

A Systematic Review of Strategies to Improve Prophylaxis for Venous Thromboembolism in Hospitals

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Objective: To assess the effectiveness of different strategies for increasing the uptake of prophylaxis for venous thromboembolism (VTE) in hospitalized patients through a systematic review of the literature.

Methods: Literature databases and the Internet were searched from 1996 to May 2003. Studies of strategies to improve VTE prophylaxis practice were included. Studies where no policy or guideline was implemented or where the focus of the study was not VTE prevention were excluded.

Results: Thirty studies were included. The quality of the available evidence was average with the majority of studies being uncontrolled before and after design and thus limited by the historical nature of much of the available data. Adherence to guidelines and the provision of adequate prophylaxis were poor in studies which relied on passive dissemination of guidelines. In general, the use of multiple strategies was more effective than a single strategy used in isolation. The most effective strategies incorporated a system for reminding clinicians to assess patients for VTE risk, either electronic decision-support systems or paper-based reminders, and used audit and feedback to facilitate the iterative refinement of the intervention. There were no studies adequately powered to demonstrate a reduction in rates of VTE. Insufficient evidence was available to make useful comparisons of strategies in terms of costs and resource utilization.

Conclusions: Passive dissemination of guidelines is unlikely to improve VTE prophylaxis practice. A number of active strategies used together, which incorporate some method for reminding clinicians to assess patients for DVT risk and assisting the selection of

appropriate prophylaxis, are likely to result in the achievement of optimal outcomes.

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Venous thromboembolism (VTE) is a significant problem for surgical and medical hospitalized patients, leading to the possibility of serious illness and risk of death. A number of clear evidence-based guidelines are available which outline the appropriate use of prophylaxis to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE).^{1–10} In spite of the existence of such evidence, the problem of VTE in hospitalized patients persists, and it is clear that evidence-based guidelines and recommendations are underutilized. The challenge of translating evidence into practice is a widespread problem across a range of healthcare settings and clinical problems. It is clear that there is no “one-size-fits-all” solution which will be effective for every setting and every health problem. A systematic review was undertaken which aimed to evaluate strategies used to increase the uptake of VTE prophylaxis for hospitalized patients and to make recommendations about the effectiveness of different strategies.

MATERIALS AND METHODS

Inclusion Criteria

Studies of all types regarding prophylaxis for DVT or PE were included (randomized controlled trials (RCTs), historical and/or nonrandomized comparative studies, case series, case reports, surveys, and clinical audit reports). All studies were retrieved without language restriction and subsequently excluded if they did not add substantially to the English language evidence base. Studies were excluded if there was no evidence regarding the success of DVT policy implementation (ie, at least postimplementation outcomes) or where no results, either quantitative or qualitative, could be extracted from the study. The included papers contained information on at least 1 of the following outcomes: out-

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comes of care (such as rates of DVT), processes of care (such as adequacy of prophylaxis), processes of change (such as adherence to guidelines), and resource utilization and costs. Two reviewers independently examined all retrieved references, and any disagreement over inclusion or exclusion was discussed and a consensus reached.

Search Strategy

Ovid PreMEDLINE and MEDLINE, Current Contents, Cochrane Library's Controlled Trials Register and Database of Systematic Reviews, DARE and NHS-EED, and EMBASE from 1996 up to and including May 2003 were all searched. The UK National Research Register (NRR), NIH ClinicalTrials.gov database, PubMed, and HTA Assessment database were also searched in May 2003. Gray literature was also extensively searched from 1996 up to May 2003. Pearl-ing was then undertaken to locate articles that may have been missed by the electronic database searches.

Specific search terms to retrieve articles were *venous thromboembolism (VTE)*, *deep vein (venous) thrombosis (DVT)*, *pulmonary embolism (PE)*, *prophylaxis*, *prevention guidelines*, *protocol*, *policy*, *implementation*, *clinical practice*, *hospital*, *postoperative* in PreMEDLINE, MEDLINE, Current Contents, EMBASE, and PubMed. In other databases (Cochrane Library, NHS HTA databases, Clinical Trials database, NRR, SIGLE), the search terms used were *venous thromboembolism (VTE)*, *deep vein (venous) thrombosis (DVT)*, *pulmonary embolism (PE)*.

Data Extraction and Analysis

Data were extracted from each included study using standardized study profile tables developed *a priori*. Each included study was critically appraised for its study quality and "level of evidence" according to the hierarchy of evidence developed by the National Health and Medical Research Council of Australia.¹¹ Study quality was assessed on a number of parameters such as the quality of the study methodology reporting, methods of randomization and allocation concealment (for RCTs), blinding of patients or outcomes assessors, attempts made to minimize bias, sample sizes, and the ability of the study to measure "true effect." The applicability of results outside the study sample was also examined, as were the appropriateness of the statistical methods used to describe and evaluate the study data.

RESULTS

Thirty studies were identified which met the inclusion criteria (Table 1). Only 1 RCT comparing different strategies to increase VTE prophylaxis uptake could be identified.¹² The majority of studies reported the results of an audit cycle prior to, and following, the implementation of VTE practice guidelines or a local protocol. Three of these studies were concurrently controlled,¹³⁻¹⁵ with the remainder being histor-

ically controlled or case series (see Table 1). The available data were weakened by their historical nature, with the possibility of bias introduced by differences in data collection or recording methods, changes in other hospital procedures over time, as well as changes in personnel or management structures. The majority of studies were not adequately powered to detect changes in rare patient outcomes such as rates of DVT or PE. There was also the strong possibility that much of the data was subject to the Hawthorne effect, such that behavior may have changed within the study setting as a result of the research process itself; for example, as a result of focusing on VTE prevention. As this may be seen as a positive outcome from a clinical perspective, there is little incentive for clinical researchers to seek to minimize this effect. As a result of the nature of the available data, conclusions were more easily made with regard to changing clinician behavior than with regard to influencing patient outcomes.

Strategies Used in the Included Studies

Strategies for increasing the uptake of VTE prophylaxis included passive dissemination, audit and feedback, computer-based decision aids, documentation aids, continuing education, quality assurance activities, advertising, appointment of specific implementation staff, and recruitment of local change agents or opinion leaders.

Studies Using Passive Dissemination

Six studies were identified which relied on the passive dissemination of guidelines (via international or local publication) to change VTE prophylaxis practice (see Table 2).¹⁶⁻²¹ Adherence to guidelines and the provision of adequate prophylaxis was poor in these studies, with no more than 50% of patients receiving appropriate prophylaxis, despite dissemination of the guideline. These 6 studies underline the problem of uptake of VTE prophylaxis practices and suggest that the dissemination of evidence-based guidelines alone will not be enough to ensure that the majority of patients in need of prophylaxis receive it, nor that the prophylaxis provided is appropriate for the patient. It seems likely that a lack of knowledge regarding risk classification for VTE and appropriate treatment may be contributing to the poor practices documented in these 6 studies.

Studies Using a Single Active Strategy

Twelve studies used 1 of 4 active strategies in isolation to improve VTE prophylaxis (see Table 3).^{13,14,22-31} The 4 strategies used were computer-based clinical decision support systems, audit and feedback, documentary aids, and quality-assurance activities (in this case, active monitoring of VTE prophylaxis policy). While all of the strategies resulted in improvements in VTE prophylaxis practice, the most effective strategy for increasing adherence to guidelines and adequacy of prophylaxis appeared to be the computer-based clinical decision-support systems, with rates for each of these

TABLE 1. Included Studies by Broad Category of Implementation Strategy

Study	Year	Strategy Used	Level of Evidence	No.
Ageno ¹⁶	2002	Passive	IV	165 Patients
Ahmad ¹⁷	2002	Passive	IV	185 Patients; 194 clinicians
Arnold ¹⁸	2001	Passive	IV	245 Patients
Bratzler ¹⁹	1998	Passive	IV	419 Patients
Burns ²⁰	2001	Passive	Survey study	117 Surgeons
Villemur ²¹	1998	Passive	IV	505 Patients; 30 Clinicians
Aouizerate ²²	1998	Active	III-3	1165 Patients
Durieux ¹³	2000	Active	III-2	1971 Patients; 14 surgeons
Fagot ²³	2001	Active	III-3	279 Prescriptions
Harianth ²⁴	1998	Active	III-3	200 Patients
Huang ¹⁴	2000	Active	III-2	200 Patients
Macdonald ²⁵	2002	Active	III-3	5008 Patients
McEleny ²⁶	1998	Active	III-3	1108 Patients
Miller ²⁷	1996	Active	III-3	997 Patients
Oghoetuoma ²⁸	2001	Active	III-3	196 Patients
Patterson ²⁹	1998	Active	III-3	2013 Patients; 54 surgeons
Taylor ³⁰	2000	Active	III-3	529 Patients
Williams ³¹	1997	Active	III-3	74 Patients
Anderson ¹²	1994	Multiple	II	3158 Patients
Birks ^{32,33}	2002	Multiple	III-3	266 Patients
Bridges ³⁴	2003	Multiple	III-3	177 Patients
Devlin ³⁵	1999	Multiple	IV	50 Patients
Frankel ³⁶	1999	Multiple	III-3	200 Patients
Hall ³⁷	2000	Multiple	IV	192 Patients; 79 wards
Hohlt ³⁸	2000	Multiple	III-3	Not Stated
McCarthy ^{39,40}	1998	Multiple	III-3	757 Patients
Peterson ⁴¹	1999	Multiple	III-3	500 Patients
Pritts ¹⁵	1999	Multiple	III-2/3	337 Patients
Ryskamp ⁴²	1998	Multiple	IV	209 Patients
Stratton ⁴³	2000	Multiple	IV	1907 Patients

outcomes approaching 100%.^{13,25,29,30} In comparison, the other 3 strategies generally resulted in rates of around 80% for adherence to guidelines and adequacy of prophylaxis.^{14,22–24,27,28,31} However, in one study using audit and feedback, an iterative process was used to modify existing guidelines based on the results of the audit, and this produced outcomes similar to those obtained by the studies using computer-based decision aids.²⁶

This variability in outcomes may be attributed to 2 factors. The outcomes achieved by using the computer-based decision systems are likely to have resulted from the use of automatic reminders to assess VTE risk or assist in correct prescription of prophylaxis, which removed the element of human error from VTE prophylaxis practice. By comparison, in the 3 studies which used paper-based documentation aids, the reminder process was not automated, and thus the element of human error may still have affected the use of the various

documentary aids. The effectiveness of the audit strategy used by McEleny et al²⁶ appears to have hinged on the iterative process used to modify existing guidelines, and the possibility that in some departments/hospitals within the health system studied, VTE prophylaxis was already a priority area (as evidenced by the existence of local protocols).

Studies Using Multiple Strategies

Twelve studies used multiple strategies to increase uptake of VTE prophylaxis (see Table 4).^{12,15,32–43} Adherence to guidelines and adequacy of prophylaxis improved in all the studies where it was reported.^{12,32,33,36,39–41} The majority of studies used 3 strategies in combination, and all but 2 studies^{39,40,43} used continuing education. However, the studies with the best outcomes also used audit and feedback to facilitate iterative refinement of either prophylaxis policy or implementation strategy and/or used a documentary aid

TABLE 2. Studies Using Passive Strategies

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Ageno et al. 2002, ¹⁶ Italy, Oct-Dec 2000 medical patients	Departments of Internal Medicine at 2 hospitals (1 university-based teaching hospital, 1 nonteaching)	IV	ACCP 2000 guideline ³	Adequacy of prophylaxis	52/112 (46.4%) Patients where prophylaxis was indicated received prophylaxis Patients with acute respiratory failure 5.6 times more likely to receive prophylaxis than patients with acute ischaemic stroke ($P = 0.02$) and 5.2 times more likely than heart failure ($P = 0.01$)
	165 Patients discharged during study period			Suspected DVT during hospitalization	5/165 (3%) Suspected DVT during hospitalization, 3 receiving prophylaxis, 2 not receiving prophylaxis; DVT excluded in 4 and positive in 1 (not on prophylaxis because of concomitant bleeding)
Ahmad et al. 2002, ¹⁷ Australia, dates of study not stated; surgical and medical patients	Major teaching hospital; 185 patients and 194 clinicians	IV	1997 International Consensus ¹ and Australian National guidelines ⁶	Correct prophylaxis according to risk assessment	Prophylaxis was correct in 26% of cases overall: 97% of low-risk patients, 23% of moderate-risk patients, and 5% of high-risk patients.
				Clinicians' knowledge of risk classification	Knowledge of risk classification ranged from 76% to 89% correct for low risk, 9% to 51% for moderate risk, and 36% to 64% for high risk in different clinician groups.
				Clinicians' knowledge of correct prophylaxis for risk categories	Knowledge of correct prophylaxis ranged from 0% to 66% for low risk, 0% to 75% for moderate risk, and 14% to 88% for high risk in different clinician groups.
Arnold et al 2001, ¹⁸ Canada Oct 1996 to Oct 1997, surgical and medical patients	Teaching hospital	IV	ACCP 1995 guidelines ⁵	Adequacy of prophylaxis	Of 65 patients who subsequently developed VTE, 44/65 (68%) prophylaxis inadequate (ie VTE preventable) and 21/65 (22%) prophylaxis given but VTE occurred anyway (ie VTE not preventable)
	245 Patients with objectively diagnosed DVT/PE (253 cases, 230 DVT, 48 PE, 25 DVT + PE)			Reasons for inadequacy of prophylaxis	(n = 44) Omitted (48%), duration inadequate (23%), incorrect (20%), frequency of dosing inadequate (14%), delayed (7%), dose inadequate (7%)

(Continued)

such as a paper-based reminder system to ensure that practitioners assessed patients for VTE risk and prescribed the appropriate prophylaxis. For example, in the Birks et al^{32,33} study, compliance with guidelines increased significantly

with successive refinements in implementation strategy. Compliance with guidelines was initially 47% and reached 86% only when the strategy included not simply continuing education but also the introduction of a reminder label.

TABLE 2. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Bratzler et al 1998, ¹⁹ United States, Apr-Dec 1995, surgical patients	20 Community hospitals (urban and rural)	IV	ACCP 1992–1995 guidelines ^{4,5}	Patients receiving prophylaxis	Of patients at risk for VTE 38% (35% at moderate risk, 40% at high risk, and 39% at very high risk) received prophylaxis
	419 Medicare (US) patients aged over 65 y undergoing major surgery			Adequacy of prophylaxis	Of those who received prophylaxis, 100% of patients at moderate risk, 75% patients at high risk, and 66% of patients at very high risk received adequate prophylaxis
Burns et al. 2001, ²⁰ UK, dates of study not stated, surgical patients	Postal survey of general surgeons in Scotland	NA	SIGN ² and THRIFT ⁴⁵ guidelines	Adequacy of prophylaxis for 6 clinical scenarios (not actual patients)	Under-treatment - 35% of responses
	117 surgeons				Overtreatment, 16% of responses; appropriate treatment, 49% of responses
Villemur et al, 1998, ²¹ France, Apr 1995 to Apr 1996 surgical patients	16 Private clinics and university hospitals	IV	Local hospital consensus developed by all 16 hospitals	Adequacy of prophylaxis	Under-treatment - 36% of patients
	505 Patients, 30 cardiologists			Prevalence of DVT	DVT prevalence, 14% (in undertreated, prevalence 19% vs 11% for appropriate treatment, RR = 1.7, <i>P</i> = 0.01)
				Relative risk of DVT	1.6 Times higher in patients over 70 (<i>P</i> = 0.04) 2.2 Times higher for general anesthesia (<i>P</i> = 0.03) 2.1 Times higher for reduced mobility (<i>P</i> = 0.01)

ACCP indicates American College of Chest Physicians; SIGN, Scottish Intercollegiate Guidelines Network; THRIFT, Thromboembolic Risk Factor Consensus Group.

McCarthy et al³⁹ and Byrne et al⁴⁰ demonstrated a similar progression in adequacy of prophylaxis, with successive increases occurring as the use of a documentation aid was refined to make it easier to access and finally when compliance with its use was actively monitored by a nurse. Adequacy of prophylaxis in this case increased from 51% with only verbal instruction to 94% after the final modification to the strategy.

Surgical Versus Medical Patients

Only 3 studies focused on the use of thromboprophylaxis in medical rather than surgical patients or reported results for medical patients separately from surgical patients.^{12,16,23} Anderson et al¹² (Level II) found that the improvement in prophylaxis practice was significantly better for

surgical than for medical patients, regardless of which intervention was used to increase use of prophylaxis. However, in the 2 groups of hospitals using active implementation strategies, there was a significant improvement in prophylaxis practice for medical patients compared with patients in the control hospitals. There was no clear advantage of continuing medical education plus quality-assurance activities compared with continuing education alone. Ageno et al¹⁶ documented relatively poor prophylaxis practice for medical patients in 2 Italian hospitals where passive dissemination of guidelines had occurred, with only 46% of patients receiving appropriate prophylaxis. Ageno et al¹⁶ noted a difference in practice, depending on the presenting condition, with patients with acute respiratory failure nearly twice as likely to receive

TABLE 3. Studies Using 1 Active Strategy in Isolation

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Studies using computer-based clinical decision support systems					
Durieux et al, 2000, ¹³ France, Dec 1997 to Jul 1999, surgical patients	Urban teaching hospital	III-2	Local guidelines developed by local hospital experts	Compliance with guidelines	Improved compliance in group using computer-based decision aid (intervention group 95%, control group 83%)
	1971 Orthopedic surgery patients, 14 surgeons			Adequacy of prophylaxis	Adequacy of prophylaxis better in intervention group (95%) than in control group (83%), particularly for patients at moderate risk (intervention 90%; control 6%)
	Intervention, 859 patients			Reasons for noncompliance	86% Decrease in physicians ignoring computer recommendation for prophylaxis (from 5.0% to 0.8%), a 59% decrease in wrong dosage (from 6.6% to 2.7%), and a 66% decrease in physicians ignoring recommendation for no prophylaxis (from 4.8% to 1.6%)
	Control, 1112 patients			Rates of diagnosed DVT	Control 1; intervention 0
				Rates of diagnosed PE	Control 2; intervention 2
Macdonald et al, 2002, ²⁵ Canada, Jul 1994 to Dec 1998 and Jan 1993 to Jul 1994; follow-up: June 1996; surgical patients	Tertiary care orthopedic hospital	III-3	Published guidelines for warfarin prescription	Compliance with guidelines (therapeutic test range)	In range: intervention 62%; control 52% Above range: intervention 13%; control 32% Below range: intervention 24%; control 32%
	Control 4729 joint arthroplasty patients, 51,810 test results				
	Intervention 279 joint arthroplasty patients, 2889 test results				
	Follow-up (random sample): 430/4729			Major and minor bleeding episodes	Less than 5% for both intervention and control groups
				Readmission rates for VTE	Intervention 3%; control 4% (<i>P</i> = 0.089)
				Rates of DVT at follow-up	Suspected DVT, 19/430; 16 cases clinically proven (3.7%)
				Rates of PE at follow-up	1/430 (0.2%) PE at postoperative day 42

(Continued)

TABLE 3. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
				Costs	Potential savings per patient of 11 min of nursing time or CAN\$5.50/patient daily; annual savings \$5.50 × 10,152 patient-days/y = Canadian \$55,836
Patterson et al, 1998 ²⁹ United States, Nov 1997 to Jan 1998, surgical patients	Tertiary-care teaching hospital	III-3	1995 ACCP guidelines ⁵	Patients receiving prophylaxis as indicated	85% Preintervention vs 99% postintervention ($P < 0.001$)
	921 Patients where prophylaxis indicated preintervention, 1092 postintervention and 54 surgeons			Compliance with guidelines	47/54 (87%) Surgeons had no cases of missed prophylaxis, 6 surgeons missed 1 case, 1 surgeon missed 2 cases (of the 8 cases where prophylaxis missed, in 2 prophylaxis was contraindicated)
				Computer errors (mislabeling of patients)	Overall 89/921 (8%), 76/89 computer suggested prophylaxis when not indicated
Taylor et al, 2000, ³⁰ UK, Dec 1996 to May 1997 and Jan 1998 to Jun 1998	Single NHS hospital 270 Caesarean section patients pre-intervention and 259 caesarean section patients post-intervention	III-3	1995 RCOG guidelines ¹⁰	Adequacy of prophylaxis	Patients receiving adequate prophylaxis increased from 192/270 (71%) preintervention to 231/259 (89%) postintervention
SURGICAL PATIENTS					
Studies using documentation aids					
Fagot et al, 2001, ²³ France, May 1998 to Apr 1999, medical patients	Nonsurgery department of hospital	III-3	French National guidelines	Compliance with guidelines	Significant difference following introduction of patient-specific prescription order form for patients with 2 risk factors for VTE (10% Pre vs 21% Post, $P = 0.01$)
	279 Prescriptions for LMWH made on data collection days				Significant reduction in number of nonconforming prescriptions (from 54% Pre to 35% Post, $P = 0.001$)
					No significant difference for high-risk patients
					Excluding patients in oncology and radiology did not change significance of findings

(Continued)

TABLE 3. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Harianth and St John, 1998, ²⁴ UK, 1996 onwards: second audit 2 mo after intervention; surgical patients	General surgical ward 100 Patient preintervention and 100 patients postintervention admitted to hospital	III-3	1992 THRIFT guidelines ⁴⁵	Compliance with guidelines	Significant improvement in thromboprophylaxis practice for all patients following introduction of risk score sheet for use during admission of patients (64% Pre to 79% Post $P = 0.03$) and for high risk patients (15% to 58% $P = 0.001$) Undertreatment: 35% Pre vs 21% Post
Oghoetuoma et al, 2001, ²⁸ UK, Nov 1998 to Dec 1998 (second audit), surgical patients	General urban hospital 86 Caesarean section patients preintervention and 110 patients postintervention	III-3	1995 RCOG guidelines ¹⁰	Adequacy of prophylaxis Patients receiving prophylaxis as indicated	Overtreatment: 3% Pre vs 6% Post Significant improvement in thromboprophylaxis practice after introduction of risk assessment score sheet for all patients (from 14% Pre to 73% Post $P = 0.0002$) Patients undergoing emergency caesarean section who received prophylaxis increased from 0% Pre to 73% Post
Studies using audit and feedback cycle					
Aouizerate et al, 1998, ²² France, dates of study not stated but postaudit 1 year after dissemination of guidelines, surgical and medical patients	General hospital 550 Patients audit 1 and 615 patients audit 2	III-3	French National guidelines	Patients receiving prophylaxis Adequacy of prophylaxis	No difference audit 1 to audit 2 (20.5%) Significant improvement in correct prescription (from 52% audit 1 to 81% audit 2, $P < 0.0001$) and significant reduction in overprescription (from 49% audit 1 to 17% audit 2, $P < 0.0001$) and in underprescription (from 4% audit 1 to 2% audit 2, $P < 0.03$)

(Continued)

TABLE 3. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
McEleny et al, 1998, ²⁶ UK, 1996 (4 wk) and 1997 (4 wk), surgical and medical patients	Single NHS hospital	III-3	1995 SIGN guidelines ²	Adherence to specific protocol (platelet monitoring)	Increase in adherence from 85% audit 1 to 92% audit 2 with an increase in sufficient monitoring from 44% audit 1 to 72% audit 2
	574 Patients admitted to hospital during audit 1 and 534 admitted during audit 2			At-risk patients receiving prophylaxis	Significant improvement in proportion of at-risk patients receiving prophylaxis after completion of audit cycle (and second audit; from 73% audit 1 to 97% in audit 2 $P < 0.001$)
Miller et al, 1996, ²⁷ UK, Nov 1990 to Nov 1992 and Feb 1993 to Feb 1994, surgical patients	Urban general hospital	III-3	Not stated	Adequacy of prophylaxis	Significant improvement in correct prophylaxis following audit cycle (from 55% audit 1 to 96% audit 2 $P < 0.001$)
	591 Patients Audit 1 and 406 Audit 2			Rates of DVT	DVT: Audit 1, 3/591 (0.7%); audit 2, 2/406 (0.4%)
Williams and Macdonald, ³¹ UK, dates not stated but 2 audits 3 mo apart, surgical patients	Orthopedic department of hospital	III-3	Locally developed departmental prophylaxis policy	Rates of PE	PE: Audit 1, 1/591 (0.2%); audit 2, 0/406
	35 Primary and revision hip and knee arthroplasty or femur neck fracture patients in Audit 1 and 39 in Audit 2			Major complications	Significantly fewer major complications Pre compared with Post ($P < 0.05$)
				Compliance with guidelines	Departmental protocol was followed in 50% of patients in audit 1 and improved to 70% in audit 2
					There was a significant improvement in the prescription of compression stockings and subcutaneous heparin for arthroplasty patients and for inclusion in a randomized trial of pulmonary embolism treatments for femur neck fracture patients.

(Continued)

TABLE 3. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Studies using quality assurance activities					
Huang et al, 2000, ¹⁴ UK, Oct 1997, surgical patients	District general hospital	III-2	1992 THRIFT guidelines ⁴⁵	Adequacy of prophylaxis	In intervention group, significant improvement in provision of prophylaxis to patients requiring compression stockings only (from 37% Pre to 71% Post, $P = 0.05$) and compression stockings + heparin (from 29% Pre to 70% Post, $P = 0.001$) No significant difference for any patients in control group
	50 Intervention and 50 control elective and emergency surgery patients preintervention and 50 intervention and 50 control patients postintervention				

ACCP indicates American College of Chest Physicians; LMWH, low-molecular-weight heparin; RCOG, Royal College of Obstetricians and Gynaecologists; SIGN, Scottish Intercollegiate Guidelines Network; THRIFT, Thromboembolic Risk Factors Consensus Group.

prophylaxis as patients with acute ischemic stroke or heart failure. Fagot et al²³ demonstrated that the provision of a patient-specific prescription order form improved compliance with French national guidelines for VTE prophylaxis and improved the accuracy of prescription in patients at moderate risk of VTE. However, no significant difference was found for patients at high risk.

Patient Outcomes and Resource Utilization

No studies were able to demonstrate a reduction in rates of DVT or PE as a result of the interventions to increase VTE prophylaxis, primarily due to a lack of power to detect these events. In 2 studies,^{25,34} length of hospital stay was reduced, leading to a cost saving in treating these patients. However, insufficient evidence was available to make useful comparisons of strategies in terms of costs and resource utilization.

DISCUSSION

Study Limitations

The conclusions which can be drawn from this review of literature regarding the uptake of VTE prophylaxis are limited by the nature of the available data. Only 1 RCT comparing different strategies to increase VTE prophylaxis uptake could be identified from the literature published within the last 10 years. The majority of studies report the results of an audit cycle where current practice is documented, a new

policy or program to improve practice is implemented, and then practice is reaudited following this. To the extent that such studies concentrate on process of change outcomes, such as compliance with guidelines, or process of care outcomes, such as adequacy of prophylaxis, the retrospective comparative study design provides reasonable information regarding changes in prophylaxis practice. However, since much of the data is obtained from chart review, it is impossible to control for differences in data collection or recording methods, changes in other hospital procedures over time, as well as changes in personnel or management structures. Furthermore, the majority of studies do not contain a sufficient number of participants to obtain adequate statistical power to detect changes in rare patient outcomes such as rates of DVT or PE. There is also the strong possibility that much of the data is subject to the Hawthorne effect. This may be seen as a positive outcome from a clinical perspective, and thus there may be little incentive for clinical researchers to seek to minimize this effect. As a result of the nature of the available data, conclusions are more easily made with regard to changing clinician behavior than with regard to influencing patient outcomes.

Effectiveness of Various Strategies to Increase Uptake of VTE Prophylaxis

The evidence identified for this review included only 1 study which made a direct comparison between different

TABLE 4. Studies Using Multiple Strategies

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Anderson et al, 1994, ¹² United States, Jul 1985 to Dec 1986 and Jul 1988 to Dec 1989, surgical and medical patients	15 Short-stay hospitals providing acute-care (teaching and nonteaching)	II (cluster randomized trial)	1986 NIH consensus statement on VTE prophylaxis ⁷	High-risk patients receiving prophylaxis	Significant increases in proportions of patients receiving prophylaxis in all hospitals (including control hospitals) between 2 study periods (from 29% to 52%; $P < 0.001$)
Strategies: continuing medical education (including documentation aids) or CME plus quality assurance	3 Groups of 5 hospitals: CME, CME + QA, Control				Increase in patients receiving prophylaxis significantly greater in hospitals using continuing medical education compared to control hospitals (11% vs 28%; $P < 0.001$), but there was no significant difference between hospitals using CME together with quality assurance activities and those using CME alone
	Preintervention: 466 patients in 5 control hospitals, 679 patients in 5 hospitals using CME and 702 patients in 5 hospitals using CME + QA				Improvement in prophylaxis significantly higher for surgical than medical patients in all hospitals
			Prophylaxis for different types of patients (medical/surgical)	Significant increase in prophylaxis in surgical patients in all hospitals (including control hospitals); similar improvement in hospitals using either intervention and intervention hospitals significantly greater than control hospitals	
	Postintervention: 342 patients in control hospitals, 513 patients in CME hospitals and 456 patients in CME+QA hospitals				Significant increase in prophylaxis in medical patients for both groups of intervention hospitals but no significant increase in control hospitals

(Continued)

strategies.¹² In that study, adding quality-assurance activities to a continuing medical education program did not significantly improve prophylaxis practice compared with using the continuing education strategy alone. The majority of avail-

able evidence consists of indirect comparisons of postintervention rates of compliance with guidelines or adequacy of prophylaxis practice for studies using different implementation strategies. To facilitate such comparisons, Figures 1 and

TABLE 4. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Pritts et al, 1999, ¹⁵ United States, 1995 to 1996 (24 mo in total), surgical patients	Urban university hospital	III-2/3	Not applicable (study focused on reducing length of stay for patients undergoing bowel resection by developing clinical pathway)	Rates of DVT	There were no statistically significant differences in rates of DVT between the Pre and Post implementation studies or between patients on the clinical pathway and those not on the clinical pathway
Strategies: documentation aids, continuing education	167 Patients undergoing bowel resection pre-implementation and 170 patients post-implementation (60 on the clinical pathway and 101 not on clinical pathway)				
Birks et al, 2002, ³² George et al, 1998; ³³ UK, dates not stated but postimplementation after 12 mo, surgical patients	Department of surgery	III-3	1992 THRIFT guidelines ⁴⁵	Compliance with guidelines	Improved with each audit as implementation strategies became more active from 47% at Audit 1 (baseline) to 77% at Audit 2 (after introduction of single local policy) to 78% at Audit 3 (after modifications to policy) to 86% at Audit 4 (after introduction of reminder label)
Strategies: audit cycle, documentation aids, continuing education, advertising	80 Patients for audit 1, 75 patients for audit 2, 60 patients for audit 3, 51 patients for audit 4			Adequacy of prophylaxis	Significant reduction in unacceptable protocol violations over course of 4 audits (from 30% to 14% of all patients, $P = 0.02$) and a 63% reduction in protocol violations for high risk patients (from 6 to 1)
				Patients receiving no prophylaxis	Reduction in moderate- to high-risk patients receiving no prophylaxis from 17% at audit 1 to 7% at audit 4
Bridges et al, 2003, ³⁴ United States, Aug 2000 to Jul 2001 and Jun 1999 to Jun 2000, surgical patients	Regional trauma center	III-3	2000 ACCP guidelines ³ and Eastern Association for the Surgery of Trauma 2001 VTE Practice Guidelines ⁸	Mean length of stay	Significant reduction of 4.4 d ($P < 0.002$) in intervention group on LMWH Expedited Anticoagulation Program (LEAP) compared to control group not on LEAP

(Continued)

TABLE 4. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
Strategies: continuing education, quality-assurance activities, appointment of specialist implementation staff	108 Admitted patients for intervention and 69 patients for control			Mean inpatient days on warfarin	Significant reduction of 3.8 d ($P < 0.0001$) in LEAP compared to control patients
				Rates of DVT	No DVT detected in either group
				Cost	4.4 d Reduction in length of stay resulted in a saving of US \$1800/patient, but there were additional costs of early discharge from hospital
Frankel et al, 1999, ³⁶ United States, dates not stated but 2 mo pre- and 2 mo postintervention, surgical patients	Level I urban, academic, trauma center	III-3	Locally developed guidelines based on review of the evidence for trauma patients	Compliance with guidelines (for both VTE prophylaxis and stress ulcers)	Significant improvement in compliance with guidelines 9 mo after guidelines introduced (from 48% Pre to 74% Post, $P = 0.001$)
Strategies: documentation aids, continuing education, quality-assurance activities	84 Trauma patients admitted pre-intervention and 116 admitted post-intervention			Adequacy of prophylaxis	Significant reduction in overtreatment (from 19% Pre to 2% Post, $P = 0.03$) but no significant change in undertreatment (from 26% Pre to 32% Post)
				Rates of DVT/PE	No significant change in rates of DVT (7% Pre to 5% Post) or PE (1% Pre to 1% Post)
Hohlt, 2000, ³⁸ United States, 1997–1998, surgical patients	Orthopaedic unit of Level I trauma center	III-3	Individual guidelines for each surgeon developed based on expert opinion and current literature	Patient mortality from PE	Mortality from PE reduced following implementation of interdisciplinary educational program from 4 cases Pre to 0 cases Post
Strategies: continuing education, documentation aids, quality-assurance activities, local change agents/opinion leaders	Sample size not stated			Incidence of DVT	Incidence of DVT reduced from 6 cases Pre to 1.3 cases Post (as reported in paper)

(Continued)

2 graph each of the studies which reported these 2 outcomes. The slope of the line connecting the pre- and postintervention scores for each study provides an indication of how large an improvement was achieved, with steeper lines indicating a greater improvement than flatter lines. It should be kept in mind that these rates may be dependent on factors in each

study setting which are not directly related to the strategy used for implementation, so that any comparison between studies must be made with caution.

Nevertheless, some patterns are evident in Figures 1 and 2. In Figure 1, it can be seen that 5 studies achieved rates of adherence to guidelines above 90%.^{13,22,26,39,40,42} In terms of

TABLE 4. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
McCarthy et al, 1998; ³⁹ Byrne et al, 1996; ⁴⁰ UK, dates of study not stated, surgical patients	District general hospital	III-3	1992 THRIFT guidelines ⁴⁵	Adequacy of prophylaxis	Appropriate prophylaxis prescriptions increased with each audit as implementation strategies became more active from 51% at audit 1 (verbal instruction to carry out risk assessment) to 54% at audit 2 (risk assessment sheet included in case notes) to 94% at audit 3 (miniaturized risk assessment sheet on reverse of prescription order form, nurse to check if completed and contact doctor if not); in replication hospital, 85%, and in both hospitals combined, 90%
Strategies: passive instruction, documentation aids, quality-assurance activities	195 General surgery patients for audit 1, 159 patients for audit 2, 203 patients for audit 3 and intervention replicated in 200 patients second hospital (replication hospital)			Adherence to specific guideline (completion of risk assessment sheet)	Introduction of miniaturized risk assessment sheet significantly increased completion of risk assessment from 37% to 97% ($P < 0.005$)
Peterson et al, 1999, ⁴¹ Australia, Feb 1997 to Dec 1997, surgical patients	Acute-care teaching hospital	III-3	1992 THRIFT guidelines ⁴⁵	Length of hospital stay	No change following intervention (median 2 d, mean 9.9)
Strategies: documentation aids, continuing education, advertising, local change agents	250 Surgical patients pre-intervention and 250 patients post-intervention			Compliance with guidelines	Significant improvement in adherence to guidelines following intervention (from 60% Pre to 70% Post, $P < 0.05$); biggest improvement for patients at high risk (26% Pre to 76% Post)
Devlin et al, 1999, ³⁵ United States, Mar 1999 to May 1999, surgical patients	Level I trauma center	IV	Locally developed guidelines based on review of evidence for trauma patients	Patients receiving prophylaxis	36/50 (72%)
Strategies: continuing education, appointment of specialist staff	50 Consecutive trauma patients admitted to surgery department with major orthopedic or spinal injuries			Adequacy of prophylaxis	Prophylaxis prescribed when indicated 53% of the time
				Rates of DVT	2/50 (4%)

(Continued)

TABLE 4. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
				Rates of PE	1/50 (2%)
				Rates of thrombocytopenia	1/50 (2%)
				Major bleeding episodes	3/36 (8%) Of patients prescribed prophylaxis (enoxaparin)
Hall and Eccles, 2000, ³⁷ UK, Sep 1996 to Jan 1999, surgical and medical patients	2 Urban acute care trusts	IV	1992 THRIFT guidelines ⁴⁵	Guideline use	56% Of wards were using guidelines with 40% of wards in Trust 1 using them and 75% of wards in Trust 2
Strategies: continuing education, advertising, local change agents/opinion leaders	79 Wards and 192 patient charts (10 patients randomly selected from each ward) with DVT risk assessment			Patients receiving prophylaxis	53% Of patients received prophylaxis; low risk: 16%; moderate risk: 62%; high risk: 78%
				Adequacy of prophylaxis	24% Patients did not receive prophylaxis when it was indicated
				Adherence to specific protocol (for use of reminder sticker)	32% Of patient files adhered correctly to guideline
Ryskamp and Trotter, 1998, ⁴² United States, Aug 1995 to Oct 1995; surgical and medical patients	Closed medical-surgical intensive care unit of large community teaching hospital	IV	1993 algorithm for VTE prophylaxis in medical patients	Adequacy of prophylaxis	86% Of patients received prophylaxis within 24 h of admission
Strategies: continuing education, quality-assurance activities	209 Patients admitted to ICU where prophylaxis indicated			Compliance with guidelines	Compliance with guidelines increased as implementation strategies became more active from 73% at baseline to 87% with the introduction of a dosing nomogram to 96% with the introduction of nurse monitoring of prophylaxis practice; when nurse monitoring ceased compliance with guidelines reduced to 86%
Stratton et al, 2000, ⁴³ United States (multicenter study), Jan 1996 to Feb 1997, surgical patients	10 Hospitals (9 teaching, 5 university, 4 private, 1 county)	IV	1995 ACCP guidelines ⁵	Patients receiving prophylaxis	89% Of patients in the 4 surgical groups received prophylaxis
Strategies: passive dissemination, documentation aids, quality-assurance activities	1907 Patients at high risk for DVT/PE (50 randomly selected from each hospital for each of 4 surgical procedures)			Adequacy of prophylaxis	64% Of patients received appropriate prophylaxis (ranging from 45% of hip-fracture-repair patients to 84% of total-hip-replacement patients)

(Continued)

TABLE 4. (Continued)

Study and Location	Setting and Patients	Level of Evidence	Guidelines	Outcomes Measured	Results
					Use of appropriate prophylaxis was significantly and independently associated with surgical group and clinical site ($P < 0.001$) but not with preexisting risk factors When preexisting risk factors and clinical site were removed from the analysis, appropriate prophylaxis was significantly associated with multiple therapies ($P < 0.001$) and shorter length of hospital stay ($P < 0.01$)

ACCP indicates American College of Chest Physicians Abbreviations: CME, continuing medical education; LMWH, low-molecular-weight heparin; NIH, National Institutes of Health; QA, quality assurance; THRIFT, Thromboembolic Risk Factors Consensus Group.

strategies used, these 5 studies are characterized by having either an iterative process of audit and feedback used to improve practice or refine implementation strategy^{22,26,39,40,42} or an active reminder process in place.^{13,39,40} On the other hand, of the 5 studies with the lowest rates of guideline adherence, only 1 used an audit and feedback strategy,³¹ and in this study no active iterative process was in place to improve practice after the audit. The other 4 studies relied primarily on continuing education to improve compliance with guidelines. The largest improvements in this outcome were also seen in the 3 studies using multiple strategies,^{32,33,39,40,42} which used successive audits to refine prophylaxis policy and implementation strategy.

In Figure 2, it is apparent that passive strategies for improving prophylaxis practice are not as effective as any of the active strategies. In general, it would appear that computer-based clinical-decision support systems are among the most effective strategies for improving prescribing practice, presumably because they minimize errors made by individual clinicians with varying degrees of interest, knowledge, and motivation for DVT and PE prevention. For this outcome, the highest scores were obtained in those studies which used either the computer-based decision support systems as discussed,^{13,29,30} or audit and feedback incorporating an iterative process.^{26,32,33,39,40,42} As with guideline compliance, lower scores were obtained in studies without an audit and feedback cycle,^{36,37,43} or where the documentation aid used did not provide an active reminder to assess VTE risk, or assistance to prescribe the appropriate prophylaxis.^{24,28} The quality-assurance strategy described by Huang et al¹⁴ resulted in

adequate prophylaxis being provided to around 70% of patients, which was a significant improvement on rates in the control group. However, it seems likely that the single strategy of actively monitoring compliance is not sufficient for optimizing prophylaxis practice.

Are Multiple Strategies Better Than a Single Strategy?

In the studies included in this review, it was evident that for any intervention to significantly improve VTE prophylaxis practice, it needs to have at least 2 elements. First, it must help clinicians remember to assess the risk status of patients for VTE, and second, it must assist clinicians to prescribe the prophylaxis appropriate for the risk classification. Thus, it is unlikely that acceptable VTE prophylaxis practices will result from a reliance on passive dissemination of guidelines (either through international publication or local dissemination within a workplace). Rather, an active implementation process is required, and a number of active strategies used in combination are likely to be more effective than a single active strategy used in isolation. While improving clinician knowledge of VTE risk assessment and prophylaxis should help to improve practice, the evidence suggested that increased knowledge may not be particularly effective without the additional step of actively reminding clinicians to assess patients for VTE risk. Having reminded clinicians to assess patients for VTE risk and prescribe appropriate prophylaxis, a further effective step is then to simplify the prescription process. The excellent results obtained in the

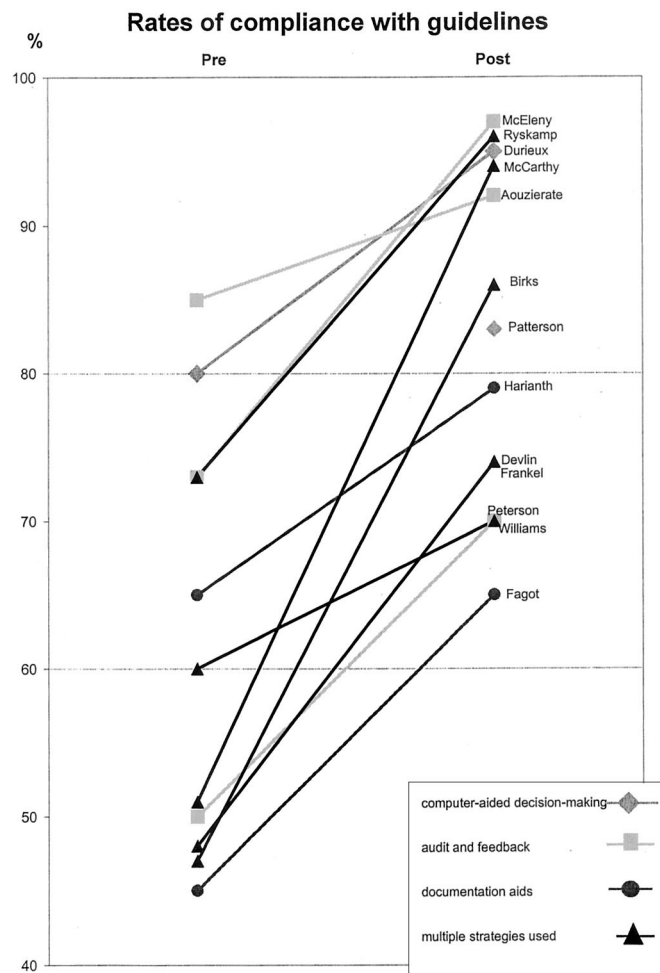


FIGURE 1. Rates of compliance with guidelines pre- and postimplementation of prophylaxis strategy. The slope of the line indicates the extent of improvement with steeper lines indicating greater improvement.

studies which used computer-based systems to facilitate risk assessment and prophylaxis prescription suggest that such systems may offer a promising method for achieving these 3 steps, by controlling sources of error which are inherent in variable clinician knowledge and practice. It is impossible to determine from the available evidence whether a computer-based system would be sufficiently more effective than a less technologically based alternative to justify the initial capital costs of developing and implementing such a system. It is likely that local circumstances would play a large role in determining how complex and costly the development of such a computer-based system would be. The alternative of a paper-based reminder system with active monitoring of adherence may offer an equally effective solution. However, it would appear that for any intervention to succeed in increasing the uptake of VTE prophylaxis, it needs to incorporate an

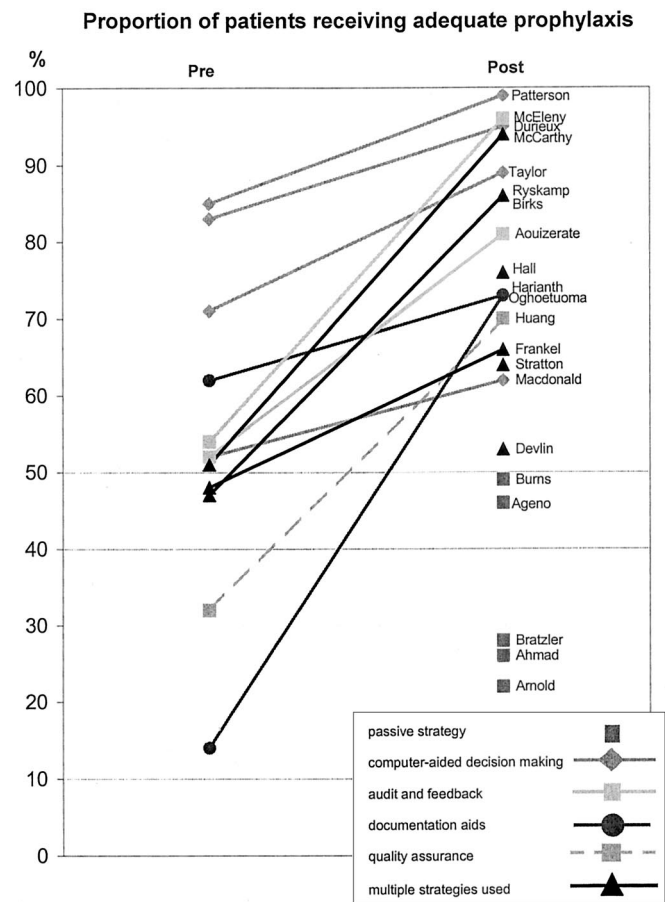


FIGURE 2. Proportion of patients receiving adequate prophylaxis pre- and postimplementation of prophylaxis strategy. The slope of the line indicates the extent of improvement with steeper lines indicating greater improvement.

iterative process so that the intervention, policy, or strategy can be improved as successive audits provide information about its effectiveness.

In terms of improving patient outcomes, in particular rates of DVT and PE, no clear evidence was found that suggests any one strategy was more effective than any other. However, this is most likely due to the limitations of the available data as previously discussed. The study designs and sample sizes used may not be sufficiently powerful to detect changes in the incidence of VTE.

Barriers and Facilitators

A number of barriers and facilitators to increasing VTE prophylaxis were evident in the included studies. Variability in clinician knowledge of risk assessment and appropriate prophylaxis and motivation regarding the need for prophylaxis appeared to play a role in the success or otherwise of implementation strategies (although such outcomes were rarely measured directly). A further complication is that there

does not appear to be universal acceptance that the evidence found in guidelines or consensus statements for VTE prophylaxis practice are suitable or appropriate in all clinical situations. This appeared to be the case particularly for recommendations regarding medical patients. Although not always directly studied, the interest and enthusiasm of local clinical management for VTE prophylaxis seemed to have influenced performance in some studies, even in the control groups where no active intervention was undertaken.

Walker et al⁴⁴ studied the introduction of the SIGN guidelines for VTE prophylaxis in Scotland and found that barriers to guideline implementation included a lack of supportive systems, including systems for data collection and audit; problems with individual staff responsible for implementation; a lack of acceptance of guidelines; and a perceived lack of need in particular clinical areas. On the other hand, facilitators were almost always individuals or groups of individuals who were enthusiastic and proactive and, in particular, who were given adequate time to promote good prophylaxis practice. Not surprisingly, Walker et al⁴⁴ found that barriers were reported more often by hospital trusts, which were not actively implementing guidelines compared with those trusts which were. In these trusts, more facilitators than barriers were identified.

Recommendations

Research

The question of which strategies are most effective in increasing uptake of VTE prophylaxis could best be answered by cluster randomized trials comparing 1 or more strategies. At this stage, it does not seem necessary to include a placebo arm since there is sufficient evidence to suggest that passive dissemination alone will not result in adequate prophylaxis practice. Rather, research questions could focus on which of the various active strategies is more effective, in particular, comparisons of more complex (and probably more costly) interventions with simpler (and probably cheaper) interventions. A full evaluation of different strategies would ideally seek to identify barriers and facilitators to implementation so that an iterative process of improvement can occur such as was described in a number of the included studies. To study the key patient outcomes of DVT and PE rates, large multicenter studies would probably be necessary to provide sufficient power to detect these outcomes. Cost and resource use issues would need to be studied carefully and thoroughly, ensuring that the balance between the cost of implementing strategies and the potential clinical savings is taken into account, to determine whether there are cost benefits associated with particular strategies.

Clinical Practice and Policy

To effect change in VTE prophylaxis practice requires clinical leadership, improved clinician knowledge of risk

assessment and prescribing, and a supportive system which removes some of the individual barriers which presently result in less-than-optimal practices. Any intervention designed to improve thromboprophylaxis practice should ideally contain the following components:

A process for demonstrating to clinicians the importance and relevance of VTE prophylaxis in their local clinical setting; for example, by conducting a local audit of current practice and presenting this to clinical staff

A process for improving clinician knowledge about VTE risk assessment and prophylaxis practice (probably through a continuing education process)

A method of reminding clinicians to assess patients for VTE risk (and possibly documentary aids to assist in the process)

A process for assisting clinicians to prescribe the appropriate prophylaxis

A method for assessing the effectiveness of any changes and for refining local policy to further improve practice; clinical audit and feedback may be the most effective method for achieving this.

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