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ORIGINAL ARTICLE

Impact of a Program to Improve Venous Thromboembolism Prophylaxis on Incidence of Thromboembolism and Bleeding Rates in Hospitalized Patients During Implementation of Programs to Improve Venous Thromboembolism Prophylaxis

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Abstract

Objective: To study the impact of multiphase quality improvement efforts to enhance appropriate use of chemical and mechanical venous thromboembolism (VTE) prophylaxis (VTEP) on the rate of hospital-acquired VTE and determine whether efforts have been associated with increased bleeding complications.

Patients and Methods: All adult inpatients discharged between January 1, 2005, and December 31, 2015, were included in the study. Retrospective interrupted time series analysis compared VTEP performance, VTE outcomes, and unintended consequences (derived from linked administrative and clinical data) across 5 improvement phases: baseline (January 1, 2005-December 31, 2006), paper order set phase (January 1, 2007-February 9, 2009), electronic order set phase (February 10, 2009-December 16, 2009), active reminder phase (December 17, 2009-May 31, 2012), and maintenance phase (June 1, 2012-September 30, 2015).

Results: Guideline VTEP plan adherence at the end of the study period (including documenting contraindications) reached 88.8% (654,138 of 736,384 patient days). Delivery of pharmacological VTEP increased from 43.9% (49,155 of 111,906 patients) to 60.8% (75,784 of 124,676 patients); delivery of mechanical or pharmacological VTEP increased less (65.0% [431,791 of 664,087 patient days] to 67.4% [496,625 of 736,384 patient days]). Mean VTE rates decreased from 4.6 per 1000 hospitalizations (21.7 VTEs per month) at baseline to 4.3 per 1000 hospitalizations (18.0 VTEs per month) during the maintenance phase ($P<.001$). More than 97% of patients who had development of VTE (534 of 548) received VTEP, but 65.7% (360 of 548) experienced gaps of 1 or more days in VTEP delivery. Measured in-hospital bleeding rates were fairly consistent over the study (4.6% [5,198 of 111,906 patients] at baseline to 5.3% [6,662 of 124,676 patients] during the reminder phase). There was little change in rates of 7-day readmission with bleeding or VTE.

Conclusion: Our VTEP project improved guideline compliance, increased the proportion of patients receiving VTEP, and was associated with a decrease in VTE. Gaps in VTEP delivery occurred despite protocoled order sets and electronic feedback. Further improvements in VTE may require new approaches.

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Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), is considered a preventable complication of surgical and medical hospitalizations.[1,2] Multiple clinical guidelines for VTE prophylaxis (VTEP) have emerged identifying acceptable practices.[3-5] However, multicenter studies have

Affiliations are at the end of this article.

reported use of appropriate VTEP in only 60% of medical and 42% of surgical inpatients.[6,7]

This study focuses on how deploying a standardized system ensuring that every patient receives a VTE risk evaluation and those above "low risk" receive active orders for pharmacological and/or mechanical prophylaxis as per guidelines influenced what prophylaxis patients received and VTE occurrence outcomes, as well as potential complications of VTEP. Specifically, our guidelines recommended that every patient would receive chemical VTEP, as appropriate, unless it was considered by the attending physician that either chemical VTEP was contraindicated, in which case mechanical VTEP was selected, or the patient was at low risk for VTE, in which case no VTEP was required. Our high-risk patient populations had both chemical and mechanical VTEP prechecked in our standardized order sets. However, for any patient declared to be at low risk, a reassessment of risk or contraindication was required every 3 days. In addition, any time VTEP orders were placed on hold for a procedure or other reason, the VTEP order was again requested after 24 hours.

At our institution, we have been working to improve VTEP for many years, utilizing several approaches. Prior studies elsewhere had identified several candidate methods to improve appropriate VTEP, including passive diffusion of guidelines, enhanced education, general and targeted reminders, audit and feedback, and use of order sets.[8,9] We determined that (1) embodying local expert consensus regarding accepted published guidelines into order sets and then (2) mandating order set use at critical times (admission or transfer) would be our initial approach for improvement, as previously reported.[10] This process was implemented by placing mandatory sections addressing VTEP initially into our paper order sets and subsequently into electronic admission and transfer order sets. During these efforts, we transitioned to full computerized physician order entry. By making the clinician's decision regarding risk for VTE and type of VTEP discrete via the order set, we enabled logic to automate computer surveillance with electronic prompts directing clinicians to make decisions regarding VTEP throughout the hospitalization period.[10,11] Similar to prior studies that suggested multimodality approaches (including education, prompts, forcing functions, audit and feedback), we found that combining approaches had the best chance of sustained improvement[8,9] and resulted in more consistent ordering of guideline-appropriate VTEP.[10] Our recent reports show 0 defects in initial VTEP for more than a year in most of our institutions, including Mayo Clinic Hospital.[11] It is difficult to conclude, however, that efforts to improve ordering of VTEP or that current standardized quality metrics result in actual reductions in hospital-acquired VTE.

We have previously reported our efforts to improve the use of VTEP in our institution.[10,11] The aim of this study was to investigate whether our quality improvement efforts for VTEP over time have improved the rate of hospital-acquired VTE and whether efforts have been associated with increased bleeding complications.

PATIENTS AND METHODS

According to policy activities that constitute research at our institution, this work met criteria for operation improvement activities exempt from ethics review. This study is an interrupted time series assessment of VTEP efforts, VTE outcomes, and potential adverse consequences of our approach to improve VTEP.

Study Population and Setting

The study population included all adult inpatients discharged between January 1, 2005, and December 31, 2015, at Mayo Clinic Hospital in Rochester, Minnesota. Mayo Clinic Hospital is a large academic medical center with a level I trauma center and provides services ranging from primary care including obstetrics and pediatrics to tertiary and quaternary care. It has 2207 hospital beds spread over 2 campuses and averaged between 5500 and 6000 hospital discharges per month during the study.

VTEP Improvement Program

The improvement efforts are broken into 5 phases:

(1) Baseline (January 1, 2005-December 31, 2006). Venous thromboembolism prophylaxis practices were managed independently by each attending physician.

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(2) Paper order set phase (January 1, 2007-February 9, 2009). Paper-based VTEP sections were developed and included in all major postoperative and admission order sets. No "forcing function" existed other than policy with local reinforcement by pharmacists. There was also no consistent electronic record of the physician's decision against VTEP, such as contraindication or low risk.

(3) Electronic order set phase (February 10, 2009-December 16, 2009). The clinician was forced to use an electronic admission, postoperative, or transfer order set that contained a mandatory VTEP section. Physicians needed to specify if a patient was at low risk and explain why none of the VTEP options applied. Otherwise, an active VTEP order was required. These decisions were stored electronically and were available for analysis.

(4) Reminder phase (December 17, 2009-May 31, 2012). Because the clinician's decision regarding the VTEP plan was stored discretely and resulted in an active order, computer surveillance to detect guideline deviations, such as a pharmacological VTEP withheld for 24 hours or low-risk hospitalization for 72 hours or longer, was possible. When these types of conditions were met, ordering physicians were confronted with reminders to address VTEP.

(5) Maintenance phase (June 1, 2012-September 30, 2015). Electronic orders and reminders remained active throughout the maintenance phase. During this phase, we monitored the rate of VTEP orders and intervened by specific inquiry whenever a given service or physician exceeded the mean reminder rate by 3 SDs. This situation was rare and usually reflected a change in practice or order set or a provider who was not well acquainted with our electronic health record system. Although we could monitor orders for VTEP and the rate of VTE occurrence throughout the entire study period, we were only able to assess VTEP delivery through May 31, 2012, because of constraints on medication record access.

Statistical Analyses

Taking advantage of the natural experiment of implementing a series of VTEP interventions, we performed interrupted time series analysis (ITSA) using Markov chain Monte Carlo (MCMC) models on a monthly basis for the entire institution, comparing rates of prophylaxis performance, VTE outcomes, and unintended consequences incorporating random effects for time to adjust for autocorrelation.[12]

All data utilized in this study were retrospectively gathered from clinical and administrative databases. Medication administration information, mechanical prophylaxis use, hospital admissions data, laboratory measurements, and blood product utilization were obtained from clinical sources for the entire time frame. All data were extracted by person and date. Clinical data were found for all discharges identified.

To assess VTEP implementation, we measured daily rates of VTEP delivery. Pharmacological prophylaxis was determined by the administration of selected anticoagulants with specified dosage volume obtained from medication administration data (Supplemental Appendix 1, available online at https://mcpiqojournal.org/) to count as meeting daily pharmacological prophylaxis. Documentation of utilization of specified devices from nursing flow sheets was counted as meeting mechanical prophylaxis. Overall daily rates of prophylaxis reflect the average percentage of days in the hospital with any evidence of either chemical and/or mechanical prophylaxis.

During the electronic order set and reminder phases, any specific reasons to not order VTEP were recorded in the electronic record. During these periods, we assessed both VTEP delivered and the compliance with clinical guidance examining the order. Guideline adherence was assumed if there was either VTEP delivered or specific documentation of accepted reasons to not use VTEP, such as low risk of VTE or contraindication to both pharmacological and mechanical VTEP. Although these data may have been included in the hospital notes during the earliest 2 stages, it remained infeasible to extract.

Our primary outcome was assessed by the presence of an acquired VTE, defined as a PE or DVT not present at hospital admission. To identify VTE, we used *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes from hospital billing data as used by the Agency for Healthcare Research and Quality Patient Safety Indicators

TABLE 1. General Descriptive Patient Information for Each of the Venous Thromboembolism Prophylaxis Program Phases

Variable	Baseline (N=59,869)	Paper order set phase (N=49,799)	Electronic order set phase (N=17,847)	Reminder phase (N=81,693)	Maintenance phase (N=87,878)
Phase duration (mo)	24	25	11	29	40
Discharges per period	111,906	116,946	45,593	124,676	166,926
Patient age (y), mean ± SD	59±18.61	59±18.54	58±18.48	58±18.71	59±18.96
Length of stay (d), mean ± SD	5.0±7.6	5.1±7.9	4.9±7.5	5.0±7.3	5.0±7.5
Surgical cases, No. (%)	36,267 (50.3)	32,148 (51.0)	12,431 (54.7)	47,132 (48.8)	52,303 (47.8)

(PE: 415.1, 415.11, 415.19; DVT: 451.11, 451.19, 451.2, 451.81, 451.9, 453.40, 453.41, 453.42, 453.8, 453.9).[13] We report the percentage of patients admitted each month with an acquired VTE not present on admission, and each occurrence of VTE was examined individually.[14]

One concern with pharmacological VTEP is increasing risk for bleeding. We focused on 4 potential countermeasures: indications of bleeding during the hospitalization, readmissions to the hospital or emergency department within 7 days for bleeding, readmissions for a DVT/PE, and hospital readmissions within 7 days for any other reason. We used readmissions within 7 days to focus on issues related to the hospitalization rather than issues related to the transition of care or postacute period. Readmissions for other reasons were included to assess secular trends and help determine whether readmissions for VTE or bleeding were affected by VTEP changes. Other institutional initiatives were trying to reduce all readmissions.

To consistently and objectively identify patients with bleeding over time, we used a modification of the TIMI bleeding criteria,[14] whereby the patient needed at least 2 of 4 possible criteria: (1) notable decrease in hemoglobin level (≥4 g/dL), (2) use of any blood products, (3) clinical diagnosis of bleeding in problem list, or (4) return to surgery for bleeding among patients with interventional procedures or surgery. Requiring 2 criteria has been found to reduce the rate of false-positive identification. We have published details of these criteria and summarize them in Supplemental Appendix 2 (available online at https://mcpiqojournal.org/).[15] To be counted as a readmission for VTE or bleeding, the condition could either be present on the readmission or develop during the readmission.

To further assess the linkage between the intervention and the outcomes, we examined the prophylaxis status of the cases with VTE during the electronic order set and reminder stages of our improvement program.

Monthly rates of the variables of interest were analyzed using an ITSA model. This model was fit using MCMC methods via an interface to the JAGS software through the R statistical programming language (R Foundation for Statistical Computing). The MCMC technique is well known to be a reliable and robust approach to fitting complex mixed-effects models.[12] Weakly informative prior distributions were assumed for all parameters, and results were not dependent on the specification of prior distributions within any reasonable range. All estimates reported are the posterior mean of the corresponding model parameter comparing the baseline, paper, and reminder phases (maintenance phase was included with reminder for VTE outcomes). Uncertainty is represented via 90% credible intervals. Effects corresponding to a parameter with a credible interval that does not include 0 (or equivalently does not include 1 for a corresponding hazard ratio [HR]) are deemed significant.

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TABLE 2. Admissions and Hospital Days Patients Received Venous Thromboembolism Prophylaxis According to Improvement Phase[a,b]

Variable	Baseline (N=59,869 patients and 664,087 days)	Paper order set phase (N=49,799 patients and 708,623 days)	Electronic order set phase (N=17,847 patients and 267,907 days)	Reminder phase (N=87,878 patients and 736,384 days)
Any prophylaxis per discharge				
Mechanical	47,907 (42.8)	53,267 (45.5)	20,410 (44.8)	48,279 (38.7)
Chemical	49,155 (43.9)	61,514 (52.6)	25,372 (55.6)	75,784 (60.8)
Either	74,810 (66.9)	86,711 (74.1)	34,644 (76.0)	94,078 (75.5)
Neither	37,096 (33.1)	30,235 (25.9)	10,949 (24.0)	30,598 (24.5)
Daily prophylaxis status				
Mechanical delivered[c]	263,441 (39.7)	285,378 (40.3)	98,473 (36.8)	216,527 (29.4)
Pharmacological delivered[c]	298,645 (45.0)	362,846 (51.2)	143,164 (53.4)	406,279 (55.2)
Both delivered[c]	130,295 (19.6)	154,638 (21.8)	54,010 (20.2)	126,181 (17.1)
Either delivered[c]	431,791 (65.0)	493,586 (69.6)	187,627 (70.0)	496,625 (67.4)
Neither pharmacological nor mechanical delivered	232,296 (35.0)	215,037 (30.4)	80,280 (30.0)	239,759 (32.6)
Physician declared VTEP not indicated	NA[d]	NA[d]	66,242 (34.8)	322,133 (43.8)
Either VTEP delivered or not indicated	431,791 (65.0)[d]	495,405 (69.9)[d]	228,657 (85.4)	654,138 (88.8)

[a]NA = not available; VTEP = venous thromboembolism.
[b]Data are presented as No. (percentage) of patients or hospital days.
[c]Mechanical includes documented patient refusals in numerator. Chemical includes therapeutic treatments delivered in numerator.
[d]During these phases, there was unreliable documentation of "not indicated" in the record.

Because the time frame for electronic orders (11 months) was considered a phase-in for decision support, we excluded the electronic orders set phase for this analysis. Additionally, run charts were developed to visually assess potential changes.

RESULTS

General descriptive information on 399,121 adult inpatient encounters included in the analysis across the study phases (mean, 54,000 patients per year) is shown in Table 1. During the improvement efforts, compliance with VTEP guidelines (including documenting contraindications) improved to 88.8% (654,138 of 736,384 patient days) (Table 2). The proportion of patients who received VTEP at any time during hospitalization and the proportion of hospital days patients received any kind of VTEP is shown in Table 2. Generally, patients either received VTEP or had documentation that VTEP was not indicated on 85.4% (228,657 of 267,907) to 88.8% (654,138 of 736,384) of their hospital days and received active VTEP at some time during their stay 66.9% (74,810 of 111,906 patients) to 75.5% (94,078 of 124,676 patients) of the time (Table 2).

Table 2 the number of days patients received prophylaxis increased from 65.0% (431,791 of 664,087) at baseline to 69.6% (493,586 of 708,623) during the paper order set phase but declined to 67.4% (496,625 of 736,384) during the reminder phase. Delivered pharmacological VTEP increased from 43.9% (49,155 of 111,906 patient discharges) at baseline to 60.8% (75,784 of 124,676 patient discharges) during the reminder phase, but simultaneously, there was a decline in use of mechanical prophylaxis from 42.8% (47,907 of 111,906 patient discharges) at baseline to 38.7% (48,279 of 124,676 patient discharges) in the reminder phase.

Hospital-Acquired VTE

Venous thromboembolism rates increased in the more passive phases and then decreased during the reminder and maintenance phases (Figure 2). Mean VTE rates decreased from 4.6 per 1000 hospitalizations (21.7 VTEs per month) at baseline to 4.3 per 1000 hospitalizations (18.0 VTEs per month) during the maintenance phase ($P<.001$). Based on the ITSA

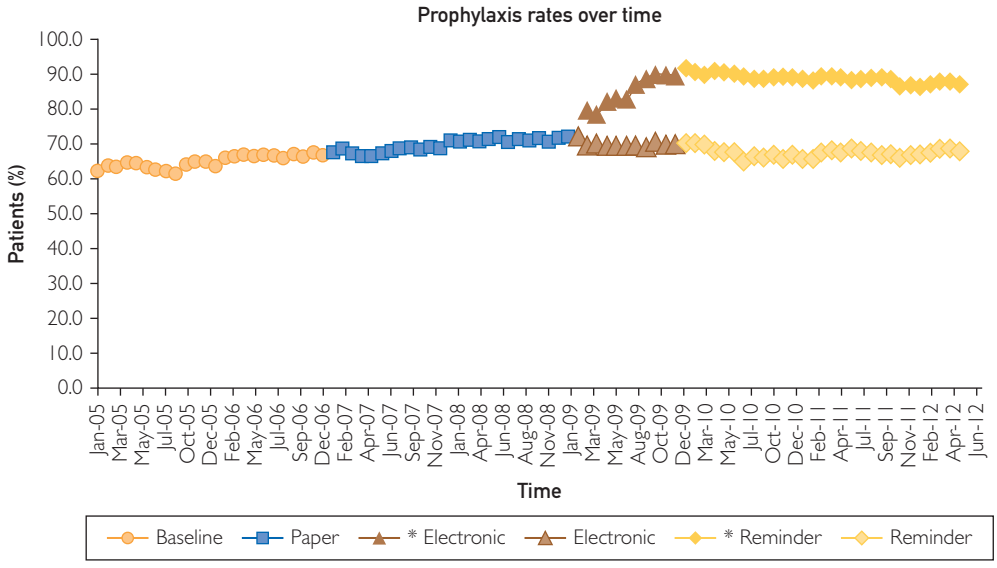

FIGURE 1. Prior to January 2009, we were only able to capture in the numerator patients who were given some form of venous thromboembolism prophylaxis (VTEP) (either mechanical or pharmacological). Beginning in January 2009, the electronic order set methods allowed routine documentation of circumstances in which the physician considered VTEP either not indicated or contraindicated. Figure shows the rates of delivered mechanical or pharmacological prophylaxis in the lower line after January 2009, and the upper line marked with an asterisk shows the total percentage of patients who had documentation of either delivered VTEP or documentation of indications why not ordered.

model, the VTE rate significantly decreased, with 30.9% fewer occurrences of VTE within the reminder period (537 of 123,256 patients [0.44%]) compared with the paper period (612 of 116,946 patients [0.52%]) ($P<0.001$). Improvements in VTE were noted in surgical patients (6.5 per thousand at baseline, 6.1 per 1000 during reminder phase), while no change was noted for medical patients (2.7 per 1000). Deep venous thrombosis rates accounted for the overall VTE rate changes. A significant decrease was observed in the DVT rate from the paper to the reminder phase ($P<0.001$). Pulmonary embolism rates gradually increased from baseline through the reminder period but returned to baseline levels during the maintenance phase.

Countermeasures

Seven-day readmission rates with any diagnosis of VTE declined significantly during the reminder phase (3.0 per 1000 at baseline, 3.4 per 1000 during the paper phase, 2.5 per 1000 during the reminder phase; $P<0.001$).The rates of all-cause 7-day readmissions decreased with each analyzed phase (7.2% [8,006 of 111,906 patient discharges] at baseline, 6.8% [7,947 of 116,946 patient discharges] during the paper phase, 6.6% [9,650 of 145,776 patient discharges] during the reminder phase).

Measured bleeding rates increased over time (4.6% [5,198 of 111,906 patient discharges] at baseline, 3.9% [4,592 of 116,946 patient discharges] during the paper phase, 5.3% [6,662 of 124,676 patient discharges] during the reminder phase), with the rate in reminder phase being 1.23 times higher than during the paper phase (HR, 1.23; 95% CI, 0.97-1.49). This increase was significant among those with chemical prophylaxis (HR, 1.25; 95% CI, 1.00-1.53; $P=0.05$). When we focused on patients without any pharmacological prophylaxis, bleeding rates remained stable. Readmission rates due to bleeding were consistent over time (1.3% [1,394 of 111,906 patient discharges] at baseline, 1.1% [1,299 of 116,946 patient discharges] during

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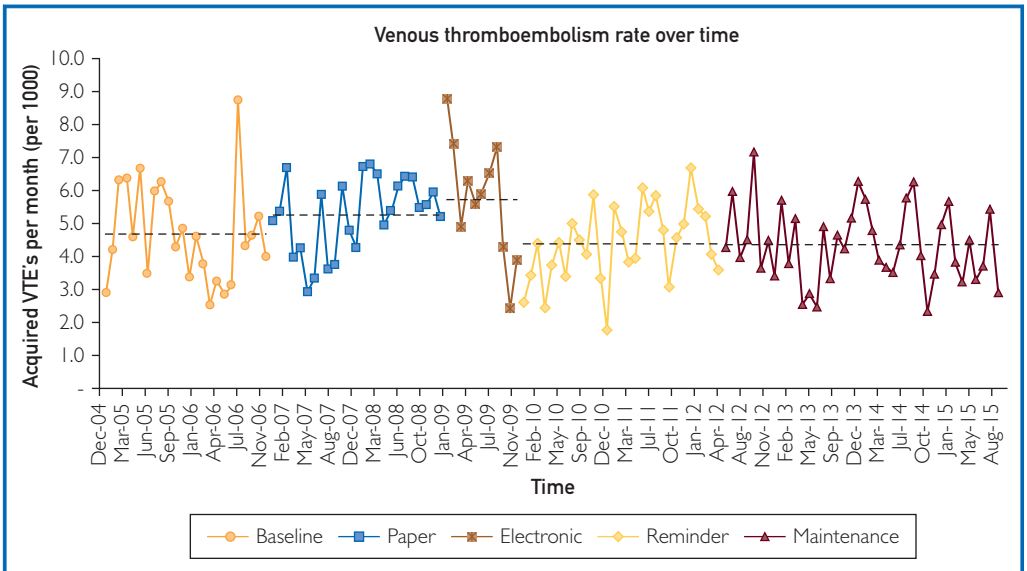

FIGURE 2. Actual rates of confirmed venous thromboembolism are shown during the 5 phases of the improvement project. Actual rates of venous thromboembolism improved in a sustained way from the mean of 4.6 per 1000 discharges during baseline to 4.3 per 1000 discharges during the maintenance phase.

the paper phase, 1.3% [1,929 of 145,776 patient discharges] during the reminder phase).

Prophylaxis History for Patients with VTE Events

During the index hospitalization, 196 DVTs and 93 PEs were identified (257 with either) during the electronic orders phase. During the reminder phase, there were 333 DVTs and 285 PEs (548 with either). Table 3 provides information on prophylaxis type prior to the identification of the VTE for these inpatients. Only 6 of 257 patients (2.3%) with hospital VTE during the electronic phase and 14 of 548 patients (2.6%) during the active reminder phase through May 2012 had no documented VTEP prior to their event. About half of the patients with VTE had both chemical and mechanical prophylaxis recorded. The gap in delivery of VTEP was different during these phases between those with VTE (534 of 805 cases with ≥1 day gap [66.3%] and 5,024 of 23,475 days without VTEP [21.3%]) and those without

TABLE 3. Prophylaxis Type Used Before VTE Event

Variable	Discharges with VTE	Prophylaxis type (%)					Discharges with ≥1 d without prophylaxis (%)	Days without prophylaxis/total days (%)
		None	Chemical	Mechanical	Either	Both		
Electronic order set phase								
DVT	196	4 (2.0)	186 (94.9)	113 (57.7)	192 (98.0)	107 (54.6)	141 (71.9)	1,265/6,301 (20.1)
PE	93	2 (2.2)	91 (97.8)	60 (64.5)	91 (97.8)	60 (64.5)	55 (59.1)	322/2,305 (14.0)
Either	257	6 (2.3)	245 (95.3)	151 (58.8)	251 (97.7)	145 (56.4)	174 (67.7)	1,390/7,423 (18.7)
Reminder phase								
DVT	333	5 (1.5)	317 (95.2)	195 (58.6)	328 (98.5)	184 (55.3)	227 (68.2)	1,869/9,471 (19.7)
PE	285	9 (3.2)	274 (96.1)	159 (55.8)	276 (96.8)	157 (55.1)	180 (63.2)	2,021/8,929 (22.6)
Either	548	14 (2.6)	521 (95.1)	305 (55.7)	534 (97.4)	292 (53.3)	360 (65.7)	3,634/16,052 (22.6)

DVT = deep venous thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

VTE (92,888 of 169,464 cases with ≥1 day gap [54.8%] and 394,096 of 1,173,074 days without VTEP [33.6%]). More than 97% of patients who had development of VTE (534 of 548) received VTEP, but 65.7% (360 of 548) experienced gaps of 1 or more days in VTEP delivery.

DISCUSSION

Our VTEP quality improvement project was associated with notably increased internal VTEP guideline compliance ordering but only a small increase in actual VTEP delivery. The daily delivery of either pharmacological or mechanical VTEP increased only very modestly from 65.0% to 67.4%. This system performance was associated with only a small decrease in actual rate of VTE over the study period (4.6 per 1000 discharges to 4.3 per 1000 discharges from baseline to maintenance). This finding suggested that gaps in care might be responsible for the lack of improvement. Considering the entire inpatient population, the gap between receiving a guideline-consistent VTEP order and VTEP delivery was between 4.8% and 11.2% (difference between "not indicated" and "neither delivered" in Table 2). However, as we further analyzed what proportion of patients with VTE had gaps in VTEP, we found that although less than 3% of patients with a hospital-acquired VTE did not receive at least one form of VTEP during hospitalization, there were between 18.7% and 22.6% of days when no VTEP was delivered even when ordered (Table 3). This finding suggests the possibility that improved consistency in VTEP delivery might result in actual reductions in VTE. Our data do not help us determine why there were such gaps in delivery. It is possible that lapses occurred when clinical circumstances suggested to nurses, physicians, and/or patients that pharmacological or mechanical VTEP was unwanted because of a sense of increased risk or was no longer indicated—perhaps reflecting a tendency by clinicians to underestimate VTE risk. A recent study found that although various members of the health care team might be aware that acutely ill patients in the intensive care unit without contraindications should receive VTEP, translating that knowledge into individual patient care decisions may falter and that this translation may be most manifest in patients with higher severity of illness.[16] Another possibility is that VTEP used in mixed populations in real practice may not produce the expected reductions in VTE. For example, Stelfox et al[17] found that improvement efforts resulting in increased utilization of low-molecular-weight heparin from 45.9% to 78.3% did not result in a significant difference in the adjusted odds of VTE in a critically ill population. One other consideration is the potential role for surveillance bias, in which our efforts to educate physicians about the risk of VTE may have resulted in greater testing for VTE and thereby detecting more VTEs.[18,19] Our study design does not permit evaluation of this contribution to the less than hoped for decline in VTE.

We also determined that our improvement efforts may have increased the risk for bleeding. Delivery of pharmacological VTEP increased substantially from 45.0% to 55.2% (Table 2). Over the same period, bleeding rates increased from 4.6% at baseline to 5.3% in the reminder phase. Although this finding bears further exploration, there was no increase in bleeding-related readmission rates. Meanwhile, we saw reduced 7-day VTE-related readmissions, suggesting that appropriate admission use of VTEP during the index hospitalization may have prevented postdischarge incidence or discovery of VTE.

The improvement in guideline adherence and VTEP delivery in our center was similar to that previously reported, with improvements seen at each phase of the intervention.[9,20] The Johns Hopkins Venous Thromboembolism Collaborative saw an improvement with paper order sets to reduce symptomatic VTE and increase appropriate VTEP prescriptions from 27% to 98% in one area and from 33% to 62% in a sample of 226 patients.[20] When adding electronic ordering and clinical decision support to their model, findings were similar to ours in that VTE rates decreased. However, the Johns Hopkins group reported no difference in major bleeding.[21] Bleeding definitions used in that study were based on the International Society on Thrombosis and Haemostasis definition (hemoglobin decline of ≥2 g/dL or transfusion of 2 or more units of blood or bleeding into a critical organ such as the brain,

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gastrointestinal tract, or eye), whereas we additionally included use of any blood product or any clinical note listing bleeding in the problem list.

Despite an increase in VTEP use, we found gaps in VTEP delivery in up to 22.6% of patients who had VTEs. Ma et al[22] reported gaps in 40% of patients who had development of VTE in their series after improvement efforts involving education and consensus policy implementation. In their population, in addition to lapses in dosing, they found that up to 50% of patients received no VTEP. A recent analysis of academic hospital patients reported some VTEP use in only 54% of medically ill patients.[23] These rates contrast with ours, in which more than 97% of patients received at least some VTEP. These results highlight the common finding that clinician education and policy alone are rarely sufficient to eliminate practice variations. In a recent study evaluating what interventions were considered most influential in an improvement effort to increase VTEP among intensive care unit patients, local champions, verbal reminders to prescribers, and changes to the computer order entry system were most highly valued.[24] We found that achieving higher levels of reliable delivery of VTEP required forcing functions (order sets) and reminders, in addition to consensus guideline formation and education.[11]

The finding of increased bleeding in patients receiving pharmacological VTEP is concerning. Khanna et al[25] studied the effect of implementing paper order set prompts to use VTEP. They found a small increase in the use of pharmacological VTEP (51% to 58%) but did not find an actual increase in overall bleeding. Their study involved only 26,064 admissions and may have been underpowered to detect a small increase in actual hemorrhage. We must consider if our system—which tends to promote VTEP—might be increasing the bleeding risk for some patients. Our system relies on clinicians to properly determine the relative risk and benefit ratios; data analytics may improve the assessment.

Perceptions and attitudes about the need for VTEP in the new era of medical and surgical care are continually debated.[26] Some surgical studies using administrative rather than clinical data have suggested no clear relationship between delivery of VTEP and VTE outcomes.[27,28] In our study, we found relatively small, but important, reductions in VTE rates associated with improvements in VTEP delivery in a medical/surgical hospital population. The varied results, combined with our findings of a slight increase in bleeding, suggest the need for new randomized controlled trials in surgical practice areas where surgical technique and implementation of enhanced recovery pathways put us in a new paradigm of care with less trauma/invasiveness for patients.

Our study had several limitations, including that it was performed at a single academic medical center. However, we believe it would be informative if these measures and analyses were replicated in other settings. The reliance on diagnosis codes to identify DVT and PE is another limitation. However, our definitions for DVT and PE were based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes used by the Agency for Healthcare Research and Quality Patient Safety Indicators, the validity of which has been studied.[29] Although we could electronically determine whether chemical or mechanical VTEP was provided each day, not until electronic orders were implemented in 2009 were we able to determine whether those not receiving VTEP were clinically indicated.

CONCLUSION

Improving adherence to VTEP guideline therapy using a multimodality approach that included forcing functions via order sets and logic-driven reminders resulted in a small reduction in actual VTE. Despite these functions, there were missed opportunities for VTEP delivery in up to one-quarter of patients who experienced VTE. Over half of the patients with new VTEs had received both pharmacological and mechanical VTEP throughout their hospitalization. We saw a slight increased risk for bleeding. These findings suggest that a new approach to VTEP is needed, stressing convenience and effectiveness of VTEP, and improved analytics to guide risk assessments and clinical reminder systems.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **DVT** = deep venous thrombosis; **HR** = hazard ratio; **ITSA** = interrupted time series analysis; **MCMC** = Markov chain Monte Carlo; **PE** = pulmonary embolism; **VTE** = venous thromboembolism; **VTEP** = VTE prophylaxis

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REFERENCES

1. Leibson CL, Needleman J, Buerhaus P, et al. Identifying in-hospital venous thromboembolism (VTE): a comparison of claims-based approaches with the Rochester Epidemiology Project VTE cohort. *Med Care*. 2008;46(2):127-132.
2. Heit JA. Venous thromboembolism: disease burden, outcomes and risk factors. *J Thromb Haemost*. 2005;3(8):1611-1617.
3. 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;133(6, suppl):381S-453S.
4. Qaseem A, Chou R, Humphrey LL, Starkey M, Shekelle P. Clinical Guidelines Committee of the American College of Physicians. Venous thromboembolism prophylaxis in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2011;155(9):625-632.
5. Treasure T, Hill J. NICE guidance on reducing the risk of venous thromboembolism in patients admitted to hospital. *J R Soc Med*. 2010;103(6):210-212.
6. Cohen AT, Tapson VF, Bergmann JF, et al. ENDORSE Investigators. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study [published correction appears in *Lancet*. 2008;371(9628):1914]. *Lancet*. 2008;371(9610):387-394.
7. Tapson VF, Decousus H, Pini M, et al. IMPROVE Investigators. Venous thromboembolism prophylaxis in acutely ill hospitalized medical patients: findings from the International Medical Prevention Registry on Venous Thromboembolism. *Chest*. 2007;132(3):936-945.
8. Tooher R, Middleton P, Pham C, et al. A systematic review of strategies to improve prophylaxis for venous thromboembolism in hospitals. *Ann Surg*. 2005;241(3):397-415.
9. Kahn SR, Morrison DR, Cohen JM, et al. Interventions for implementation of thromboprophylaxis in hospitalized medical and surgical patients at risk for venous thromboembolism. *Cochrane Database Syst Rev*. 2013;7:CD008201.
10. Morgenthaler TI, Lovely JK, Cima RR, et al. Using a framework for spread of best practices to implement successful venous thromboembolism prophylaxis throughout a large hospital system. *Am J Med Qual*. 2012;27(1):30-38.
11. Morgenthaler TI, Rodriguez V. Preventing acute care-associated venous thromboembolism in adult and pediatric patients across a large healthcare system. *J Hosp Med*. 2016;11(suppl 2):S15-S21.
12. Gelman A, Hill J. *Data Analysis Using Regression and Multilevel/Hierarchical Models*. New York, NY: Cambridge University Press; 2007.
13. Farrow NE, Lau BD, JohnBull EA, et al. Is the Meaningful Use Venous Thromboembolism VTE-6 measure meaningful? a retrospective analysis of one hospital's VTE-6 cases. *Jt Comm J Qual Patient Saf*. 2016;42(9):410-416.
14. Moriarty JP, Finnie DM, Johnson MG, Huddleston JM, Naessens JM. Do pre-existing complications affect the failure to rescue quality measures? *Qual Saf Health Care*. 2010;19(1):65-68.
15. Moriarty JP, Daniels PR, Manning DM, et al. Going beyond administrative data: retrospective evaluation of an algorithm using the electronic health record to help identify bleeding events among hospitalized medical patients on warfarin. *Am J Med Qual*. 2017;32(4):391-396.
16. Sauro K, Bagshaw SM, Niven D, et al. Barriers and facilitators to adopting high value practices and de-adopting low value practices in Canadian intensive care units: a multimethod study. *BMJ Open*. 2019;9(3):e024159.
17. Stelfox HT, Brundin-Mather R, Soo A, et al. A multicentre controlled pre-post trial of an implementation science intervention to improve venous thromboembolism prophylaxis in critically ill patients. *Intensive Care Med*. 2019;45(2):211-222.
18. Bilimoria KY, Chung J, Ju MH, et al. Evaluation of surveillance bias and the validity of the venous thromboembolism quality measure. *JAMA*. 2013;310(14):1482-1489.
19. Ju MH, Chung JW, Kinnier CV, et al. Association between hospital imaging use and venous thromboembolism events rates based on clinical data. *Ann Surg*. 2014;260(3):558-564.
20. Streiff MB, Lau BD, Hobson DB, et al. The Johns Hopkins Venous Thromboembolism Collaborative: multidisciplinary team approach to achieve perfect prophylaxis. *J Hosp Med*. 2016;11(suppl 2):S8-S14.
21. Zeidan AM, Streiff MB, Lau BD, et al. Impact of a venous thromboembolism prophylaxis "smart order set": improved compliance, fewer events. *Am J Hematol*. 2013;88(7):545-549.

22. Ma KA, Cohen E, Kahn SR. Venous thromboembolism in hospitalized patients: an updated analysis of missed opportunities for thromboprophylaxis at a university-affiliated tertiary care center. *Vasc Med*. 2014;19(5):385-391.
23. Khanna R, Maynard G, Sadeghi B, et al. Incidence of hospital-acquired venous thromboembolic codes in medical patients hospitalized in academic medical centers. *J Hosp Med*. 2014;9(4):221-225.
24. Sauro KM, Brundin-Mather R, Parsons Leigh J, et al. Improving the adoption of optimal venous thromboembolism prophylaxis in critically ill patients: a process evaluation of a complex quality improvement initiative. *J Crit Care*. 2019;50:111-117.
25. Khanna R, Vittinghoff E, Maselli J, Auerbach A. Unintended consequences of a standard admission order set on venous thromboembolism prophylaxis and patient outcomes. *J Gen Intern Med*. 2012;27(3):318-324.
26. Louis SG, Sato M, Geraci T, et al. Correlation of missed doses of enoxaparin with increased incidence of deep vein thrombosis in trauma and general surgery patients. *JAMA Surg*. 2014;149(4):365-370.
27. JohnBull EA, Lau BD, Schneider EB, Streiff MB, Haut ER. No association between hospital-reported perioperative venous thromboembolism prophylaxis and outcome rates in publicly reported data. *JAMA Surg*. 2014;149(4):400-401.
28. Nicholas LH, Osborne NH, Birkmeyer JD, Dimick JB. Hospital process compliance and surgical outcomes in Medicare beneficiaries. *Arch Surg*. 2010;145(10):999-1004.
29. Henderson KE, Recktenwald A, Reichley RM, et al. Clinical validation of the AHRQ postoperative venous thromboembolism patient safety indicator. *Jt Comm J Qual Patient Saf*. 2009;35(7):370-376.