JAMA Surgery | Review

Venous Thromboembolism Prevention in Emergency General Surgery
A Review

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IMPORTANCE Venous thromboembolism (VTE) is the most preventable cause of morbidity and mortality in US hospitals, and approximately 2.5% of emergency general surgery (EGS) patients will be diagnosed with a VTE event. Emergency general surgery patients are at increased risk of morbidity and mortality because of the nature of acute surgical conditions and the challenges related to prophylaxis.

OBSERVATIONS MEDLINE, Embase, and the Cochrane Database of Collected Reviews were searched from January 1, 1990, through December 31, 2015. Nearly all operatively and nonoperatively treated EGS patients have a moderate to high risk of developing a VTE, and individual risk should be assessed at admission. Pharmacologic prophylaxis in the form of unfractionated or low-molecular-weight heparin should be considered unless an absolute contraindication, such as bleeding, exists. Patients should receive the first dose at admission to the hospital, and administration should continue until discharge without missed doses. Certain patient populations, such as those with malignant tumors, may benefit from prolonged VTE prophylaxis after discharge. Mechanical prophylaxis should be considered in all patients, particularly if pharmacologic prophylaxis is contraindicated. Studies that specifically target improved adherence with VTE prophylaxis in EGS patients suggest that efficacy and quality improvement initiatives should be undertaken from a system and institutional perspective.

CONCLUSIONS AND RELEVANCE Operatively and nonoperatively treated EGS patients are at a comparatively high risk of VTE. Despite gaps in existing literature with respect to this increasing patient population, successful best practices can be applied. Best practices include assessment of VTE risk, optimal prophylaxis, and physician, nurse, and patient education regarding the use of mechanical and pharmacologic VTE prophylaxis and institutional policies.

JAMA Surg. 2018;153(5):479-486. doi:10.1001/jamasurg.2018.0015
Published online March 14, 2018.

Supplemental content

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Venous thromboembolism (VTE) represents the most preventable cause of morbidity and mortality in hospitalized patients,[1] and the Agency for Healthcare Research and Quality (AHRQ) suggests appropriate VTE prophylaxis as a top patient safety practice.[2] The burden of operative and nonoperative emergency general surgery (EGS) is increasing and represents 7% of all hospital admissions in the United States. The reported rate of VTE among patients undergoing EGS is approximately 2.5%.[3]

Numerous observational studies,[4] quality improvement studies,[5] randomized clinical trials,[6] reviews,[7] and practice management guidelines[8] are available to guide acute care surgeons in VTE prevention for patients with trauma. However, little guidance is available for the emergency general surgeon. Patients undergoing EGS represent a challenge regarding VTE prevention.[9] Despite the substantial number of annual EGS admissions, little is known about the risk of VTE or the use of mechanical and/or pharmacologic prophylaxis in EGS patients. Furthermore, although guidelines for VTE prophylaxis are available,[10,11] they are difficult to interpret in the context of admission to an EGS service for an acute condition, particularly when admissions to such services include as many as 70% of patients who do not require operative intervention.[9] The purpose of this narrative review is to apply the existing literature on VTE prophylaxis to this challenging group of EGS patients and offer recommendations using the best available evidence.

Methods

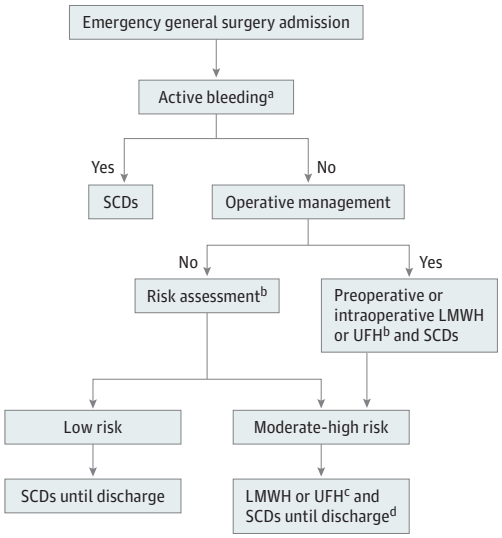
We performed an electronic literature search of MEDLINE, EMBASE, and the Cochrane Database of Collected Reviews from January 1,

Table 1. Summary of Studies on VTE Prophylaxis in EGS Patients

Source	Study Design	Included Patients	No.	Intervention	Process Improvement	VTE Rate
Bergqvist et al,[13] 1996	RCT	Emergency abdominal surgery	80	Placebo vs LMWH	NA	Placebo (22%) and LMWH (8%)
Stevenson et al,[14] 2007	Prospective cohort	Acute surgical unit	793	QI intervention	Appropriate VTE prophylaxis increase from 73% to 86%	Not reported
McKenna et al,[15] 2008	Prospective cohort	Acute surgical admission	51	QI intervention	Appropriate VTE prophylaxis increase from 37% to 88%	Not reported
Kreckler et al,[16] (2013), and McCulloch et al,[17] 2010	Prospective cohort	EGS ward	2083	QI intervention	Appropriate VTE prophylaxis increase from 35% to 87%	0.75% to 0.30% After intervention
Wandling et al,[18] 2017	Retrospective cohort	Operative and nonoperative EGS patients	2091	None	NA	0% (Nonoperative appendicitis) to 2.4% (nonoperative cholecystitis)

Abbreviations: EGS, emergency general surgery; LMWH, low-molecular-weight heparin; NA, not applicable; QI, quality improvement; RCT, randomized clinical trial; VTE, venous thromboembolism.

Figure. Algorithm Used to Assess Emergency General Surgery Patients and Decision on How to Provide Venous Thromboembolism Prophylaxis



LMWH indicates low-molecular-weight heparin; SCDs, sequential compression devices; and UFH, unfractionated heparin.

[a] Clinical, radiographic, or laboratory evidence.

[b] Risk assessment is shown in Table 3.

[c] Some patients, such as those with pelvic malignant tumors, may benefit from 28 days of LMWH treatment.

[d] Institution-specific, weight-based.

1990, through December 31, 2015, for randomized clinical trials, meta-analyses, systematic reviews, and observational studies (eTable in the Supplement). We also manually reviewed the most widely cited guidelines regarding VTE prophylaxis and institutional guidelines and policies. Emphasis was given to articles that specifically examined EGS patients, but similar patient cohorts were considered, specifically emergency surgery patients within the National Surgical Quality Improvement Program. Nonoperatively treated EGS patients are difficult to define, but for this review, we used the American Association for the Surgery of Trauma definition.[12] Overall, there was a paucity of studies that reported VTE prophylaxis in EGS patients (**Table 1**).[13-18] Because of a lack of level I evidence regarding VTE prophylaxis in EGS patients, we did not specifically grade the quality of evidence. However, we attempted to interpret heterogenic data from numerous published works (eg, primary research, guidelines, and epidemiologic studies) to make general recommendations for EGS patients based on the entire body of evidence (**Figure**).

Discussion

Clinical Risk Assessment

Available guidelines and risk assessment tools do not specifically address operatively or nonoperatively treated EGS patients but rather focus on VTE prevention and prophylaxis for acute care medical admissions, trauma, and elective surgical patients (**Table 2** and **Table 3**). Compared with elective surgical patients, operatively treated EGS patients are at an increased risk of VTE; the risk varies based on the underlying diagnosis. This underlying risk may range from 0.2% (appendectomy)[19] to 4% (colectomy)[20] in addition to patient-specific factors (eg, a history of VTE). Certain subpopulations, such as those undergoing EGS for malignant tumors or inflammatory bowel disease, may be at an even greater risk.[21,22] For instance, patients undergoing emergency colectomy for ulcerative colitis are at a nearly 2-fold increased risk of VTE (9%) compared with elective colectomy (5%).[23] Venous thromboembolism is more than 2.5 times more common after nonelective procedures than elective procedures for a broad range of major abdominal operations.[24] Although no study, to our knowledge, has directly compared rates of VTE in specific elective and EGS operations, in general, the morbidity and mortality associated with EGS is significantly higher than that associated with elective operations.[25,26] A pilot study[18] of EGS patients in the National Surgical Quality Improvement Program suggested rates of VTE as high as 2.4% in nonoperative treatment of acute cholecystitis.

The UK National Institute for Health and Care Excellence guidelines recognize that nearly all EGS patients are at an increased risk of VTE.[11] Specifically, the guidelines suggest that a patient with an "acute surgical admission with inflammatory or intra-abdominal condition"[11(p12)] is at an increased risk for VTE (Table 2). The American College of Chest Physicians guidelines do not specifically comment on nonoperatively treated surgical patients or nonelective surgical patients; rather, they recommend an assessment of thrombotic risk using a validated tool.[27] The AHRQ outlines methods for quality improvement, including the development of risk assessment

tools; however, no such validated tool exists for EGS patients.[28] For elective surgical patients, the Caprini[29] and Rogers scores[30] (Table 3) are 2 of the most commonly accepted risk assessment tools in medical and surgical patients. Attempting to apply these risk assessment tools is problematic in patients who are not undergoing elective surgery or who are admitted to a surgical service but treated nonoperatively. The Johns Hopkins clinical decision support tool for VTE risk assessment (Table 3) has been published examining a group of all patients admitted to surgical services, but data were not stratified to examine EGS patients specifically.[31] Although these tools have not been validated in the EGS patient population when considered, most if not all EGS patients are at moderate to high risk (Caprini score >2) for developing VTE. This finding is demonstrated on a population level when considering available descriptive data from the National Inpatient Sample[9] and the American College of Surgeons' National Surgical Quality Improvement Program.[3,32] Of all acute care surgical admission patients, more than 80% are older than 40 years, and 30% undergo an operative intervention,[9] most of which are laparoscopic procedures (appendectomy and cholecystectomy) that exceed 45 minutes in duration.[19] Among patients undergoing surgery, more than 70% have a body mass index (calculated as weight in kilograms divided by height in meters squared) greater than 25 (overweight), 40% have sepsis, and 80% have American Society of Anesthesiologists class 2 or greater disease.[33] When completing a VTE risk assessment at the individual level, one should consider the use of birth control or hormone replacement therapy, immobility, and underlying comorbidities, such as heart and lung disease or prior stroke.[31] We recommend the use of a standard, validated risk assessment tool (ie, Caprini, Rogers, Hopkins tools) for all EGS patients, and further research should attempt to validate VTE risk assessment in operatively and nonoperatively treated EGS patients.

Choice of Prophylaxis

The optimal VTE prophylaxis prevention strategy balances an individual patient's risk of VTE and the risk of bleeding. The 2 primary modalities of VTE prophylaxis are mechanical (eg, graduated compression stockings, intermittent pneumatic compression, sequential compression devices, and foot pumps) and pharmacologic (unfractionated heparin or low-molecular-weight heparin [LMWH]). Mechanical VTE prophylaxis works by reducing venous stasis that results in endothelial injury and clot formation and stimulates endothelial secretion of tissue plasminogen activator that promotes clot dissolution. Unlike pharmacologic prophylaxis, mechanical prophylaxis is not associated with an increased risk of bleeding complications. There are few contraindications to mechanical prophylaxis, but notable contraindications include lower-extremity wounds and severe peripheral arterial disease. Although the evidence supporting the use of graduated compression stockings is mixed, intermittent pneumatic compression and sequential compression devices are beneficial in reducing VTE events in many cohorts and in meta-analyses when used in isolation or in conjunction with pharmacologic prophylaxis.[34] However, it is important to frequently assess patients to ensure appropriate sizing to avoid development of pressure ulcers associated with mechanical prophylaxis use.[35] In the context of mechanical prophylaxis, ambulation is often misunderstood as adequate prophylaxis; however, the efficacy of ambulation and the amount of ambulation required to be effective is unknown and likely overstated.[36] On the basis of the available evidence, we recommend the use of mechanical prophylaxis with sequential compression devices in most patients and in particular those in whom pharmacologic VTE prophylaxis is contraindicated. We have stopped the routine use of graduated compression stockings for VTE prophylaxis in part because their use is associated with high rates of device-related pressure injury in the surgical intensive care unit.[35]

Pharmacologic VTE prophylaxis with unfractionated heparin or LMWH is highly effective for VTE prevention in hospitalized patients.[37,38] To our knowledge, there is only 1 randomized trial report[13] on the use of pharmacologic VTE prophylaxis (LMWH) in EGS patients. Bergqvist et al[13] found a reduction of postoperative VTE from 22% to 8% with the use of LMWH compared with placebo (Table 1). Pharmacologic prophylaxis is associated with a modest risk of bleeding complications. Contraindications to pharmacologic prophylaxis include active bleeding or the presence of disorders associated with a significant risk of bleeding, such as thrombocytopenia or coagulopathy. Furthermore, the pain of injections and the

Table 2. Summary of Guidelines for VTE Prophylaxis in Medical and Surgical Patients

Guideline	VTE Risk	Recommendations
National Institute for Health and Care Excellence	Acute surgical admission with inflammatory or intra-abdominal condition, surgery >60 min, significant reduction in mobility, additional risk factors related to Caprini[29] or Rogers[30] score	Risk stratify at admission, mobilize (not quantified), pharmacologic VTE prophylaxis,[a] mechanical VTE prophylaxis[b]
American College of Physicians	Individualized risk assessment of the risk of VTE and bleeding before initiating VTE prophylaxis	Pharmacologic VTE prophylaxis[a] in medical (including stroke) patients unless assessed risk of bleeding outweighs likely benefits, recommend against the use of mechanical VTE prophylaxis[b]
American College of Chest Physicians		
Nonorthopedic surgical patients	Assess risk with Caprini[29] or Rogers[30] score	Very low risk (<0.5%) (ambulation [not quantified]), low risk (1.5%) (mechanical VTE prophylaxis[b]), moderate risk (3%) (pharmacologic VTE prophylaxis[a]), high risk (6%) (pharmacologic[a] and mechanical VTE prophylaxis[b])
Medical patients	Acutely ill medical patients with active cancer, sepsis, IBD, or confined to bed	Pharmacologic VTE prophylaxis[a]
Thrombosis Canada		
General surgical patients	Assess risk as individual (Caprini score[29]) or as part of a group (undergoing surgery)	LMWH in most cases until discharge and for up to 30 d in patients at high risk for cancer
Medical patients	Balance risk factors (eg, acute inflammatory condition, recent surgery, or acute infectious disease) with bleeding risk	Patients at an increased risk for VTE (>1%) should receive LMWH unless at high risk for bleeding

Abbreviations: IBD, inflammatory bowel disease; LMWH, low-molecular-weight heparin; VTE, venous thromboembolism.

[a] Fondaparinox, LMWH, or unfractionated heparin (renal impairment).

[b] Antiembolic stocking, foot impulse devices, or intermittent pneumatic compression devices.

Table 3. Summary of Risk Assessment for VTE

Risk Factor	Caprini Score,[29] Points	Rogers Score,[30] Points	Johns Hopkins Risk Factors (Yes/No)[a]
Patient factors			
Age, y			Yes
41-60	1	NA	
61-74	2	NA	
≥75	3	NA	
Obesity (BMI>25)	1	NA`	NA
Female	NA	1	NA
Oral contraceptives or HRT	NA	NA	Yes
Congestive heart failure	NA	NA	Yes
Inflammatory bowel disease	1	NA	Yes
Swollen legs	1	NA	NA
Varicose veins	1	NA	NA
Major surgery within 1 mo	1	NA	NA
COPD	1	NA	NA
Malignant tumor (past or present)	2	2	NA
Chemotherapy within 30 d	NA	2	NA
History of DVT or PE	3	NA	NA
Hypercoaguable disorder	3	NA	Yes
Family history of thrombosis	3	NA	NA
Pregnancy or postpartum	1	NA	Yes
Unexplained stillbirth	1	NA	NA
Stroke (within 1-3 mo)	5	NA	Yes
Sepsis (within 1 mo)	1	NA	Yes
Immobility or bed rest	2	NA	Yes
Acute myocardial infarction	1	NA	NA
Multiple trauma (<1 mo)	5	NA	NA
Hip, pelvis, or leg fracture (<1 mo)	5	NA	NA
Perioperative factors			
Emergency	NA	1	NA
Major surgery (>45 min)	2	NA	NA
Major surgery (>2 h)	NA	NA	Yes
Laparoscopic surgery (>45 min)	2	NA	NA
Central venous access	2	NA	Yes
Operative location			NA
Respiratory tract	NA	9	
Stomach, intestines	NA	4	
Hernia	NA	2	
Arthroscopic	2		
ASA classification			NA
2	NA	1	
≥3	NA	2	
Work RVU			NA
10-17	NA	2	
>17	NA	3	
Transfusion >4 U of pRBCs	NA	2	NA
Ventilator dependent	NA	2	Yes
Serum sodium level >145 mEq/L	NA	2	NA
Wound classification 3 or 4	NA	1	NA
Albumin level <0.0035 g/dL	NA	1	NA
Preoperative hematocrit <38%	NA	1	NA
Preoperative bilirubin level <1.0 mg/dL	NA	1	NA

(continued)

Table 3. Summary of Risk Assessment for VTE (continued)

Risk Factor	Caprini Score,[29] Points	Rogers Score,[30] Points	Johns Hopkins Risk Factors (Yes/No)[a]
Risk stratification for VTE (total score)	NA	NA	NA
Very low	0	<7	
Low	1-2	7-10	
Moderate	3-4	>10	
High	≥5	NA	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; HRT, hormone replacement therapy; NA, not applicable; PE, pulmonary embolism; pRBCs, packed red blood cells; RVU, relative value unit; VTE, venous thromboembolism.

SI conversion factors: to convert sodium to millimoles per liter, multiply by 1; albumin to grams per liter, multiply by 10; hematocrit to proportion of 1, multiply by 0.01; and bilirubin to micromoles per liter, multiply by 17.104.

[a] The Johns Hopkins algorithm recommends that any surgical patients with any risk factor without risk of bleeding receive pharmacologic VTE prophylaxis.

associated costs are also worth considering, particularly when attempting to improve adherence with respect to VTE guidelines or implementing quality improvement initiatives.[39]

Because most operatively and nonoperatively treated EGS patients are at moderate to high risk of developing VTE, there should be consideration for pharmacologic VTE prophylaxis in all EGS patients unless an absolute contraindication, such as active bleeding, exists. This guideline is in keeping with recommendations by the UK National Institute for Health and Care Excellence and the American College of Chest Physicians for patients at moderate to high risk of developing VTE (Table 2). Thrombosis Canada, guided by the Canadian Patient Safety Institute, recommends that all general surgery patients, including EGS patients, receive standard prophylaxis, including heparin, until discharge unless contraindicated.[40] The choice of unfractionated heparin or LMWH varies among institutions, and specific recommendations for EGS patients are challenging to make. Review of the best available evidence in other patient populations, such as trauma,[41] suggests LMWH to be more effective with respect to VTE prevention, with a lower risk of bleeding and heparin-induced thrombocytopenia than unfractionated heparin. Further benefits include once-daily dosing, which reduces patient discomfort, reduces nursing time, and may improve adherence. Because of these benefits, our suggestion is to prescribe LMWH for all admitted EGS patients.

Finally, if contraindications to pharmacologic VTE prophylaxis exist, mechanical VTE prevention strategies should be considered even if the patient is ambulating. A reassessment of contraindications, such as bleeding, should be performed daily while the patient is in hospital.

Initiation and Discontinuation of Prophylaxis

The timing of initiation of VTE prophylaxis is an understudied area particularly in those patients thought to be at high risk of bleeding because of an underlying diagnosis, such as gastrointestinal tract bleeding. The safety of early VTE prophylaxis in EGS patients has not been specifically studied to our knowledge, but safety has been well accepted in elective surgical patients, which has resulted in lower VTE rates without an increase in transfusions.[42] All EGS patients should be risk stratified at admission, and VTE prophylaxis (mechanical and/or pharmacologic) should be initiated as soon as possible even if an operation is planned. The need for transfusions, hemodynamic instability, and a decreasing hemoglobin level all individually or additively indicate active bleeding and therefore may preclude pharmacologic but not mechanical prophylaxis.

In addition to initiating pharmacologic prophylaxis as early as possible, recent literature has highlighted the need to ensure that patients do not miss any doses of pharmacologic prophylaxis. In patients who miss 1 or more doses, the rate of VTE events is nearly 5-fold higher with a single missed dose.[43,44] Doses may be missed for a number of reasons: patient preference, nursing concerns, drug delivery, or withholding of doses by prescriber before a planned operation for fear of bleeding.[39,45,46] Pharmacologic VTE prophylaxis should not preclude the safety of most EGS operations and is regularly given during elective general surgery. Unless specific regional anesthetic techniques, including epidural placement, are planned, pharmacologic VTE prophylaxis does not need to be withheld for any amount of time preoperatively. Further challenges arise when prophylaxis is withheld and the operation is delayed or canceled resulting in patients missing 1 or more doses.[47]

Timing of discontinuation of VTE prophylaxis also raises difficulties in EGS patients. We advocate that all EGS patients continue to receive appropriate VTE prophylaxis for their entire hospital stay even when ambulation is improving. Although ambulation is overall likely to be beneficial to patients, few data support its use as primary VTE prophylaxis.[36] Furthermore, evidence suggests that a cohort of surgical patients may benefit from extended VTE prophylaxis after discharge, most notably patients undergoing pelvic and oncologic operations.[48] In these patients, who remain at increased risk of VTE even after discharge from the hospital, continuing pharmacologic VTE prophylaxis after discharge reduces the rate of VTE by half within 90 days.[49] No literature currently exists on the risk of VTE after discharge in EGS patients as a discrete population, but it seems reasonable to extrapolate the existing evidence for nonemergency surgically managed colon malignant tumors to those managed immediately because of bleeding or obstruction. This topic is an area that warrants future research within the EGS patient population. It is likely that a substantial subgroup of EGS patients are at risk of VTE after discharge.[21]

Prophylaxis Measurement and Adherence

The many challenges of managing acutely ill EGS patients necessitates a systems approach to VTE prophylaxis with engagement of frontline staff, including surgeons, residents, nurses, pharmacists, and other health care professionals, in addition to actively engaging patients.[50] Because of the requirement to document quality metrics, many institutions now quantify and record VTE risk at admission to the hospital. Such measures are often linked to a decision aid (computerized or paper based) to assist the practitioner in selecting the optimal VTE prophylaxis strategy. Studies suggest that the use of decision support tools increases practitioner awareness and adherence[5,51] and eliminates disparities in care.[52] This method relies on practitioners accurately assessing patient risk and prescribing appropriately but also ensuring that patients are educated and receive the prescribed prophylaxis.

A few studies[14,16,17] have examined quality improvement projects aimed, in part, to increase adherence with recommendations for VTE prophylaxis and have demonstrated significant improvements (Table 1). Although limited by the use of physician orders as a surrogate to determine optimal prophylaxis (as opposed to actual medication administration records), these studies also highlight the generally poor adherence rates.[53] Within EGS, several studies have found improved VTE prophylaxis prescribing from 73% to 86%[14] and 35% to 87%[16,17] after initiating a quality improvement initiative that specifically targets VTE prophylaxis. One study[16] found a 50% reduction in VTE events after implementation of a quality improvement initiative.

The AHRQ recommends institutions first accurately measure adherence to determine whether there is a need for change. This measurement requires pursuance by administrators and practitioners with stakeholder buy-in to actively reduce VTE risk.[31] Many strategies are available, including education of patients and practitioners, the use of protocols, proformas, or decision support tools built into the electronic medical record. Accurate measurement before and after any planned intervention should be undertaken to refine methods locally. This measurement may take the form of identifying those who do not prescribe optimal prophylaxis or engaging other health care professionals in a culture of patient safety to raise concerns when VTE prophylaxis is not prescribed.[54-56] Measuring and improving VTE adherence in EGS patients and other cohorts remain the most significant challenges with respect to VTE prophylaxis.

Conclusions

Increased recognition of the relatively higher VTE risk in EGS patients is required to improve patient safety. A number of factors, including the patient's disease process and the complexity of coordinated care, make EGS patients a challenging group to whom to provide adequate VTE prophylaxis, and there remain numerous gaps in the literature. Adherence with VTE prophylaxis is a well-established quality metric, and many institutions are beginning to recognize the need for prospective measurement and improving the culture of safety at the individual and institutional levels. This narrative review applied the existing literature to a heterogenic EGS patient population to make recommendations, improve patient safety and quality of care, and identify avenues for future research. We recommend using a validated system for risk assessment and prescribing LMWH for all operative and nonoperative EGS admissions and mechanical prophylaxis if pharmacologic prophylaxis is contraindicated.

ARTICLE INFORMATION

Accepted for Publication: November 11, 2017.

Published Online: March 14, 2018. doi:10.1001/jamasurg.2018.0015

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Statistical analysis: Vogt.
Obtained funding: Lau.
Administrative, technical, or material support: Murphy, Vogt, Streiff.
Study supervision: Murphy, Vogt, Lau, Parry, Streiff, Haut.

Conflict of Interest Disclosures: Dr Haut reported serving as a paid consultant and speaker for the Preventing Avoidable Venous Thromboembolism—Every Patient, Every Time VHA/Vizient IMPERATIV Advantage Performance Improvement Collaborative and the Illinois Surgical Quality Improvement Collaborative, receiving royalties from Lippincott, Williams, Wilkins for the book *Avoiding Common ICU Errors*, and being a paid author of a paper commissioned by the National Academies of Medicine titled *Military Trauma Care's Learning Health System: The Importance of Data Driven Decision Making*, which was used to support the report titled *A National Trauma Care System: Integrating Military and Civilian Trauma Systems to Achieve Zero Preventable Deaths After Injury*. Dr Strieff reported consulting for Janssen and Portola and receiving grants from Janssen, Boehringer Ingelheim, and Roche. No other disclosures were reported.

Funding/Support: Mr Lau and Dr Haut are supported by grant 1R01HS024547 from the Agency for Healthcare Research & Quality titled "Individualized Performance Feedback on Venous Thromboembolism Prevention Practice," by contract CE-12-11-4489 from the Patient-Centered Outcomes Research Institute (PCORI) titled "Preventing Venous Thromboembolism: Empowering Patients and Enabling Patient-Centered Care via Health Information Technology," and by contract CE-12-11-4489 from PCORI titled "Preventing Venous Thromboembolism (VTE): Engaging Patients to Reduce Preventable Harm from Missed/Refused Doses of VTE Prophylaxis." Mr Lau is supported by the Institute for Excellence in Education Berkheimer Faculty Education Scholar Grant and contract AD-1306-03980 from the Patient-Centered Outcomes Research Institute entitled "Patient Centered Approaches to Collect Sexual Orientation/Gender Identity Information in the Emergency Department."

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

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