Practices to prevent venous thromboembolism: a brief review

Brandyn D Lau,1,2 Elliott R Haut1,3,4,5,6

ABSTRACT
Background Venous thromboembolism (VTE) is a common cause of preventable harm for hospitalised patients. Over the past decade, numerous intervention types have been implemented in attempts to improve the prescription of VTE prophylaxis in hospitals, with varying degrees of success. We reviewed key articles to assess the efficacy of different types of interventions to improve prescription of VTE prophylaxis for hospitalised patients.

Methods We conducted a search of MEDLINE for key studies published between 2001 and 2012 of interventions employing education, paper based tools, computerised tools, real time audit and feedback, or combinations of intervention types to improve prescription of VTE prophylaxis for patients in hospital settings. Process outcomes of interest were prescription of any VTE prophylaxis and best practice VTE prophylaxis. Clinical outcomes of interest were any VTE and potentially preventable VTE, defined as VTE occurring in patients not prescribed appropriate prophylaxis.

Results 16 articles were included in this review. Two studies employed education only, four implemented paper based tools, four used computerised tools, two evaluated audit and feedback strategies, and four studies used combinations of intervention types. Individual modalities result in improved prescription of VTE prophylaxis; however, the greatest and most sustained improvements were those that combined education with computerised tools.

Conclusions Many intervention types have proven effective to different degrees in improving VTE prevention. Provider education is likely a required additional component and should be combined with other intervention types. Active mandatory tools are likely more effective than passive ones. Information technology tools that are well integrated into provider workflow, such as alerts and computerised clinical decision support, can improve best practice prophylaxis use and prevent patient harm resulting from VTE.

INTRODUCTION
Venous thromboembolism (VTE), comprised of deep vein thrombosis (DVT) and/or pulmonary embolism (PE), is estimated to account for 5–10% of all deaths among hospitalised patients.1 2 In addition, non-fatal VTE events are associated with significant morbidities. In 2008, the US Surgeon General issued a Call to Action to Prevent DVT and PE. The report brings to light the huge numbers of patients afflicted by DVT (~350 000–600 000) and killed by PE (~100 000) every year in the USA.3

Both pharmacological and mechanical prophylactic interventions have been demonstrated to be highly effective in preventing many, but not all, VTE.1 4 It has been estimated that best practice prophylaxis may reduce the incidence of DVT by up to 70%.1 The underlying pharmacological mechanism of all prophylaxis medications is to decrease clotting, and therefore they may increase the risk of bleeding. The balance between bleeding and clotting must be considered, and the harms and benefits must be weighed before administering these drugs.5 Blanket approaches that give the same medication at the same dose and frequency to all patients may not be beneficial and may even cause more harm than benefit.6–8 Therefore, individual patient risk assessment is paramount to ensure that all patients receive optimal prophylaxis.

Most hospitalised patients have one or more risk factors for VTE. Evidence based, best practice prophylaxis varies by individual patient risk factors (ie, cancer, advanced age, immobility, history of VTE) and primary clinical service (eg, medicine, surgery, trauma, orthopaedics).1 Specialty specific guidelines are
often available in addition to general VTE prevention guidelines.\textsuperscript{1,9,10}

Despite high quality, randomised controlled trials (RCTs) showing the clinical effectiveness of prophylactic medications and mechanical devices to reduce the risk of VTE,\textsuperscript{11,12} numerous studies continue to show that many hospitalised patients are not prescribed risk appropriate VTE prophylaxis. One USA registry study found that only 42% of patients diagnosed with DVT during hospitalisation had received prophylaxis.\textsuperscript{13} These findings are not localised; another recent study across 32 countries found that only 59% of at risk surgical and 40% of at risk medical patients received guideline recommended VTE prophylaxis.\textsuperscript{14} Even as recently as Coagulation Day 2010, guideline adherence was reported to be 40% across Austrian intensive care units.\textsuperscript{15}

In 2001, the Agency for Healthcare Research and Quality (AHRQ) ‘Making health care safer’ report called the delivery of appropriate prophylaxis against VTE “the number one patient safety practice”\textsuperscript{16} and one that can prevent inhospital death.\textsuperscript{17} The AHRQ has recently placed ‘interventions to improve prophylaxis for VTE’ on its top 10 list of strongly encouraged patient safety practices.\textsuperscript{18,19}

Varied types of interventions aimed to improve adherence to VTE prophylaxis have been attempted. A systematic review of interventions to improve VTE prophylaxis use, based on literature searches from 1996 to 2003, found 30 eligible studies. Strategies included passive dissemination, which had little effect (50% compliance), single strategy studies (12 studies—audit and feedback, documentation aids and quality assurance activities all produced about 80% compliance) and clinical decision support systems (approached 100% compliance). Twelve studies incorporated two or more strategies, usually including an educational component, and all demonstrated improvements in the use of VTE prophylaxis. Most studies evaluated change in provider behaviour, not patient outcome, and no study that evaluated outcomes demonstrated a reduction in DVT or PE rates, often due to lack of adequate power.\textsuperscript{20} As computerised provider order entry systems are increasingly adopted in hospitals, an opportunity exists to incorporate clinical decision support into these systems.
The purpose of this review is to provide an update on the most effective interventions aimed at improving adherence to guidelines on the use of VTE prevention strategies.

METHODS
As part of the AHRQ sponsored ‘Making health care safer II’ report,\(^{18} {\text{21}}\) we conducted a MEDLINE search to identify studies that assessed interventions designed to improve the use of VTE prophylaxis in hospitalised patients published between 2001 and October 2012. We selected articles to show a representative sample of the diversity in types of interventions. Interventions were classified as education only, paper based, computerised, real time audit and feedback, or combinations of interventions. Interventions were considered educational only if they involved retrospective audit and feedback, general guidelines, policies and protocols, and/or grand rounds type presentations. Because VTE prophylaxis is multifactorial, requiring risk assessment, prescription and administration, we liberally included a wide possible range of heterogeneous educational interventions, targeting both clinicians and patients. Paper based interventions were tangible, patient specific VTE risk assessment and prophylaxis recommendation tools, such as risk assessment forms or preprinted paper order sets. Computerised clinical decision support tools were intangible, patient specific VTE risk assessment and prophylaxis recommendation tools, such as electronic alerts, reminders or computerised order sets. Real time audit and feedback involved third party review, non-prescriber mediated intervention (eg, nurses or pharmacists risk stratifying and/or alerting prescribers). Combined interventions included multiple components from at least two categories. We included studies that employed three commonly used valid quality improvement designs: RCTs, non-randomised studies with concurrent controls or controlled before and after studies.\(^{22}\)

Process outcomes of interest were the use of any VTE prophylaxis and best practice VTE prophylaxis defined within individual studies. Clinical outcomes of interest were both symptomatic and asymptomatic VTE and potentially preventable VTE, defined as VTE that occurs in patients not prescribed appropriate prophylaxis.\(^{23}\)

RESULTS
Sixteen articles were included in this review. Two studies employed education only, four implemented paper based tools, four used computerised tools, two evaluated audit and feedback strategies, and four studies used combinations of intervention types (table 1).

Education only interventions
Scaglione et al evaluated the impact of implementing a hospital guideline on the appropriateness of VTE prophylaxis prescription for hospitalised patients. They sampled the medical records of two cohorts of patients, one before and the other after implementation of the guideline. The authors found that after implementation, prescription of appropriate prophylaxis in those at high risk for VTE improved for both medical (42% vs 25%, \(p=0.0075\)) and surgical (97% vs 64%, \(p=0.0004\)) hospitalised patients. The authors also reported a significant decrease in VTE in the 2 years after implementation (adjusted OR 0.68, 95% CI 0.62 to 0.75) (table 2).\(^{24}\)

In an effort to address a recently discovered cause of suboptimal prophylaxis,\(^{25}\) patient refusal,\(^{26}\) Piazza et al launched a pharmacist mediated intervention to individually educate hospitalised patients on the importance of VTE prophylaxis. They targeted all hospitalised patients prescribed pharmacological VTE prophylaxis during their study period (n=528) and evaluated medication adherence. Patient education sessions were conducted within 24 h of the initial prescription for VTE prophylaxis. Compared with their pre-implementation group, administration of prescribed pharmacological VTE prophylaxis was higher after the patient education intervention (94.4% vs 89.9%, \(p<0.0001\)), and documentation of patient refusal significantly decreased (29.3% vs 43.7%, \(p<0.001\)) (table 2).\(^{27}\)

Paper based interventions
As part of an effort to reduce prescription errors, the National Inpatient Medication Chart, a standardised paper based medication chart, was incorporated in Australian public hospitals. Liu et al evaluated a National Inpatient Medication Chart based VTE risk stratification and prophylaxis guidance tool on improving the quality of VTE prophylaxis. They followed consecutive medical and surgical patients

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<tr>
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<tr>
<td>Scaglione (2005)</td>
<td>Appropriate prophylaxis prescription</td>
<td>Appropriate VTE prophylaxis prescription significantly improved for medical (42% vs 25%, (p=0.0075)) and surgical (97% vs 64%, (p=0.0004)) patients</td>
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<td>Piazza (2012)</td>
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VTE, venous thromboembolism.
for those patients at risk before and after implementation (OR 0.7, 95% CI 0.2 to 1.8, \( p=0.44 \)) (table 3).\(^{30}\)

Streiff et al reported significant improvement (26% to 68%, \( p<0.0001 \)) in the proportion of surgical patients prescribed risk appropriate VTE prophylaxis after implementation of a paper based order set at the Johns Hopkins Hospital. This paper based order set has now been replaced entirely with a computerised approach (table 3).\(^{31}\)

**Computerised interventions**

Lesselroth et al developed a clinical decision support enabled order menu in their computerised patient record system to recommend appropriate VTE prophylaxis at the time medications are prescribed at the Portland Oregon VA Medical Center. After identifying and addressing some key initial limitations (providers could unintentionally or intentionally bypass the order menu and recommended guidelines), use of the order menu increased from 20% to 80%. This study underscores the need for interventions to integrate well into provider workflow and ideally be mandatory without any possibility of ignoring or bypassing the VTE algorithm. Alerts and systems are only effective if they consistently reach their intended target.\(^{32}\) These findings also highlight the fact that even ‘mandatory’ tools do not result in 100% prophylaxis prescription compliance for all patients (table 4).

In a study by Beeler et al, an electronic alert was displayed in the chart of every hospitalised medical patient who did not have pharmacological or

### Table 3

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<thead>
<tr>
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<tr>
<td>Liu (2012)</td>
<td>Prophylaxis prescription</td>
<td>Prophylaxis prescription improved for medical (66.5% vs 52.7%) and surgical (89.1% vs 77.5%) patients ( (p&lt;0.001) )</td>
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<td></td>
<td>Appropriate prophylaxis</td>
<td>Appropriate VTE prophylaxis prescription significantly improved for medical (71.0% vs 55.6%) and surgical (75.6% vs 53.6%) patients ( (p&lt;0.01) )</td>
</tr>
<tr>
<td></td>
<td>VTE</td>
<td>No significant change in VTE (risk ratio 0.88, 95% CI 0.48 to 1.62)</td>
</tr>
<tr>
<td>O’Connor (2009)</td>
<td>Prophylaxis prescription</td>
<td>Patients more likely to be prescribed VTE prophylaxis with order set than free text orders (44.0% vs 20.6%, ( p&lt;0.0001 ))</td>
</tr>
<tr>
<td>Fontaine (2006)</td>
<td>Prophylaxis prescription</td>
<td>Prescription aids did not improve VTE prophylaxis prescription ( (0.7, 95% \text{ CI } 0.2 \text{ to } 1.8, p=0.44) )</td>
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<tr>
<td>Streiff (2012)</td>
<td>Appropriate prophylaxis prescription</td>
<td>Appropriate prophylaxis prescription significantly improved for surgical patients (26% to 68%, ( p&lt;0.0001 ))</td>
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mechanical VTE prophylaxis prescribed within 6 h after admission and had documented VTE risk. This system, which reacts to a lack of prescription for VTE prophylaxis, made improvements but may not be optimal as more proactive systems that prompt the appropriate care on admission. Rates of VTE prophylaxis orders among medical patients significantly increased from pre-implementation rates of 43.4% to 66.7% (p<0.0001) during the 4 months after implementation. The following year, VTE prophylaxis orders increased further to 73.6% (p=0.011). The rates of prophylaxis among these medical patients still did not reach those for surgical patients (approximately 90%) who were used as the control arm (table 4).

Kucher et al actively searched for hospitalised patients at risk for developing VTE who were not prescribed prophylaxis (pharmacological or mechanical). In this randomised trial, electronic alerts that the patient was at risk for VTE were sent to providers of patients in the intervention group. Patients in this intervention group were significantly more likely to receive mechanical prophylaxis (p<0.001) and significantly more likely to receive prophylactic doses of unfractionated heparin (p<0.001). There were no significant changes to orders of enoxaparin (p=0.18) or warfarin (p=0.11) between intervention and control groups. In addition, patients in the intervention group were significantly more likely to be free from DVT or PE after 90 days (p<0.001) (table 4). This computerised approach is effective, but is also reactive—it identifies patients who were not initially ordered prophylaxis and then attempts to correct the patient safety problem, rather than proactively suggesting appropriate prophylaxis at the time of initial treatment.

In 2008, a mandatory, computerised, decision support enabled VTE risk stratification order set was implemented in the computerised provider order entry system at the Johns Hopkins Hospital to recommend guideline appropriate, service specific (eg, medicine, general surgery, trauma, etc) prophylaxis for an individual patient’s risk stratum. This system requires proactive risk stratification during the completion of the admission order set for all admitted patients and therefore is nearly 100% effective at forcing providers to assign a risk stratum to all patients within 24 h of hospital arrival. Within the first year, adherence to guideline appropriate VTE prophylaxis increased significantly hospital-wide and rates of VTE have been on a decreasing trend. Within the trauma service, prescription compliance increased from 66.2% to 84.4% (p<0.001) and preventable harm (defined as VTE in patients not ordered appropriate prophylaxis) significantly decreased from 1.0% to 0.17% (p=0.04) and was eliminated for 2 full years after implementation (table 4).

However, this system remains fallible as the guideline suggested VTE prophylaxis is merely a recommendation; it is not required and may be overridden by the ordering clinician.

### Real time audit and feedback interventions

Piazza et al conducted a multicentre RCT to study a real time alert to the attending physicians of patients at high risk of VTE who are not receiving prophylaxis. Patients whose physicians were alerted were more likely to receive VTE prophylaxis than control subjects (46.0% vs 20.6%, p<0.0001); however, the rate of VTE was not significantly different between the two groups (2.7% vs 3.4%, HR 0.79; 95% CI 0.50 to 1.25) (table 5).

In a study by Mahan et al, pharmacists prospectively reviewed patients’ medical records to determine risk factors for VTE and the current prescribed prophylaxis. When the prophylaxis prescription was inadequate for their risk level, the pharmacist alerted the attending physician (in person or via telephone communication). After implementation of this intervention, the proportion of patients prescribed appropriate prophylaxis increased from 23.8% in 2006 to 37.9% (OR 1.8, 95% CI 1.6 to 2.1, p<0.0001), and preventable VTE decreased by 74% (95% CI 44% to 88%, p=0.0006) (table 5).

### Combinations of interventions

In response to poor documentation of VTE risk and inadequate use of appropriate prophylaxis, a clinical guideline was implemented at one hospital in the UK to enhance the culture of documenting VTE risk and prescribing VTE prophylaxis. The guideline was implemented using a multidisciplinary team and multimodal strategy involving education, information technology, verbal and written reminders, and with frequent optimisation based on feedback from end users. An immediate post-implementation review found that adherence to VTE prophylaxis guidelines increased from 56% to 96%. Unfortunately, there was a significant drop-off over time in adherence

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<td>Mahan (2012) Appropriate prophylaxis prescription</td>
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noted in a follow-up analysis, with only a 69% compliance rate reported (table 6). The authors suggest the cause may be due to over prophylaxis of patients who, on retrospective chart review, did not have indications for pharmacological prophylaxis.

Gallagher et al evaluated the impact of several interventions implemented over a 3 year period to improve the use of VTE prophylaxis at one hospital in Australia. Interventions included educating providers on the burden of VTE, the failure to apply guidelines and the development of a printed hospital-wide risk assessment tool incorporated into routine clinical practice with VTE related feedback to clinicians. Comparing the first three quarters with the final three quarters, the authors found a statistically significant increase in VTE prophylaxis use (48% to 74%, p=0.01) accompanied by a significant reduction in VTE after implementation (RR 0.68, 95% CI 0.47 to 0.99, p=0.04) over the 3 year study period (table 6).40

Stinnett et al found that 75% of patients admitted to the medical service were at increased risk for VTE yet only 43% of those patients received any type of VTE prophylaxis. The authors designed an intervention that consisted of education and a combination VTE prevention tool, which included a VITE risk stratification scheme, a standard admission order form that presented optimal VTE prevention regimens. After implementation of this intervention, the authors found that 71% of patients at high risk for VTE received prophylaxis (table 6).41

Maynard et al implemented a computerised risk assessment form linked to preferred VTE prophylaxis options. In addition, approximately one educational session was held per quarter, and feedback was provided to the clinical staff when audits indicated that their patient was prescribed inadequate prophylaxis. Prescription of appropriate VTE prophylaxis increased each year after implementation of the intervention, from 58% at baseline in year 1 to 78% and 93% during study years 2 and 3, respectively (p<0.001). Overall, the risk of developing hospital acquired VTE decreased significantly after implementation (RR 0.69, 95% CI 0.47 to 0.79) while the risk of developing preventable VTE decreased by 86% (95% CI 0.06 to 0.31) (table 6).42

**DISCUSSION**

Numerous interventions have been implemented in attempts to improve the use of VTE prophylaxis for hospitalised patients with varying degrees of success. The most successful interventions are those that integrate well into the prescriber workflow and, as demonstrated in numerous quality improvement interventions,20, 43, 44 should be coupled with ongoing education to re-emphasise the importance of VTE prophylaxis for hospitalised patients.31

Public reporting of VTE prophylaxis processes and outcomes is another possible approach to improve VTE prophylaxis, through feedback and public reporting or the financial incentive of non-payment for VTE events. The Centres of Medicare and Medicaid Services placed VTE after orthopaedic hip/knee replacement on their list of ‘never events’ for which providers will not be reimbursed. However, as has been seen in numerous clinical trials, even with best practice prophylaxis, not all VTE events can be prevented,3, 45 especially in the orthopaedic patient population.

Another potential limitation to the use of VTE rates alone to measure quality is the significant problem caused by surveillance bias; many DVTs are clinically silent and therefore go undetected without routine screening which is differentially applied to various patient populations and hospitals.23 For example, in the field of trauma surgery, clinical ambiguity persists regarding the clinical and cost effectiveness of screening high risk asymptomatic trauma patients for DVT with duplex ultrasound.23 As a result, certain providers and hospitals report higher DVT rates due entirely to higher rates of diagnostic testing—a classic example of surveillance bias.46-48 Because of these issues—and variation in patient risk—unadjusted VTE rates alone are likely not appropriate for public reporting as they may be more misleading than helpful.

The updated evidence for VTE prophylaxis in selected patients has been well described in a variety of recent evidence based clinical guidelines and systematic reviews.1, 7, 9 The evidence for clinical interventions for VTE prophylaxis remains strong for

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<td>Clark (2011)</td>
<td>Appropriate prophylaxis prescription</td>
<td>After implementation, appropriate VTE prophylaxis prescription increased from 56% to 96%, but waned over time to 69%</td>
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<td>Gallagher (2009)</td>
<td>Prophylaxis prescription VTE</td>
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hospitalised patients, and prophylaxis is recommended by practice guidelines for specific populations, although it should not be applied universally. As the availability of medications and condition specific evidence is rapidly evolving and these guidelines are regularly updated, we did not evaluate specific regimens within this review.

When evaluating preventable harm from VTE, we agree that the ideal definition should combine an outcome and process measure rather than relying on clinical VTE outcomes alone. It has been suggested that only VTE events occurring in patients who did not receive adequate prophylaxis should be labelled a ‘preventable VTE’. This approach and specific definition has been incorporated as one of the six meaningful quality measures related to VTE. Although there is not yet national consensus on the use of this definition, preventable harm from VTE has been shown to be a useful quality improvement measure in several single centre studies. We advocate including this measure in future clinical research studies that evaluate the impact of interventions to prevent VTE.

CONCLUSION

Strong evidence from numerous high quality trials supports the effectiveness of VTE prophylaxis for specific populations. However, there are significant potential harms and risk stratification is necessary to ensure that prophylaxis is targeted to appropriate patients. Unfortunately, rates of VTE prophylaxis remain suboptimal, and VTE continues to be a difficult and elusive crisis in patient safety. Relatively little evidence exists on which specific interventions are effective for increasing rates of VTE prophylaxis in appropriate populations. As with other patient safety interventions, educating providers on the benefits of appropriate VTE prophylaxis alone is not an effective strategy to improve use of appropriate VTE prophylaxis. Evidence, although mostly low quality (non-randomised studies without concurrent controls), supports that education combined with other quality improvement strategies and information technology approaches such as alerts and mandatory computerised clinical decision support, appear to offer the most effective approaches to promote best practice prophylaxis use and prevent patient harm resulting from VTE.

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Contributors BDL conducted the search, reviewed relevant articles, analysed the results and drafted the paper. ERH planned the concept of the paper, developed the framework for conducting the review and is the guarantor of the paper.

Competing interests ERH is the primary investigator of a Mentored Clinician Scientist Development Award K08 1K08HS017952-01 from the Agency for Healthcare Research and Quality entitled ‘Does screening variability make DVT an unreliable quality measure of trauma care?’ ERH receives royalties from Lippincott, Williams and Wilkins for a book Avoiding common ICU errors, and has given expert witness testimony in various medical malpractice cases.

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REFERENCES


Narrative review


