronic reminders on the rate of thromboprophylaxis following admissions and particularly following patient handoffs. To our knowledge, so far no studies have been published on the impact of electronic reminders following admissions and transfers.

Methods

Design and Site

The study was designed as a prospective single center clinical trial. The six departments of the hospital were randomly assigned either to the intervention or to the control group. The University Hospital Zurich provides approximately 850 inpatient beds and covers all specialties. The ethics committee approved the study and patient consent was waived.

Clinical Information System

Since 2009, inpatient care is comprehensively managed by the clinical information system (Kisim, Cistec AG, Zurich, Switzerland) including computerized physician order entry (CPOE) of all pharmacological therapies, other treatments and diagnostic procedures on all wards of the University Hospital Zurich except for intensive care units (ICUs). The system offers a number of CDS functions involving medication and laboratory data (24).

Reminders

The VTE 'reminder' (25) is displayed on the graphical user interface as a non-interruptive red bar (Figure 1) within the top section of the EHR (8, 12). Its underlying algorithm has been upgraded to be triggered by both, admissions and transfers, in order to support patient handoffs.

In the intervention group, a VTE reminder is automatically displayed in the EHR of each patient who did not receive a prophylaxis order within the first six hours of admission or transfer. To be precise, following this six hours delay the algorithm checks for thromboprophylaxis orders that are active within the time frame 0-30 hours after admission or transfer. Hence, orders placed before the patient's arrival or orders placed within the first six hours – being active or becoming active during the prospective 24 hours – suppress the reminder. Further, the time frame from displaying the reminder until 24 hours after admission or transfer was considered to reflect the immediate impact of the intervention.

Reminders were triggered only once during the uninterrupted stay of a patient on a ward in order to minimize the number of notifications. By clicking on the reminder bar a flow sheet pops up outlining the guidelines for assessing a patient's VTE risk, followed by evidence-based recommendations for appropriate prophylaxis (Figure 2). This flow sheet allowed for the re-evaluation of the risk for VTE also after transfers. The

reminder could be stopped by clicking on the 'notification acknowledged' button. Finally, each unacknowledged reminder was automatically stopped after ten days.

The patients were blinded, since they had no access to their EHR. Health professionals on wards assigned to the control group did not see any reminders. However, all professionals were informed about the study at the beginning, independent of their study group. Those professionals working on wards assigned to the intervention group could see reminders within the EHRs.

Figure 1: Synoptic view of the EHR. The mouse cursor displayed in the top right section points to the VTE reminder bar.

Figure 2: Pop-up window showing guidelines for assessing a patient's VTE risk (based on (26, 27)).

Definitions

The 'admission ward' is defined as the ward a patient is admitted to, either directly or via emergency unit. However, the emergency unit is not considered an admission ward since most inpatients are transferred within a few hours.

The 'transfer ward' is defined as the ward a patient is transferred to, either from the admission ward or a preceding transfer ward. To be precise, neither a patient's change of the room, nor health professionals' shift change are considered to be transfers or patient handoffs.

'Stay' is defined as the continuance in place of an inpatient on the very same ward, from admission or transfer until transfer or discharge. One hospitalization includes one or more stays. Only stays with durations of at least 24 hours were considered. Stays overlapping the study periods and stays in ICUs were excluded.

The 'rate of prophylaxis' is defined as the percentage of stays including at least one treatment with pharmacological or mechanical VTE prophylaxis compared to the total number.

'Adequacy' is defined as the number of stays with correctly ordered or withheld prophylaxes according to evidence-based guidelines divided by the total number of stays.

Study Periods

After the 'baseline period' (06/02/2011 to 08/31/2011; 13 weeks), the VTE reminders were activated in the intervention group for the following 13 weeks ('reminder period' until 11/30/2011).

Clinical Outcome

ICD-10 diagnosis codes (International Classification of Diseases, World Health Organization, Geneva, Switzerland) were analyzed to determine differences in the frequencies of bleeding due to anticoagulants, other bleeding events, heparin-induced thrombocytopenia and VTE events (Table 1.). All patients were included in this analysis except for hospitalizations overlapping both study periods and patients switching the study group (158 excluded patients; 1%). The electronic health records had been reviewed in order to eliminate diagnoses prevalent at admission.

Table 1. ICD-10 diagnosis codes used to determine differences in the frequencies of bleeding due to anticoagulants, other bleeding events, heparin-induced thrombocytopenia and VTE events (adapted from (28, 29) and updated).

Event	**ICD-10 diagnosis codes**
Bleeding due to anticoagulants	D68.3*
Other bleeding events	D69.9*, H11.3*, H31.3*, H35.6*, H43.1*, H45.0*, I60.*, I61.*, I62.*, K22.8*, K62.5*, K66.1*, K92.0*, K92.1*, K92.2*, M25.0*, R04.*, R23.3*, R31, R58
Heparin-induced thrombocytopenia	D69.53
Venous thromboembolism	I26.*, I80.1*, I80.2*, I80.3*, I80.8*, I80.9*, I82.1*, I82.2*, I82.3*, I82.8*, I82.9*, O22.3*, O87.1*, O88.2*

The * character is used as a wildcard that matches zero or more numeric digits.

Quality Assessment

Adequacy was assessed in computer-generated random samples of 40 inpatients determined for each week during the reminder period (resulting in a total of 520 patients). Each sample consisted of 20 patients from the intervention group (ten receiving a VTE prophylaxis, ten without prophylaxis) and 20 patients from the control group (ten receiving a VTE prophylaxis, ten without prophylaxis).

Two angiologists adjudicated the adequacy of the decisions to order or withhold VTE prophylaxis in each of these hospitalizations. The same patients were contacted by phone three months after discharge and interviewed using a questionnaire to determine whether new VTE was diagnosed (based on (30)).

Assignment of the Departments to the Study Groups

The hospital's departments are organizational structures that were defined by the management in order to simplify the handling of jointly used resources in terms of both, infrastructure and professional staff. All divisions hosting and caring for inpatients are allocated to the six considered departments.

The decision to randomize departments instead of individual patients, teams or divisions was made in order to minimize potential contamination due to physician rotations across intervention and control groups. Randomization included ranking and pairing of the departments: First, the two departments with the highest prophylaxis rate were randomized, second, the two intermediate departments, third, the two departments with the lowest prophylaxis rate.

The resulting intervention group consisted of the three interdisciplinary departments

(i) 'traumatology/reconstructive surgery/dermatology/rheumatology' (highest prophylaxis rate),

(ii) 'internal medicine/oncology/radiation oncology/hematology/infectious diseases' (intermediate prophylaxis rate) and

(iii) 'cardiac surgery/vascular surgery/thoracic surgery/angiology/cardiology/pulmonology' (lowest prophylaxis rate).

The control group consisted of the three interdisciplinary departments

(iv) 'endocrinology/diabetology/gastroenterology/nephrology/urology/abdominal surgery' (highest prophylaxis rate),

(v) 'ophthalmology/psychiatry/neurology/neuroradiology/otolaryngology/oral and maxillofacial surgery/

neurosurgery' (intermediate prophylaxis rate) and

(vi) 'gynecology/obstetrics/neonatology' (lowest prophylaxis rate).

Statistics

Levels of $p \leq 0.05$ were considered significant. Fisher's exact tests were used for 2x2 contingency tables. Comparisons of continuous variables were performed using the Wilcoxon rank-sum test.

The primary end point was the change in the rate of prophylaxis. Proportions of orders placed 6-24 hours after admissions and transfers represented the immediate impact of the reminders.

Duration of the study periods was defined to obtain sample sizes above the minimum, assuming an increase of the prophylaxis rate from 70% to 75%, a significance level of 0.01, and a power of 90%.

Calculations were performed using the software R, version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 15,736 patients were included. These patients stayed 11,770 times in admission wards and 7,780 times in transfer wards. Stays of 106 patients (0.7%) transferred from the intervention group to the control group and vice versa were included in the analyses.

In the intervention group and in the control group the mean duration of hospitalization was 8.4 and 6.4 days, the mean age was 59 and 43 years, the percentage of females was 40.2% and 59.7%, respectively (each $p<0.0001$). None of these demographics differed significantly in the intervention group between the baseline and reminder period (each $p>0.16$). In the control group, the duration of hospitalization ($p=0.54$) and the age of the patients ($p=0.67$) did not significantly differ between the periods, however, the proportions of males and females did (61.1% females during baseline period; 58.4% females during reminder period; $p=0.0083$).

The prophylaxis rate significantly increased in the intervention group by 5.1% from 69.2% to 74.3% ($p<0.0001$). In the control group, the change of the prophylaxis rate from 68.1% to 69.7% was not significant ($p=0.070$).

Stays in Admission Wards

The prophylaxis rate increased in the admission wards of the intervention group by 5.3% ($p<0.0001$; Table 2.). No significant change was observed in the control group ($p=0.21$). The proportions of prophylaxes ordered within the time frame 6-24 hours after admission significantly increased in the intervention group, reflecting the immediate impact of the VTE reminders ($p<0.0001$). No significant change of these proportions was observed in the control group ($p=0.25$).

Compared to a hypothetical algorithm that would alert immediately at the time of admission (without considering orders placed for the period 0-30h), the six hours postponed prophylaxis check reduced the number of displayed reminders by 51% in the intervention group.

Table 2. Prophylaxis rates in both study groups in the admission wards according to the timing of order entry.

	Intervention group					**Control group**				
	Baseline period		Reminder period			Baseline period		Reminder period		
	# of stays	%	# of stays	%	p	# of stays	%	# of stays	%	p
Stays with prophylaxis orders placed before admission or in the time frame 0-6h	1248	48.4	1296	50.7	0.099	1623	51.1	1766	51	0.92
Stays with prophylaxis orders placed in the time frame 6-24h after admission	223	8.6	307	12	<0.0001	242	7.6	291	8.4	0.25
Stays with prophylaxis orders placed >24h	138	5.4	127	5	0.57	114	3.6	153	4.4	0.091
Stays without prophylaxis orders	970	37.6	825	32.3	<0.0001	1195	37.6	1252	36.2	0.21
Total number of stays	2579	100	2555	100		3174	100	3462	100	

Stays in Transfer Wards

This analysis included 6,352 patients with 7,780 stays. In the intervention group, the prophylaxis rate significantly increased by 4.1% (p=0.0022; Table 3.), whereas no significant change was observed in the control group (p=0.17). The proportions of prophylaxes ordered within the time frame 6-24 hours after transfer significantly increased in the intervention group (p=0.034) and not in the control group (p=0.25).

Compared to a hypothetical algorithm that would alert immediately at the time of a patient's transfer (without considering orders placed for the period 0-30h), the six hours postponed prophylaxis check reduced the number of displayed reminders by 78% in the intervention group.

Table 3. Prophylaxis rates in both study groups in the transfer wards according to the timing of order entry.

	Intervention group					**Control group**				
	Baseline period		Reminder period			Baseline period		Reminder period		
	# of stays	%	# of stays	%	p	# of stays	%	# of stays	%	p
Stays with prophylaxis orders placed before transfer or in the time frame 0-6h	1214	75.1	1311	77.9	0.058	1512	70.6	1666	71.2	0.69
Stays with prophylaxis orders placed in the time frame 6-24h after transfer	39	2.4	63	3.7	0.034	77	3.6	100	4.3	0.25
Stays with prophylaxis orders placed >24h	43	2.7	44	2.6	1	54	2.5	71	3	0.31
Stays without prophylaxis orders	320	19.8	264	15.7	0.0022	498	23.3	504	21.5	0.17
Total number of stays	1616	100	1682	100		2141	100	2341	100	

Clinical Outcome

By analyzing the frequencies of the ICD-10 diagnosis codes no significant change was observed for the incidence of bleeding due to anticoagulants, other bleeding events, heparin-induced thrombocytopenia and VTE events (Table 4.).

Table 4. Number of patients suffering from bleeding due to anticoagulants, other bleeding events, heparin-induced thrombocytopenia or VTE events. (Multiple ICD-10 diagnosis codes per patient and category are counted as one, e.g. two different VTE codes in one patient are considered as one patient suffering from VTE.)

	Intervention group					**Control group**				
	Baseline period		Reminder period			Baseline period		Reminder period		
	# of patients	%	# of patients	%	p	# of patients	%	# of patients	%	p
Bleeding due to anticoagulants	6	0.18	4	0.12	0.54	1	0.02	1	0.02	1
Other bleeding event	29	0.87	31	0.93	0.89	11	0.26	14	0.3	0.84
Heparin-induced thrombocytopenia	1	0.03	3	0.09	0.62	0	0	0	0	1
VTE event	19	0.57	13	0.39	0.29	12	0.28	10	0.21	0.53
Total number of patients	3321	100	3332	100		4256	100	4669	100	

Quality Assessment

Regarding the adequacy of thromboprophylaxis, no significant differences were observed in a sample of 520 patients analyzed in detail (Table 5.): In the intervention group 88.1% of prophylaxis regimens were adequate, in the control group 89.2% of the prophylaxis regimens were adequate (p=0.78).

Table Assessment of adequacy of the prophylaxis regimens.

Intervention group		Prophylaxis				p
		ordered	%	withheld	%	
Decision	adequate	111	85.4	118	90.8	0.25
	inadequate	19	14.6	12	9.2	
Total		130	100	130	100	

Control group		Prophylaxis				p
		ordered	%	withheld	%	
Decision	adequate	108	83.1	124	95.4	0.0021
	inadequate	22	16.9	6	4.6	
Total		130	100	130	100	

453 of these 520 patients were contacted by phone three months after discharge (lost to follow-up: intervention 45, control 22). No difference in the frequency of post-discharge VTE was observed between the intervention group (three VTE events) and the control group (three VTE events).

Discussion

We implemented an algorithm displaying non-interruptive reminders on thromboprophylaxis. Only if no VTE prophylaxis had been ordered within the first six hours following admission or transfer including patient handoff was a reminder displayed in the EHR. The VTE reminders had a significant impact on the prophylaxis rate in the admission wards and transfer wards of the intervention group. The immediate impact of the reminders was demonstrated by increased numbers of VTE prophylaxes ordered 6-24 hours following admissions and even following transfers. None of these end points were significantly affected in the control group where the notifications were suppressed. To our knowledge, this study shows for the first time the significant impact of VTE prophylaxis reminders after both admissions and patient transfers.

The aim of the reminders was to increase the awareness of VTE prevention and to foster guideline adherence. When the user clicks on the reminder bar, a pop-up window displays evidence-based prophylaxis guidelines. Notifications featuring improved acceptance are characterized by high quality of knowledge and presenting detailed advice in a user-friendly manner (31).

It was the purpose of the study to document the improvement of the process of VTE prevention. Yet, the observed trend towards better clinical outcome in the intervention group did not reach significance (from 0.57% to 0.39%; p=0.29). To show a statistically significant reduction of VTE events due to the reminders, a much larger sample size would be required: A power calculation using data from table 4, a significance level of 0.01, two-sided, with a power of 90%, results in more than 2 x 43,000 patients to be enrolled in the intervention group. However, the clinical and economic benefit of improved adherence to evidence-based guidelines has been recognized (15, 32) and the impact of computer-based decision support on reduction of symptomatic and asymptomatic deep-vein thrombosis was shown in a landmark publication (7).

Increasing the thromboprophylaxis rate by electronic reminders might induce overuse of prophylaxis. Though, neither did the assessment of the clinical outcome in the intervention group show a trend toward increased bleeding events due to anticoagulants (from 0.18% to 0.12%), nor was the percentage of inadequately ordered prophylaxes high in the intervention group compared to the control group (14.6% vs. 16.9%). Nevertheless, the 9.2% inadequately withheld prophylaxes despite the display of reminders in the intervention group's sample indicate that there is still room for improvement. Further increase of the

adequacy of the prophylaxis regimens might be achieved by a specialist service reviewing EHRs with unacknowledged VTE reminders.

The higher prophylaxis rate observed in the transfer wards compared to the admission wards is probably a result of both, the carrying over of prophylaxis orders from preceding wards and the more complex illness of transferred patients. The latter is supported by two findings: (i) The patients included in the transfer wards analysis were hospitalized on average 11.2 days, whereas those included in the admission wards were hospitalized on average 6.2 days, whether or not they were transferred later ($p<0.0001$). (ii) The patients analyzed in the transfer wards were transferred from or to an ICU in 12.3% of the cases during their hospitalization. In contrast, the patients analyzed in the admission wards were transferred to an ICU during their hospitalization in only 6.6% of the cases ($p<0.0001$).

Reminders were displayed after a delay of six hours, thereby allowing physicians to order VTE prophylaxes proactively. Following this six hours delay, the algorithm checked for thromboprophylaxis orders that are active within the time frame 0-30 hours after admission or transfer. Hence, orders being active or becoming active during the subsequent 24 hours suppressed the reminder. Reminders were triggered only once during the uninterrupted stay of a patient on a ward in order to minimize the number of notifications. These features helped to improve the specificity: Compared to a hypothetical algorithm immediately alerting at each admission and transfer of a patient, the six hours postponed prophylaxis check reduced the number of reminder bars in the admission and transfer wards by 51% and 78%, respectively. That corresponds to an average reduction by 62%, minimizing the risk of alert fatigue (14).

A patient's need for prophylaxis varies during the hospitalization, therefore the VTE risk should be re-evaluated after transfers. This is of particular interest, since in this study, the stays in transfer wards represented 40% of the total number of stays. Triggering a single reminder after both, admission and patient handoff may be a compromise between excessive alerting and maximum impact. This approach could help to improve the transfer of important information through the change of the care team in patient handoffs (18-20).

The algorithm triggering the reminder does not identify high-risk patients based on VTE risk score calculation, since the identification of individual risk factors by computers may be unreliable, particularly if important information is lacking or not interpretable. An algorithm should preempt neither the decision to order prophylaxis nor the risk assessment by the responsible physician (33), since both, underuse and overuse

of thromboprophylaxis are known problems (34, 35). However, the described pop-up window showing evidence-based prophylaxis recommendations offers user-friendly guidance (cf. figure 2).

On the one hand, learning effects might have contributed to increased proportions of prophylaxes ordered until 6 hours after the patients' arrival, particularly regarding the admission wards of the intervention group (cf. table 2). On the other hand, the decision to order thromboprophylaxis may directly be influenced by the algorithm as soon as the reminder bar is displayed. Thus, without considering prophylaxis orders placed before the appearance of the reminders, three categories of order entry timing could be distinguished: (i) patients receiving their first order for VTE prophylaxis immediately following the notification, i.e. within the time frame 6-24 hours, (ii) patients receiving their first order beyond >24 hours (until transfer or discharge), and (iii) patients receiving no prophylaxis at all. Regarding only these 'reminder influenced categories' in the intervention group, the proportion of orders placed within the time frame 6-24 hours increased by 7.6% ([307/1259]-[223/1331]) and 7.3% ([63/371]-[39/402]) in the admission and transfer wards, respectively.

Some limitations are noteworthy interpreting this study. On the one hand, the randomization of the hospital's departments has the advantage of minimized staff exchange across the study groups allowing for more precisely measuring the impact of the reminders in the admission and transfer wards. On the other hand, this approach limits conclusions drawn with respect to prophylaxis regimens and clinical outcomes since different specialties with different views, knowledge and experience in VTE are assembled within the departments. We considered this issue by comparing not only the intervention group vs. the control group during the intervention period but also the changes within each study group before and after the implementation of the reminders. The slight increase of the prophylaxis rate in the analysis of the control group might indicate that limited contamination occurred between the study groups, e.g. due to carry-over effects of patients from the intervention group transferred to wards of the control group or due to physician rotations across the hospital departments. If a Hawthorne effect had influenced the health professionals, its contribution would have been minimal since no significant change was observed in the control group (36).

Numbers of patients with specific diagnoses according to ICD-10 codes need to be carefully interpreted because most codes are generated by medical coding staff after discharge of the patients. Noteworthy regarding the reviews of the EHRs is that only 39% of the patients with ICD-10 codes related to VTE suffered from hospital-acquired VTE (hospital-acquired conditions: cf. table 4).

The in-depth assessment of adequacy of the prophylaxis regimens revealing no significant differences between the study groups was based on a limited sample of 520 patients. Three months following discharge, 453 of these patients were available for the follow-up interviews (87%). This sample might not be large enough to detect minor – but potentially relevant – differences regarding the adequacy of prophylaxis regimens or the incidence of events after discharge.

In conclusion, the electronic reminders improved the awareness of VTE prevention in both, admission and transfer wards. This approach may contribute to better quality of care and safer patient handoffs.

Acknowledgements

We thank Gabriela Gitzelmann (University Hospital Zurich) for her relentless effort calling discharged patients and we thank Peter Amberg (Cistec AG, Zurich) for the programming of the upgraded algorithm.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing Interests Statement

The authors have no competing interests.

Contributorship Statement

P. E. Beeler designed and performed the research, analyzed and interpreted data, and wrote the manuscript. E. Eschmann performed research, analyzed data, and reviewed the manuscript. A. Schumacher and J.-D. Studt performed research, and reviewed the manuscript. B. Amann-Vesti and J. Blaser designed the research, analyzed and interpreted data, and reviewed the manuscript. All authors approved the final submitted version of the manuscript.

References

1. Shojania KG, Duncan BW, McDonald KM, Wachter RM, Markowitz AJ. Making health care safer: a critical analysis of patient safety practices. Evid Rep Technol Assess (Summ). 2001(43):i-x, 1-668.
2. Cohn SL. Prophylaxis of venous thromboembolism in the US: improving hospital performance. J Thromb Haemost. 2009 Sep;7(9):1437-45.
3. Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuunemann HJ. Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):7S-47S.
4. Cohen AT, Tapson VF, Bergmann JF, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. Lancet. 2008 Feb 2;371(9610):387-94.
5. Goldhaber SZ, Tapson VF. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. Am J Cardiol. 2004 Jan 15;93(2):259-62.
6. Tapson VF, Decousus H, Pini M, et al. Venous thromboembolism prophylaxis in acutely ill hospitalized medical patients: findings from the International Medical Prevention Registry on Venous Thromboembolism. Chest. 2007 Sep;132(3):936-45.
7. Kucher N, Koo S, Quiroz R, et al. Electronic alerts to prevent venous thromboembolism among hospitalized patients. N Engl J Med. 2005 Mar 10;352(10):969-77.
8. Kucher N, Puck M, Blaser J, Bucklar G, Eschmann E, Luscher TF. Physician compliance with advanced electronic alerts for preventing venous thromboembolism among hospitalized medical patients. J Thromb Haemost. 2009 Aug;7(8):1291-6.
9. Dexter PR, Perkins S, Overhage JM, Maharry K, Kohler RB, McDonald CJ. A computerized reminder system to increase the use of preventive care for hospitalized patients. N Engl J Med. 2001 Sep 27;345(13):965-70.
10. Durieux P, Nizard R, Ravaud P, Mounier N, Lepage E. A clinical decision support system for prevention of venous thromboembolism: effect on physician behavior. JAMA. 2000 Jun 7;283(21):2816-21.
11. Lecumberri R, Marques M, Diaz-Navarlaz MT, et al. Maintained effectiveness of an electronic alert system to prevent venous thromboembolism among hospitalized patients. Thromb Haemost. 2008 Oct;100(4):699-704.
12. Beeler PE, Kucher N, Blaser J. Sustained impact of electronic alerts on rate of prophylaxis against venous thromboembolism. Thromb Haemost. 2011 Oct;106(4):734-8.
13. Fiumara K, Piovella C, Hurwitz S, et al. Multi-screen electronic alerts to augment venous thromboembolism prophylaxis. Thromb Haemostasis. 2010 Feb;103(2):312-7.
14. van der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. J Am Med Inform Assoc. 2006 Mar-Apr;13(2):138-47.
15. Lecumberri R, Panizo E, Gomez-Guiu A, et al. Economic impact of an electronic alert system to prevent venous thromboembolism in hospitalised patients. J Thromb Haemost. 2011 Jun;9(6):1108-15.
16. Piazza G, Rosenbaum EJ, Pendergast W, et al. Physician alerts to prevent symptomatic venous thromboembolism in hospitalized patients. Circulation. 2009 Apr 28;119(16):2196-201.
17. Cohen MD, Hilligoss B, Kajdacsy-Balla Amaral AC. A handoff is not a telegram: an understanding of the patient is co-constructed. Crit Care. 2012;16(1):303.
18. Pham JC, Aswani MS, Rosen M, et al. Reducing medical errors and adverse events. Annu Rev Med. 2012;63:447-63.
19. Cook RI, Render M, Woods DD. Gaps in the continuity of care and progress on patient safety. BMJ. 2000 Mar 18;320(7237):791-4.
20. Greenberg CC, Regenbogen SE, Studdert DM, et al. Patterns of communication breakdowns resulting in injury to surgical patients. J Am Coll Surg. 2007 Apr;204(4):533-40.
21. Petersen LA, Orav EJ, Teich JM, O'Neil AC, Brennan TA. Using a computerized sign-out program to improve continuity of inpatient care and prevent adverse events. Jt Comm J Qual Improv. 1998 Feb;24(2):77-87.
22. Van Eaton EG, Horvath KD, Lober WB, Rossini AJ, Pellegrini CA. A randomized, controlled trial evaluating the impact of a computerized rounding and sign-out system on continuity of care and resident work hours. J Am Coll Surg. 2005 Apr;200(4):538-45.
23. Anderson J, Shroff D, Curtis A, et al. The Veterans Affairs shift change physician-to-physician handoff project. Jt Comm J Qual Patient Saf. 2010 Feb;36(2):62-71.

24. Beeler PE, Eschmann E, Rosen C, Blaser J. Use of an On-demand Drug-Drug Interaction Checker by Prescribers and Consultants: A Retrospective Analysis in a Swiss Teaching Hospital. Drug Saf. 2013 Jun;36(6):427-34.
25. Randolph AG, Haynes RB, Wyatt JC, Cook DJ, Guyatt GH. Users' Guides to the Medical Literature: XVIII. How to use an article evaluating the clinical impact of a computer-based clinical decision support system. JAMA. 1999 Jul 7;282(1):67-74.
26. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008 Jun;133(6 Suppl):381S-453S.
27. AWMF. S3-Leitlinie Prophylaxe der venösen Thromboembolie, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, www.awmf-leitlinien.de, version 18/3/2009 with addendum 8/5/2010. 2009, 2010.
28. Huo MH, Spencer DL, Fan Y, Borah BJ, Mills RM, Klaskala W. Thromboprophylaxis and the Risk of Post-Discharge Venous Thromboembolism and Bleeding in Patients Undergoing Total Hip or Knee Arthroplasty. Value Health. 2012 Jun;15(4):A112-A.
29. Casez P, Labarere J, Sevestre MA, et al. ICD-10 hospital discharge diagnosis codes were sensitive for identifying pulmonary embolism but not deep vein thrombosis. J Clin Epidemiol. 2010 Jul;63(7):790-7.
30. Launois R, Reboul-Marty J, Henry B. Construction and validation of a quality of life questionnaire in chronic lower limb venous insufficiency (CIVIQ). Qual Life Res. 1996 Dec;5(6):539-54.
31. Seidling HM, Phansalkar S, Seger DL, et al. Factors influencing alert acceptance: a novel approach for predicting the success of clinical decision support. J Am Med Inform Assoc. 2011 Jul-Aug;18(4):479-84.
32. Amin AN, Lin J, Johnson BH, Schulman KL. Clinical and economic outcomes with appropriate or partial prophylaxis. Thromb Res. 2010 Jun;125(6):513-7.
33. Marco P, Lopez-Abadia E, Lucas J. More on thromboprophylaxis: electronic alerts in hospitalized patients at risk of venous thromboembolism. Thromb Haemost. 2008 Oct;100(4):525-6.
34. Chopard P, Dorffler-Melly J, Hess U, et al. Venous thromboembolism prophylaxis in acutely ill medical patients: definite need for improvement. J Intern Med. 2005 Apr;257(4):352-7.
35. Kakkar AK, Mueller I, Bassand JP, et al. Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry. PLoS One. 2013;8(5):e63479.
36. McCarney R, Warner J, Iliffe S, van Haselen R, Griffin M, Fisher P. The Hawthorne Effect: a randomised, controlled trial. Bmc Med Res Methodol. 2007;7:30.

Figure Legends

Figure 1: Synoptic view of the EHR. The mouse cursor displayed in the top right section points to the VTE reminder bar.

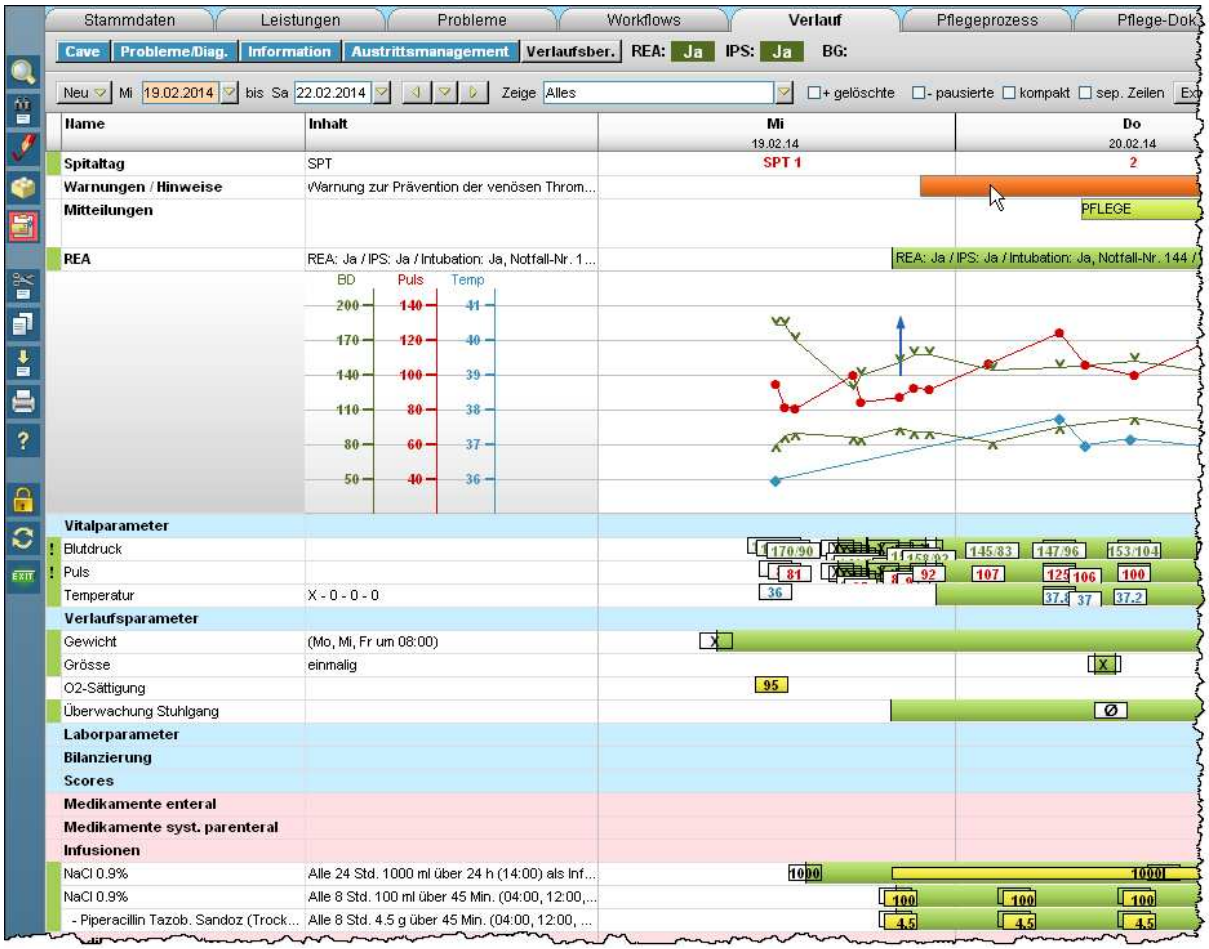

Figure 2: Pop-up window showing guidelines for assessing a patient's VTE risk (based on (26, 27)).