المجلس الصحي السعودي
Saudi Health Council

Evidence-Based Clinical Practice Guideline: Screening, Prophylaxis and Management of Venous Thromboembolism (VTE)

National Center for Evidence-Based Medicine
SAUDI HEALTH COUNCIL

First Edition
June 2021

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NICE, SIGN, ACEP
National Center for Evidence-Based Medicine
SAUDI HEALTH COUNCIL

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Table of Contents

List of Tables:

List of figures:

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Disclaimer

Clinical Practice Guidelines (CPGs) are developed to assist healthcare practitioners with decisions on appropriate healthcare. The Guidelines should be used to assist healthcare providers to exercise their clinical judgment for the benefit of patients based on the current best evidence and to reduce unnecessary variations in clinical practice. This guideline has been adapted to provide a summary of the best evidence-based information to assist healthcare providers to identify and manage patients who are at risk for venous thromboembolism (VTE). The eventual decision regarding any clinical procedure or treatment plan for a specific clinical situation must be made by the responsible healthcare professional(s). This guideline will not replace standards of care which will be determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve.

Intellectual Property Rights

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- The Saudi Health Council (SHC)
- Saudi Central Board for Accreditation of Healthcare Institutions (CBAHI)
- Scientific committee advisors of the National Centre for EBHP, Riyadh, Saudi Arabia
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- The Scottish Intercollegiate Guidelines Network (SIGN)
- The American College of Emergency Physicians
- Dr. Yasser Sami Amer, MBBCh, MSc Ped., MSc HC Inf., Clinical Practice Guidelines General Coordinator/ Advisor, Member, CPG Steering Committee, Quality Management Department, King Saud University Medical City, Riyadh, KSA, Member, G-I-N Adaptation Working Group (Steering group) and GIRAne

Abbreviations

ACEP	American College of Emergency Physicians
AES	Anti-embolism stockings
AGREE II	Appraisal of Guidelines for Research & Evaluation
APTT	Activated partial thromboplastin time
ART	Assisted reproductive technology
BMI	Body mass index
CABG	Coronary artery bypass graft
CBAHI	Saudi Central Board for Accreditation of Healthcare Institutions
CI	Confidence interval
CLOTS	Clots in Legs Or stockings after Stroke
COC	Combined oral contraceptive
CPG	Clinical Practice Guideline
CT	Computed tomography
CVC	Central venous catheter
DVT	Deep vein thrombosis
ECG	Electrocardiogram
ECRI	Emergency Care Research Institute
G-I-N	Guideline International Network
GoR	Grade of Recommendations
HIT	Heparin induced thrombocytopenia
HIV	Human immunodeficiency virus
HR	Hazard ratio
HRT	Hormone replacement therapy
ICU	Intensive care unit
INR	International Normalized Ratio
IPC	Intermittent pneumatic compression
ISI	International sensitivity index
IVC	Inferior vena cava
IVF	In vitro fertilization
Kg	Kilogram
KPIs	Key performance indicators
KSA	Kingdom of Saudi Arabia
LMWH	Low molecular weight heparin
LoE	Level of Evidence
MeSH	Medical Subject Headings
MI	Myocardial infarction
NCEBHP	National Center for Evidence Based Health Practice
NICE	National Institute of Clinical and Health Excellence
NOAC	Novel anticoagulants
NSAID	Non-steroidal anti-inflammatory drug
OHSS	Ovarian hyperstimulation syndrome
PE	Pulmonary embolism
PERC	Pulmonary Embolism Rule-out Criteria
PESI	Pulmonary Embolism Severity Index
PubMed	U.S. National Library of Medicine
PT	Prothrombin time
PTS	Post-thrombotic syndrome
RCT	Randomized controlled trial
RR	Relative risk
RV	Right ventricular
Sa,O_2	Arterial oxygen saturation
SIGN	Scottish Intercollegiate Guidelines Network
SC	Subcutaneous
SCI	Spinal Cord Injury
SHC	Saudi Health Council
sPESI	Simplified Pulmonary embolism severity index
THR	Total hip replacement
TKR	Total knee replacement
TRIP	Turning Research into Practice (TRIP) database
UFH	unfractionated heparin
US	Ultrasound
VKA	Vitamin K antagonist
VTE	Venous thromboembolism

Introduction

Acute venous thromboembolism (VTE) is associated with high morbidity and mortality. It has been reported to be responsible for about 11.3 % of deaths around the world with 30% risk of developing post thrombotic syndrome (PTS) in 10-20 years after the incidence (1). PTS is the most common chronic complication of VTE which, causes chronic limb pain, swelling and leg ulcer (2). Internationally, the true incidence of VTE is approximately 25,000 cases per year with a fatality rate of 6-10 present of the present cases. Venous thromboembolism (VTE) comprised of deep vein thrombosis (DVT) and pulmonary embolism (PE) is a relatively common disease affecting approximately 100 per 100,000 people per year (1, 3). Hence, it is estimated that approximately 25,000 people are affected in the Kingdom of Saudi Arabia (KSA) annually. The main risk factors for the development of VTE are age, surgery, antenatal, cancer, immobility trauma, puerperium, hormonal use, obesity, and inherited and acquired hypercoagulable states (3). VTE is considered a major risk to many types of patients i.e. elderly, surgical, antenatal, and patients in intensive care units (4). For example, the incidence of hospital acquired VTE is 10-40 % among surgical patients (5). In a study conducted locally at one tertiary-care hospital in Saudi Arabia, investigators identified 500 confirmed cases of VTE in one-year period with fatality rate of 20.8% and with two thirds of patients being in surgical wards and one third in the medical wards (5). Only 44.1% of surgical patients and 21.7% received appropriate thromboprophylaxis (5). Another study at seven major hospitals in Saudi Arabia found 1241 confirmed VTE cases occurred during a 12-month period (6). Most (58.3%) of the VTE cases were DVT only, 21.7% were PE, and 20% were both DVT and PE (6). Most (78.6%) confirmed VTE cases occurred in medical patients, respectively and only 40.9% of VTE cases received appropriate thromboprophylaxis (63.2% for surgical patients and 34.8% for medical patients; $P < 0.001$) (6). The mortality rate was 14.3% which represented 1.6% of total hospital deaths (6).These studies might reflect the variations in the practice and the underutilization of thromboprophylaxis for at-risk patients. Also, these studies indicated that the available guidelines might not be properly implemented. Non-adherence to the available guidelines can be attributed to several factors that include under-estimation of the risk and the absence of formal national guidelines on VTE prevention. These concerns were raised by the Saudi Central Board for Accreditation of Healthcare Institutions (CBAHI) to create a unified National guideline to be enforced in all healthcare organizations in Saudi Arabia. Hence, the aim of this adapted guideline is to provide a standard of care of VTE screening, prophylaxis, and management.

Method

This clinical practice guideline was adapted by the National Center for Evidence Based Health Practice at the Saudi Health Council in collaboration with CBAHI. The center contacted a group of clinicians and healthcare providers from various specialties to serve as an expert panel for adaptation of a National VTE guideline. The description of the methodology for the production of this CPG was fulfilled by utilizing the sequential process for trans-contextual adaptation of CPGs proposed by the ADAPTE Working group of the Guidelines International Network (G-I-N); the King Saud University Modified ADAPTE that was based on the original ADAPTE Manual and Resource Toolkit Version 2.0 (7-10). The adaptation process included three phases; set-up, adaptation, and finalization phases. This method was approved by The National Center for Evidence Based Health Practice to be the method of CPG production at the Saudi Health Council.

A search was conducted to find the available CPGs related to VTE in the last five years. The databases included Guideline International Network (**G.I.N**), National Institute of Clinical and Health Excellence (**NICE**), Turning Research into Practice (**TRIP**) database, Scottish Intercollegiate Guidelines Network (**SIGN**), Emergency Care Research Institute (**ECRI**) and the U.S. National Library of Medicine (**PubMed**). The inclusion and exclusion criteria were based on different factors (***Appendix 1***). Searches included MeSH and text words terms with combination using 'AND/ OR' Boolean operators. The search words differed between databases, but were comparable (***Appendix 2***). The recommendations were written according to the Definition of Level of Evidence (LoE) and Grade of Recommendations (GoR) (11). The classification system was adopted from the "Prevention and management of venous thromboembolism guidelines of SIGN" (Table 1). The expert panel' members agreed to be listed alphabetically as contributors.

Table 1: Level of Evidence (LoE) and Grade of Recommendations (GoR)

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS	
LEVELS OF EVIDENCE	
1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias	
1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias	
1 - Meta-analyses, systematic reviews, or RCTs with a high risk of bias	
2++ High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal	
2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal	
2 - Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal	
3 Non-analytic studies, e.g. case reports, case series	
4 Expert opinion	
GRADES OF RECOMMENDATION *Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.*	
A	*At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results*
B	*A body of evidence including studies rated as 2++, and directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+*
C	*A body of evidence including studies rated as 2+, and directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++*
D	*Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+*
GOOD PRACTICE POINTS	
✓	*Recommended best practice based on the clinical experience of the guideline development group.*

A matrix was constructed for the main possible recommendations (***Appendix 3***), which covered the following areas: screening, prophylaxis, and management. It also included different settings:

- All patients
- Outpatients/ Ambulatory care centers
- Medical patients
- Surgical and trauma patients
- Pregnant women and women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks
- Cancer associated thrombosis (it developed in up to 20% of cancer patients)
- Patients in Emergency Department
- Patients admitted to ICU
- Travel related thrombosis

The panel had 4 meetings over 9 month's period on 15th of April, 30th of April, 24th of June 2019 and 22nd of June 2020.

The first meeting addressed the followings: members concerns, selection of the questions to be answered by the guideline, agreement of adaptation methodology, and to explain the ADAPTE method using the AGREE II instrument. This tool; the **A**ppraisal of **G**uidelines for **RE**search & **E**valuation (**AGREE II**) Instrument) was developed to address the issue of variability in guideline quality and assess the methodological rigor and transparency in which a guideline is developed (12). The purpose of the AGREE II, was to provide a framework to: 1. Assess the quality of guidelines; 2. Provide a methodological strategy for the development of guidelines; and 3. Inform what information and how information ought to be reported in guidelines (12). The tool consisted of six domains; scope and purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, and Editorial Independence. The AGREE II includes two final overall assessment items that required the appraiser to make overall judgment of the guideline while considering how they rated the 23 items (***Appendix 4***). All decisions and comments during meetings were documented as minutes, which were emailed after each meeting to the members to check their accuracy. Also, a conflict of interest form

developed by the ADAPTE group was signed by each panel member (10). A decision support tool for the adaptation working panel for the current CPG was followed (***Appendix 5***).

The second meeting was conducted to inform the panel of the available CPGs addressing VTE within the last 5 years. Additionally, the panel members agreed to reach consensus regarding the appropriate CPGs for adaptation according to the inclusion and exclusion criteria. The chair of expert the panel (SA) created several taskforce groups online composed of the panel members who were required to appraise the included CPGs. All of the CPGs were uploaded in the AGREE trust website as pdf. Each member was required to register in the AGREE trust website in order to access and complete individual appraisals online. Each CPG was reviewed by two to three members of the panel using AGREE II instrument independently. Each member was given a deadline of two to four weeks to complete the appraisal.

In the third meeting, the expert panel discussed the challenges and explored their perspectives of the appraisal process. Thereafter, according to the final consensus and scoring, the included CPGs were retrieved for adaptation. Comments from reviewers were assessed and analyzed qualitatively, in order to inform and guide the adaptation of the current guideline (***Appendix 6***). Moreover, the future plan on the process of adaptation was discussed and agreed to prepare the first draft of CPG before the final meeting.

The fourth meeting was conducted to review the first draft of the adapted CPG. The reviewers rated the recommendations and their suitability to the Saudi context. Recommendations were considered suitable if they were feasible and legal. The recommendation of the included guideline that covered the same content were summarized as one entity. The Chair and the reviewers checked the recommendations to assess their readability and intelligibility. Each read the recommendations on their own and discussed them afterward as a group to reach a consensus about the intelligibility of the recommendations. Most of them were assessed as consequential and easy to understand. Only slight changes needed to be made to improve comprehensibility

and reduce complexity. The initial drafted guideline was prepared and circulated via email to all members for review. Two drafts were sent to the external reviewers for clinical content and methodological rigor. The external review included questions about whether the users approved of the draft guideline, strengths and weaknesses, and suggested modifications. The guideline recommendations were also discussed with patients and their families to address their perspectives and concern. The comments and suggestions from all these external reviews were addressed, either by modifying the guideline or by giving reasons for not taking them into account. In order to guarantee the copy rights and intellectual properties of the adapted guidelines, the Center of Evidence Based Health Practice at Saudi Health Council acquired permissions to adapt and use recommendations and pathways from the included guidelines. Moreover, a leaflet of plain language about the VTE adapted guideline in Arabic was provided to patient/public about the disease process in general, its prognosis and medications.

Results

Databases search revealed 178 guidelines. Eight met the inclusion criteria for evaluation. The panel members agreed to adapt three guidelines as they scored high compared to other included CPGs: The Scottish Intercollegiate Guidelines Network (SIGN) (13), The National Institute of Clinical and Health Excellence (NICE) (14) and The American College of Emergency Physicians (ACEP) (15).

The Scottish Intercollegiate Guidelines Network (SIGN) guideline was evaluated with an overall score of 88% and with no modification except for 1 reviewer who requested slight modification. While NICE guideline scored 88% and all expert panel agreed to adapt only the tools and pathways. The American College of Emergency Physicians guideline had an overall score of 92% with 2 reviewers recommended adapting it with no modifications and 2 requested to be added with some modification.

The scope and purpose:

Disease/Condition

Venous Thromboembolism (VTE)

Guideline Objective(s)

1- To provide an adapted high quality standardized National VTE guideline to reduce variations in the practice.
2- To screen and identify patients' group at risk of VTE aged 16 and over at different settings. It also encompasses patients includes people discharged from hospital, (including emergency room patients) with lower limb devices such as plaster casts and braces, people attending hospital for day procedures including cancer treatment and surgery, and pregnant women admitted to hospital.
3- To review and provide a comprehensive guideline for patients with different consideration (age groups, comorbidities).
4- To provide a practical implementation tools for all health practitioners.

Health / Clinical Question (PIPOH):

Questions for the current CPG were defined by the expert panel members, which were discussed and summarized using the following PIPOH format (Table2).

Table 2: VTE PIPOH questions as defined by the expert panel

Health / Clinical Question (PIPOH)	
Patients (Target Population)	Adults (> 16 years) hospitalized or outpatients at risk for VTE (medical and surgical)
	Critical Care patients.
	Patients undergoing surgery
	Patients admitted to the hospital with trauma, spinal cord injury (SCI), lower extremity injuries, or burns.
	Medical patients with risk factors for thromboembolism
	Pregnant / postpartum patients
	Patients presenting in the emergency department/ outpatient adults with suspected acute deep venous thrombosis (DVT) of the upper and lower extremity, pulmonary embolus (PE), or both (VTE).
	Patients on long travel
Interventions and Practices Considered / **CPG** Category	Screening and assessment of VTE risk factors
	Prophylaxis and Prevention of VTE
	Management of VTE
Professionals (Intended / Target Users or Stakeholders)	Physicians: surgeons, Cardiologist, Internist, hematologist, Oncologist, OBS/gynecologist, Family physician
	Nurses
	Clinical Pharmacists
	Other healthcare personnel
	Quality staff / audit
	Patient safety personnel
	Patients
Outcomes considered	Effectiveness of Screening, prevention, and treatment of patients with VTE
	VTE minor and major complications and outcomes, such as: - All-cause Mortality - Fatal PE - Bleeding - Symptomatic, proven DVT or PE - Asymptomatic DVT (proximal and distal)
Healthcare Settings	Primary, secondary, emergency and tertiary settings in Kingdom of Saudi Arabia

Key Recommendations

The current guideline recommendations were written in the following categories: screening, prophylaxis and management in different settings.

Screening of venous thromboembolism:

Preliminary assessment: All patients

D

- All patients presenting acutely or getting admitted to the hospital should be individually assessed for risk of VTE and risk of bleeding. Based on the assessment, the risks and benefits of prophylaxis should be discussed with the patient (16).
- The use of a risk assessment method checklist is recommended for this purpose (17).
- The assessment should be repeated regularly at least every 48 hours and following significant change in the clinical scenario of the patient (e.g., surgery, GI bleeding) (16).
  - ✓ Clinical assessment of venous thrombosis risk: Algorithms for assessing the risk of VTE in patients admitted to hospital have been designed and presented in (Figure 1). VTE and bleeding risks are assessed on admission to MOH hospitals using the Caprini risk assessment tool (Figure 2).
  - ✓ The risk assessment and management plan should be shared with the patient/care giver and the outcome of that discussion should be documented in the medical record.

Figure 1: Algorithm for assessing the risk of VTE

Algorithm for assessing the risk of venous thromboembolism (VTE)
Grampian risk assessment tool

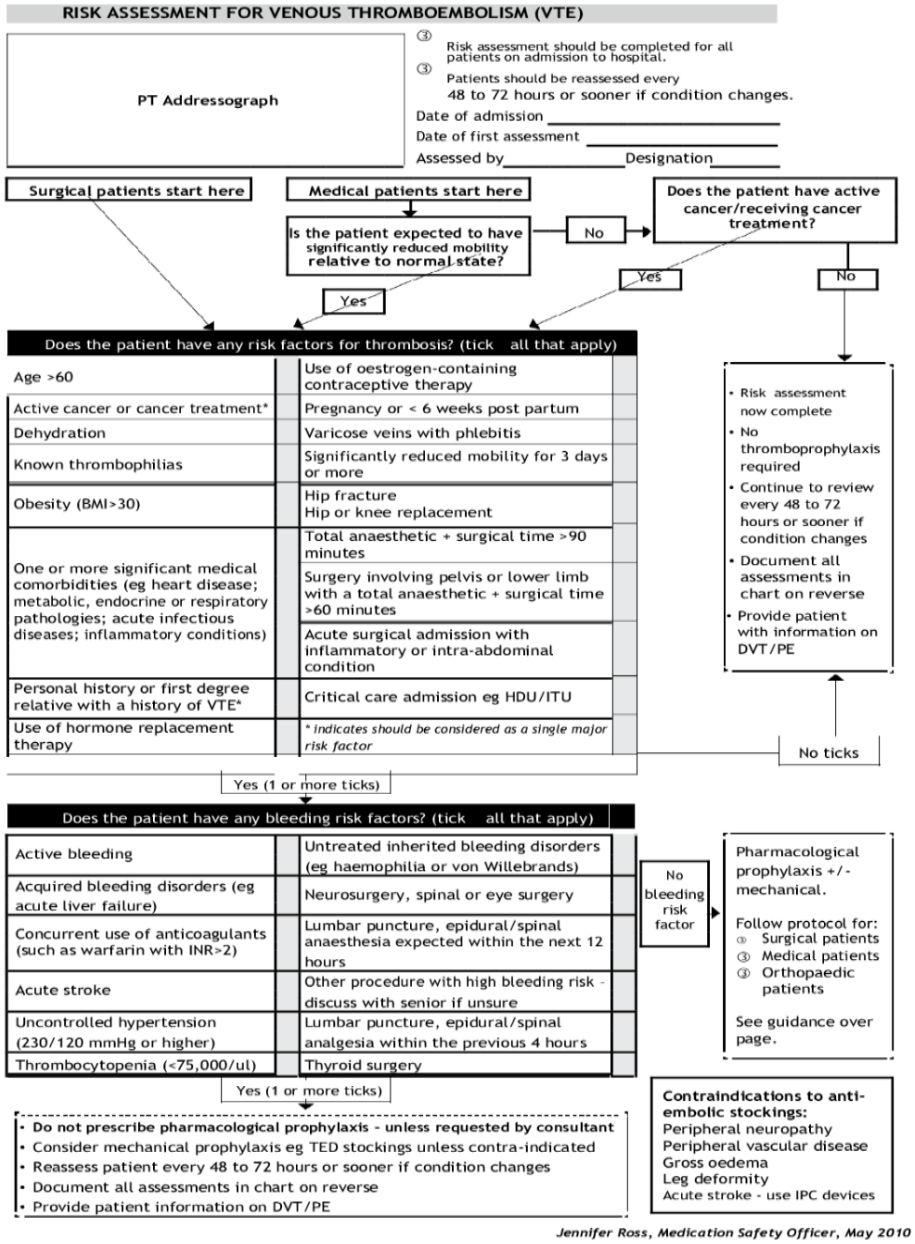
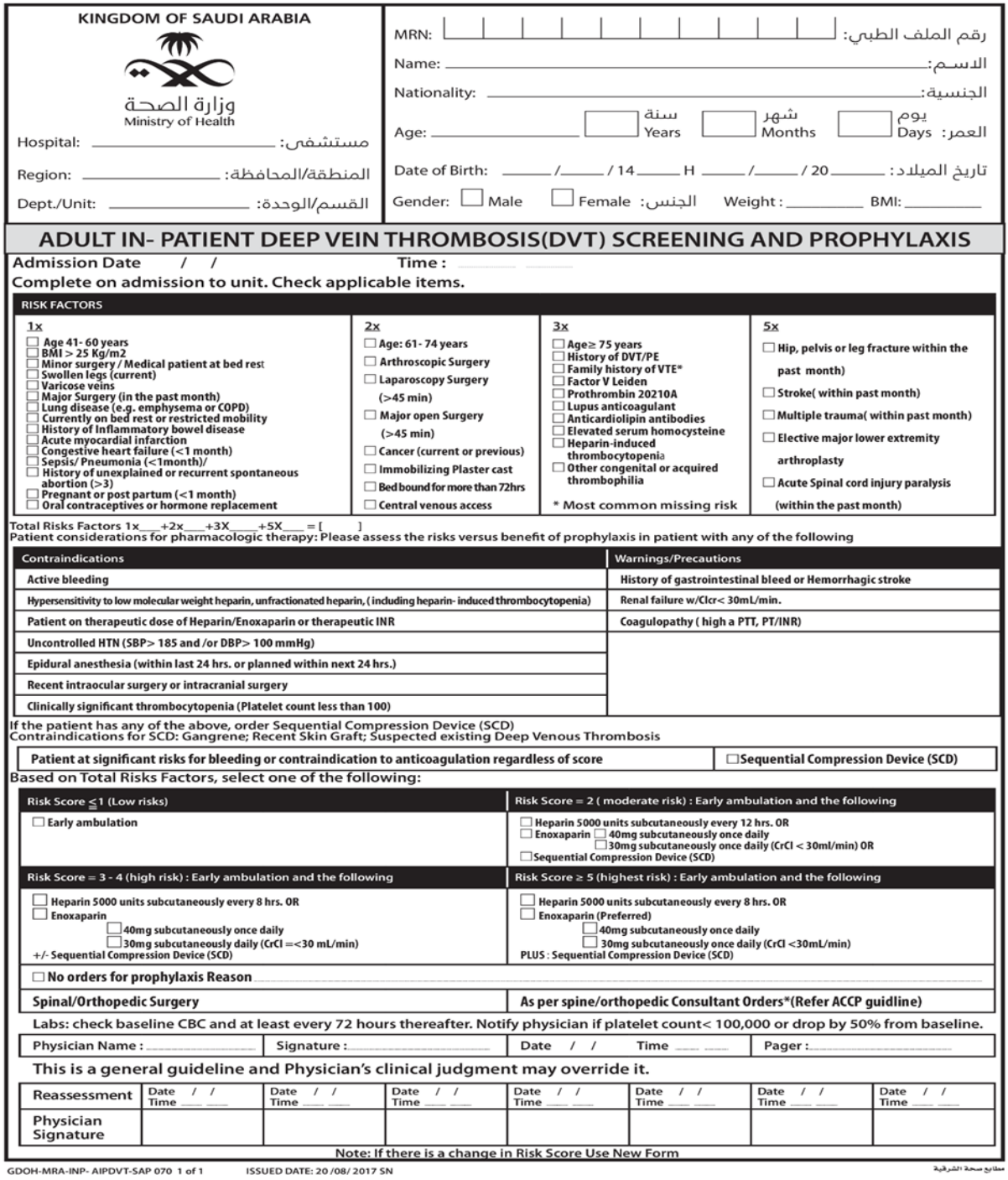


Figure 2: Adult In-Patients Deep Vein Thrombosis (DVT) Screening and Prophylaxis.



KINGDOM OF SAUDI ARABIA

وزارة الصحة
Ministry of Health

Hospital: _____ :مستشفى

Region: _____ :المنطقة/المحافظة

Dept./Unit: _____ :القسم/الوحدة

MRN: | | | | | | | | | | | :رقم الملف الطبي

Name: _____ :الاسم

Nationality: _____ :الجنسية

Age: _____ ☐ سنة Years ☐ شهر Months ☐ يوم Days :العمر

Date of Birth: ___/___/14___ H ___/___/20___ :تاريخ الميلاد

Gender: ☐ Male ☐ Female :الجنس Weight: _____ BMI: _____

ADULT IN- PATIENT DEEP VEIN THROMBOSIS(DVT) SCREENING AND PROPHYLAXIS

Admission Date / / Time :

Complete on admission to unit. Check applicable items.

RISK FACTORS

1x	2x	3x	5x
☐ Age 41- 60 years ☐ BMI > 25 Kg/m2 ☐ Minor surgery / Medical patient at bed rest ☐ Swollen legs (current) ☐ Varicose veins ☐ Major Surgery (in the past month) ☐ Lung disease (e.g. emphysema or COPD) ☐ Currently on bed rest or restricted mobility ☐ History of Inflammatory bowel disease ☐ Acute myocardial infarction ☐ Congestive heart failure (<1 month) ☐ Sepsis/ Pneumonia (<1month)/ ☐ History of unexplained or recurrent spontaneous abortion (>3) ☐ Pregnant or post partum (<1 month) ☐ Oral contraceptives or hormone replacement	☐ Age: 61- 74 years ☐ Arthroscopic Surgery ☐ Laparoscopy Surgery (>45 min) ☐ Major open Surgery (>45 min) ☐ Cancer (current or previous) ☐ Immobilizing Plaster cast ☐ Bed bound for more than 72hrs ☐ Central venous access	☐ Age≥ 75 years ☐ History of DVT/PE ☐ Family history of VTE* ☐ Factor V Leiden ☐ Prothrombin 20210A ☐ Lupus anticoagulant ☐ Anticardiolipin antibodies ☐ Elevated serum homocysteine ☐ Heparin-induced thrombocytopenia ☐ Other congenital or acquired thrombophilia * Most common missing risk	☐ Hip, pelvis or leg fracture within the past month) ☐ Stroke(within past month) ☐ Multiple trauma(within past month) ☐ Elective major lower extremity arthroplasty ☐ Acute Spinal cord injury paralysis (within the past month)

Total Risks Factors 1x___+2x___+3X___+5X___ = [ ]

Patient considerations for pharmacologic therapy: Please assess the risks versus benefit of prophylaxis in patient with any of the following

Contraindications	Warnings/Precautions
Active bleeding	History of gastrointestinal bleed or Hemorrhagic stroke
Hypersensitivity to low molecular weight heparin, unfractionated heparin, (including heparin- induced thrombocytopenia)	Renal failure w/Clcr< 30mL/min.
Patient on therapeutic dose of Heparin/Enoxaparin or therapeutic INR	Coagulopathy (high a PTT, PT/INR)
Uncontrolled HTN (SBP> 185 and /or DBP> 100 mmHg)	
Epidural anesthesia (within last 24 hrs. or planned within next 24 hrs.)	
Recent intraocular surgery or intracranial surgery	
Clinically significant thrombocytopenia (Platelet count less than 100)	

If the patient has any of the above, order Sequential Compression Device (SCD)
Contraindications for SCD: Gangrene; Recent Skin Graft; Suspected existing Deep Venous Thrombosis

Patient at significant risks for bleeding or contraindication to anticoagulation regardless of score	☐Sequential Compression Device (SCD)

Based on Total Risks Factors, select one of the following:

Risk Score ≤1 (Low risks)	Risk Score = 2 (moderate risk) : Early ambulation and the following
☐ Early ambulation	☐ Heparin 5000 units subcutaneously every 12 hrs. OR ☐ Enoxaparin ☐ 40mg subcutaneously once daily ☐ 30mg subcutaneously once daily (CrCl < 30ml/min) OR ☐Sequential Compression Device (SCD)
Risk Score = 3 - 4 (high risk) : Early ambulation and the following	**Risk Score ≥ 5 (highest risk) : Early ambulation and the following**
☐ Heparin 5000 units subcutaneously every 8 hrs. OR ☐ Enoxaparin ☐ 40mg subcutaneously once daily ☐ 30mg subcutaneously daily (CrCl =<30 mL/min) +/- Sequential Compression Device (SCD)	☐ Heparin 5000 units subcutaneously every 8 hrs. OR ☐ Enoxaparin (Preferred) ☐ 40mg subcutaneously once daily ☐ 30mg subcutaneously once daily (CrCl <30mL/min) PLUS : Sequential Compression Device (SCD)
☐ No orders for prophylaxis Reason _____	
Spinal/Orthopedic Surgery	As per spine/orthopedic Consultant Orders*(Refer ACCP guidline)

Labs: check baseline CBC and at least every 72 hours thereafter. Notify physician if platelet count< 100,000 or drop by 50% from baseline.

Physician Name : _____	Signature : _____	Date / / Time ___ ___	Pager : _____

This is a general guideline and Physician's clinical judgment may override it.

Reassessment	Date / / Time ___ ___	Date / / Time ___ ___	Date / / Time ___ ___	Date / / Time ___ ___	Date / / Time ___ ___	Date / / Time ___ ___	Date / / Time ___ ___
Physician Signature							

Note: If there is a change in Risk Score Use New Form

GDOH-MRA-INP- AIPDVT-SAP 070 1 of 1 ISSUED DATE: 20 /08/ 2017 SN

مطابع صحة الشرقية

The risk factors for VTE and recurrent VTE are listed in Tables 3 and 4. As the relative risks of bleeding and thrombosis may change over time, due to evolution of disease, interventions and treatments, there is a need to review individual circumstances throughout the period of admission and on discharge.

✓ The results of the initial assessment should be used to determine the diagnostic strategy (18, 19).

Table 3: Risk factors for venous thromboembolism

Risk	Factor Comments
Age (20-22)	Incidence of first VTE rises exponentially with age. In the general population: <40 years – annual incidence of 1/10,000 60-69 years – annual incidence of 10/10,000 >80 years – annual incidence of 100/10,000 May reflect immobility (23) and coagulation activation (24, 25)
Obesity (20, 21, 23, 25-27)	2 to 3-fold VTE risk if obese (body mass index >30 kg/m^2) May reflect immobility and coagulation activation (24, 25)
Varicose veins (28, 29)	1.5 to 2.5-fold risk after major general/ orthopedic surgery Low risk after varicose vein surgery (30, 31)
Family history of VTE	A history of at least one first degree relative having had VTE at age <50 years or more than one first degree relative with VTE history regardless of age is an indicator of increased risk of first VTE (but not of recurrent VTE) (32)
Thrombophilias (33-35)	(To be tested in patients with family history of VTE or when results will be used to improve or modify management. Testing has been suggested to assist with secondary prevention of VTE(36) Low coagulation inhibitors (antithrombin, protein C and S) Activated protein C resistance (or replaced by molecular factor V Leiden and prothrombin G20210A):the most prevalent inherited risk factors High coagulation factors (no evidence except for F VIII (I, II, including, VIII, IX, XI) Antiphospholipid antibodies High homocysteine: 1.5 to 2.5-fold VTE risk (37, 38) Elevated lipoprotein(a) >300mg/l: 1.8-fold risk of VTE (39)
Other prothrombotic states	Cancer: compared with general population overall 5 to 7-fold risk of first VTE and increased risk of recurrent VTE. Risk varies with type of cancer. Further increased risk associated with surgery, chemotherapy, use of erythropoiesis stimulating agents and central venous catheters (40, 41) Heart failure, recent myocardial infarction/stroke, metabolic syndrome: 2-fold increased risk of VTE (42) Severe acute infection Chronic HIV infection (43) Inflammatory bowel disease, nephrotic syndrome Myeloproliferative disease, paraproteinemia, Bechet's disease, paroxysmal nocturnal hemoglobinuria Sickle cell trait(should not be included) only sickle cell disease (44)

Combined oral contraceptives, hormone replacement therapy and anti-estrogens	Combined oral contraceptives (COCs): compared with non-users, COC users have 3 to 6-fold increased risk.(45, 46) Compared with users of COCs containing second generation progestogens, users of COCs containing third generation progestogens have a further 1.7- fold increase in VTE risk(47). 2.5-fold increased risk of postoperative VTE in COC users (29) No evidence that progestogen-only oral contraceptives are associated with increased VTE risk, but high-dose progestogens used to treat gynecological problems associated with 6-fold increased VTE risk Oral estrogen hormone replacement therapy (HRT) users have 2.5-fold increased VTE risk but not transdermal estrogen HRT users (48) Heritable thrombophilia further increases VTE risk in COC and oral estrogen HRT users (17, 49) Raloxifene and tamoxifen associated with a 2 to 3-fold increased VTE risk (50, 51)
Pregnancy, puerperium	Approximately 10-fold increased risk during pregnancy compared with non-pregnant and 25-fold increased risk compared with non-pregnant/ non-puerperal during puerperium (51) Pregnant and puerperal women with thrombophilia have increased risk of VTE compared to pregnant and puerperal women without an identified thrombophilia (17, 51, 52)
Immobility	For example, bed rest >3 days, plaster cast, paralysis: 10-fold increased VTE risk; increases with duration
Immobility during travel (21, 53)	2 to 3-fold increased risk
Hospitalization (21, 53)	Acute trauma, acute illness, surgery: 10-fold increased VTE risk
Anesthesia	2 to 3-fold increased risk of postoperative VTE in general compared with spinal/epidural (29, 54)
Central venous catheters	Compared with subclavian access, femoral route 11.5-fold increased risk of VTE (55) Slightly noticeable increased risk of central venous catheter (CVC) thrombosis in patients with prothrombin G20210A or factor V Leiden compared to risk in CVC patients with wild type prothrombin and factor V (56)

Table 4: Risk factors for recurrent venous thromboembolism (in patients not on long term anticoagulation)

Risk	Factor Comments
Previous unprovoked VTE (57)	Recurrence rate 5% per year after an unprovoked VTE
Male sex (58)	Compared with women, men have an increased relative risk (RR) of recurrent VTE (RR 1.6, 95% confidence interval (CI. 1.2 to 2.0). The higher relative risks reported in some studies (59, 60) may be explained by sex-specific factors present at the time of the first VTE events (61)
Obesity (62)	Hazard ratio (HR) 1.6 (95% CI 1.1 to 2.4)
Thrombophilias	Risk of recurrent VTE May be increased in patients increased in patients with either heterozygous or homozygous factor V Leiden or prothrombin gene G20210A81 or patients with antithrombin Deficiency (34, 63, 64).

Assessing the risk/ probability of developing DVT during/after hospital admission.

Ambulatory/Outpatient care centers:

B

- A validated clinical decision rule should be used in the initial assessment of outpatients presenting with suspected deep vein thrombosis or pulmonary embolism (65).

The Wells score (66) (Table 5), in either its 3 level (low, moderate or high) or 2 level (likely or unlikely) format. The wells score was validated within the Saudi context.

Table 5: The revised Wells Score or criteria for assessment of suspected DVT

Wells score or criteria: (possible score -2 to 9)

Wells score or criteria	
Criteria	**Score** (points)
1. Active cancer (treatment within last six months or palliative)	1
2. Calf swelling ≥3 cm compared to asymptomatic calf (measured 10 cm below tibial tuberosity)	1
3. Collateral superficial veins (non-varicose)	1
4. Pitting oedema (confined to symptomatic leg)	1
5. Swelling of entire leg	1
6. Localized tenderness along distribution of deep venous system	1
7. Paralysis, paresis, or recent cast immobilization of lower extremities	1
8. Recently bedridden ≥3 days, or major surgery requiring regional or general anesthetic in the previous 12 weeks	1
9. Previously documented deep-vein thrombosis	1
10. Alternative diagnosis at least as likely as DVT	subtract 2
Interpretation: For dichotomized evaluation (likely v unlikely)	
Score of 2 or higher	Deep vein thrombosis is “likely”.
Score of less than 2	Deep vein thrombosis is “unlikely”.

Patients in Emergency Department:

B For adult patients with suspected acute PE and who are at low risk for acute PE, use the Pulmonary Embolism Rule-out Criteria PERC (Table 6) to exclude the diagnosis without further diagnostic testing (67-73).

B In patients older than 50 years deemed to be low or intermediate risk for acute PE, clinicians may use a negative age-adjusted D-dimer* result to exclude the diagnosis of PE (74-77).

*For highly sensitive D-dimer assays using fibrin equivalent units (FEU) use a cutoff of ageX10 µg/L; for highly sensitive D-dimer assays using D-dimer units (DDU), use a cutoff of ageX5 µg/L.

Table 6: The Pulmonary Embolism Rule-out Criteria (PERC) rule

The Pulmonary Embolism Rule-out Criteria (PERC) rule*
Age < 50 years
Pulse < 100 bpm
Pulse oximetry > 94%
No unilateral leg swelling
No hemoptysis
No surgery or trauma within 4 weeks
No prior deep vein thrombosis or pulmonary embolism
No oral hormone use
*Patients who meet all of these eight criteria are considered to be at a very low risk for pulmonary embolism.

Medical patients:

- Assess all medical patients to identify the risks of VTE and bleeding as soon as possible after admission to hospital to maximum 24 hours. Patients to be assessed by the nurses first, then to be evaluated by physician, using a risk assessment tool for medical patients for VTE in (Table 7) (78-84).
- Balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thrombo-prophylaxis to medical patient (78-84).

Surgical and trauma patients:

- Assess all surgical and trauma patients to identify the risks of VTE and bleeding:

  As soon as possible after admission to hospital to a maximum of 24 hours. Patients to be assessed by the nurses (85-87), using the risk assessment tool for surgical patients as in (Table 7) (88-100).
- Balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis to surgical and trauma patients (88-100) .

Table 1: Risk assessment for VTE for medical and surgical patients

Risk assessment for Venous thromboembolism (VTE)					
mobility – all patients (tick one box)	**Tick**		**Tick**		**Tick**
Surgical patient		Medical patient expected to have ongoing reduced mobility relative to normal state		Medical patient NOT expected to have significantly reduced mobility relative to normal state	
Assess for thrombosis and bleeding risk below				**Risk assessment now complete**	

Thrombosis risk			
Patient related	**Tick**	**Admission related**	**Tick**
Active cancer or cancer treatment		Significantly reduced mobility for 3 days or more	
Age > 60		Hip or knee replacement	
Dehydration		Hip fracture	
Known thrombophilia's		Total an aesthetic + surgical time > 90 minutes	
Obesity (BMI >30 kg/m2)		Surgery involving pelvis or lower limb with a total an aesthetic + surgical time > 60 minutes	
One or more significant medical comorbidities (e.g. heart disease; metabolic, endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions)		Acute surgical admission with inflammatory or intra-abdominal condition	
Personal history or first-degree relative with a history of VTE		Critical care admission	
Use of hormone replacement therapy		Surgery with significant reduction in mobility	
Use of estrogen-containing contraceptive therapy			
Varicose veins with phlebitis			
Pregnancy or < 6 weeks post-partum (see NICE guidance for specific risk factors)			

Bleeding risk			
Patient related	**Tick**	**Admission related**	**Tick**
Active bleeding		Neurosurgery, spinal surgery or eye surgery	
Acquired bleeding disorders (such as acute liver failure)		Other procedure with high bleeding risk	
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR >2)		Lumbar puncture/epidural/spinal anesthesia expected within the next 12 hours	
Acute stroke		Lumbar puncture/epidural/spinal anesthesia within the previous 4 hours	
Thrombocytopenia (platelets< 75x109/l)			
Uncontrolled systolic hypertension (230/120 mmHg or higher)			
Inherited bleeding disorders (such as hemophilia and von Will brand's disease)			

Pregnant women and women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks

- Assess all women on admission to hospital or a midwife-led unit if they are pregnant or gave birth, had a miscarriage or had a termination of pregnancy in the past 6 weeks, to identify their risk of VTE and bleeding. Use risk assessment tool that was developed by the Royal College of Obstetricians and Gynecologists (101-103).
- Reassess the risks of VTE and bleeding, and assess the need for thromboprophylaxis for all women: within 6 hours of giving birth, having a miscarriage or having a termination of pregnancy or if their clinical condition changes and they are pregnant or gave birth, had a miscarriage or had a termination of pregnancy within the past 6 weeks (102, 103).

Reassessment of risk of VTE and bleeding

D

- All patients admitted to hospital or presenting acutely to hospital should be individually assessed for the risks of VTE and bleeding. The risks and benefits of prophylaxis should be discussed with the patient (16).
- The use of a risk assessment method checklist is recommended for this purpose.
- The assessment should be repeated regularly and at least every 48 hours and following significant change in the clinical scenario of the patient (e.g., surgery, GI bleeding) (16).

✓ All patients should be assessed for their individual risk of thrombosis versus increased risk of bleeding with pharmacological prophylaxis.

✓ The risk assessment should be shared with the patient/care giver and the outcome of that discussion formally recorded as part of the routine process of informed consent to treatment.

Clinical and laboratory investigations:

D All patients presenting with acute VTE should have a full clinical history and examination undertaken with the aim of detecting the underlying conditions contributing to the development of thrombosis and assessing suitability for antithrombotic therapy (104).

A Testing for inherited forms of thrombophilia (antithrombin, protein C, protein S deficiency and factor V Leiden and prothrombin G20210A) does not influence initial management of VTE and should not be performed routinely (64).

D Patients commencing treatment with UFH, LMWH and warfarin should have a baseline assessment of renal function, PT and APTT (105, 106).

- ✓ Patients commencing treatment with UFH, LMWH and warfarin should have a full blood count to:
  - Monitor for the development of HIT
  - Exclude overt myeloproliferative disease as a contributing factor in the development of VTE
  - Assess bleeding risk (107).
- ✓ Patients for whom anticoagulation is planned should be assessed for their risk of anticoagulant induced bleeding (108).

C Unselective screening for cancer in patients with deep vein thrombosis or pulmonary embolism is not indicated (109).

Prophylaxis of venous thromboembolism:

Medical patients:

General measures:

- ✓ For medical patients at VTE risk with no increased bleeding risk, pharmacologic prophylaxis should be the first choice. Mechanical prophylaxis would be an alternative if bleeding risk is high.
- ✓ Early mobilization and leg exercises should be encouraged in patients recently immobilized (110).
- ✓ Adequate hydration should be ensured in immobilized patients (111).

Mechanical Prophylaxis:

- ✓ Mechanical prophylaxis should be used for patients at risk for VTE who have increased bleeding risk.
- ✓ Intermittent pneumatic compression (IPC) devices pneumatic foot pumps or above-knee or below-knee anti-embolism stockings (AES) may be used for prophylaxis of DVT in medical patients provided that there are no contraindications and that attention is paid to correct fitting and application (112-114).
- ✓ Adequate precautions must be taken including manufacturers' guidance regarding cleaning and re-sterilization of equipment, to prevent cross-infection when mechanical devices are reused by subsequent patients.

Table 8 summarizes the contraindications for and application of anti-embolism stockings AES. It has been suggested that 15-20% of patients cannot effectively wear AES because of unusual limb size or shape. (115)

Table 8: Contraindications for and application of AES

CONTRAINDICATIONS	
Massive leg edema	Severe peripheral neuropathy
Pulmonary edema (e.g. heart failure)	Major leg deformity
Severe peripheral arterial disease	Dermatitis
APPLICATION	
Select correct size	Do not fold down
Apply carefully, aligning toe hole under toe	Remove daily for no more than 30 minutes
Check fitting daily for change in leg circumference	

Pharmacological prophylaxis:

A When the assessment of risk favors use of thromboprophylaxis, UFH, LMWH or fondaparinux should be administered, for approximately 7-10 days or the duration of hospitalization if less than 7 days. (116).

C Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in medical patients (117-119).

- ✓ If using pharmacological VTE prophylaxis for medical patients, start it as soon as possible and within 14 hours of admission, unless otherwise stated in the population-specific recommendations, no extended prophylaxis will be given post discharge.(120).

Malignant cancers:

A Patients with cancer are generally at high risk of VTE and should be considered for prophylaxis with LMWH, UFH or fondaparinux whilst hospitalized (121, 122).

A Neither heparin nor vitamin K antagonists are indicated for prolongation of survival in cancer (123).

A Neither warfarin nor heparin should be used to prevent catheter-related DVT in cancer patients (124).

Special considerations "Palliative care":

- ✓ Consider pharmacological VTE prophylaxis for people who are having palliative care. Take into account temporary increases in thrombotic risk factors, risk of bleeding, likely life expectancy and the views of the person and their family members or carers (as appropriate): Use LMWH as first-line treatment. If LMWH is contraindicated, use Fondaparinux sodium (125).
- ✓ Do not offer VTE prophylaxis to people in the last days of life (125).

For recommendations on shared decision-making in the last days of life, see the NICE guideline on care of dying adults in the last days of life. Review VTE prophylaxis daily for people who are having palliative care, taking into account the views of the person, their family members or careers (as appropriate) and the multidisciplinary team.

Special considerations "Coronary Syndromes":

- ✓ In acute coronary syndromes, patients in whom there is electrocardiogram (ECG) indication of ischemia and/or elevation of cardiac markers should receive therapeutic doses of LMWH or fondaparinux as part of the management of cardiac ischemia (126).

Special considerations "Stroke / paralysis":

A	AES should not be used routinely in stroke patients (127-129).
A	Use of IPC should be considered during hospitalization in patients with acute stroke, if tolerated (130).
A	In patients with non-hemorrhagic stroke at high risk of VTE, LMWH can be considered in addition to IPC (131).

Renal impairment (GFR < 30 ml/min):

- ✓ If using pharmacological VTE prophylaxis for people with renal impairment, choose either LMWH or unfractionated heparin (UFH). If needed, reduce the dose of LMWH and UFH for people with renal impairment (132).

Intensive Care:

A	Medical and surgical patients in Intensive care units frequently have multiple risk factors for both thrombosis and bleeding (133).
A	Anticoagulant (UFH/ LMWH) is the preferred thromboprophylaxis modality, if unable to receive anticoagulant thromboprophylaxis, mechanical prophylaxis using IPC should be used IPC use, but not AES, was associated with reduced VTE. Hence, if there is increased risk of bleeding/contraindication for pharmacologic prophylaxis (134-136).

Surgical and trauma patients:

General and abdominal Surgery:

A	Patients undergoing abdominal surgery who are at risk due to the procedure or personal risk factors should receive thromboprophylaxis with mechanical methods unless contraindicated and either subcutaneous LMWH, UFH or fondaparinux (118, 119, 137, 138).
A	AES are recommended for prophylaxis in surgical patients, in the absence of contraindications (112-114).
D	IPC devices are recommended for prophylaxis of DVT in surgical patients (139, 140).

A In patients undergoing abdominal surgery AES can be used alone when pharmacological agents are contraindicated, for example due to high bleeding risk (114).

C Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in surgical patients, as other available agents are more effective (141).

- ✓ Pharmacological thromboprophylaxis is typically continued until discharge. Extended prophylaxis should be considered on a case-by-case basis, for example when multiple thrombosis risk factors are present (142).
- ✓ The use of AES should continue until there is a return to the pre-morbid level of mobility (143-145).
- ✓ If using pharmacological VTE prophylaxis for surgical and trauma patients, start it as soon as possible and within 14 hours of admission, unless otherwise stated in the population-specific recommendations (145).

Cardiac Surgery:

D Patients undergoing CABG surgery should be offered mechanical thromboprophylaxis where feasible (146).

D Patients undergoing CABG surgery who are not at high risk of bleeding can be offered pharmacological thromboprophylaxis with UFH or LMWH in addition to mechanical Thromboprophylaxis (147).

Thoracic Surgery:

D Patients undergoing thoracic surgery should be offered mechanical prophylaxis with IPC or AES (146).

D Patients undergoing thoracic surgery who are not at high risk of bleeding should be offered pharmacological thromboprophylaxis with UFH or LMWH in addition to mechanical thromboprophylaxis (147).

Craniotomy, Spinal, Neurosurgery or Traumatic brain Surgery:

A Neurosurgical patients should routinely be offered mechanical prophylaxis (with AES or IPC) (148).

B Combining LMWH with mechanical prophylaxis may be considered in patients with additional risk factors for VTE, such as patients with intracranial neoplasm (148, 149).

Orthopedic Surgery:

A Patients undergoing THR or TKR surgery should receive pharmacological prophylaxis *(with LMWH, fondaparinux, rivaroxaban, Apixaban or dabigatran)* combined with mechanical prophylaxis unless contraindicated (146, 147, 150).

A Extended prophylaxis should be given *(146, 147, 150).*

C As other agents are more effective for prevention of DVT, aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in orthopedic patients (116, 117, 151, 152).

Patients with increased risk of bleeding should be given mechanical prophylaxis alone (141, 150, 153).

C If the bleeding risk has become acceptable then pharmacological prophylaxis should be added (154, 155).

A Pneumatic foot pumps can be considered for prophylaxis as an alternative to IPC in Orthopedic surgery patients (114, 153).

- ✓ Patients undergoing less invasive orthopedic procedures and plaster of Paris immobilization should be assessed for their thrombosis and bleeding risks and pharmacological thromboprophylaxis with heparin or fondaparinux considered, particularly in those patients who will be subject to prolonged immobility (156, 157).
- ✓ Patients with additional risk factors for VTE, such as previous VTE, should be considered for additional extended prophylaxis (158).

Urological Surgery:

D Patients having urological surgery should be offered mechanical prophylaxis with IPC or AES (159).

D Patients having urological surgery who have any additional risk factors for VTE should be offered mechanical prophylaxis and LMWH (146, 160, 161).

Vascular Surgery:

D Patients with critical limb ischemia or who are undergoing major abdominal or peripheral vascular surgery *(including amputation),* should be considered for thromboprophylaxis (140, 162-165).

D In patients undergoing varicose vein surgery who have no additional risk factors for VTE postoperative AES are recommended (31).

D In the presence of additional risk factors, the addition of UFH or LMWH is recommended (165).

Plastic and reconstructive surgery:

- ✓ Patients scheduled for plastic and reconstructive surgery should be considered for mechanical prophylaxis and pharmacological thromboprophylaxis with LMWH (166, 167).

Bariatric surgery:

- ✓ Patients undergoing bariatric surgery should receive thromboprophylaxis as recommended for those undergoing general surgery (168).
- ✓ The dosages of heparin may need to be increased in patients who are obese (169).

ENT surgery:

- ✓ Mechanical methods and pharmacological prophylaxis with LMWH may be considered for patients undergoing high-risk ENT surgery (170).

Obstetrics / gynecology patients:

D	All women should be assessed for risk factors for VTE when booking for antenatal care and at each subsequent maternity contact (171, 172).
	✓ Women should be asked about a personal and family history of VTE and whether an objective diagnosis was made (173).
D	Routine testing for thrombophilia in pregnancy is not indicated (174).
C	Low molecular weight heparins are the agents of choice for antenatal thromboprophylaxis (175, 176).
D	Antenatal thromboprophylaxis should be commenced in the first trimester of pregnancy in high risk patients (Figure 3) (177).
C	Vitamin K antagonists have adverse fetal effects and should be avoided in pregnancy. In women with mechanical heart valves, however, the risks and benefits of VKA and heparin should be assessed on an individual basis (177-180).
C	Women of childbearing age using VKA should be clearly informed of the risk of teratogenesis associated with these agents and should be advised to seek appropriate medical advice if they are planning to become pregnant or as soon as possible (and within two weeks following a first missed period) if they suspect that they may be pregnant (181, 182).
D	Pregnant women considered to be at increased risk of VTE should be advised to wear AES when immobile/hospitalized (183).
D	All women should be assessed after delivery for risk factors for VTE (184, 185).
	✓ Although there are very limited data on the safety of NOAC use during pregnancy, until evidence on the safety of NOACs in pregnancy is available, LMWH should be the anticoagulant of choice in pregnancy and NOACS should be stopped once pregnancy is recognized (186-188).

D Women with multiple risk factors for VTE should be considered for postnatal thromboprophylaxis (177, 189).

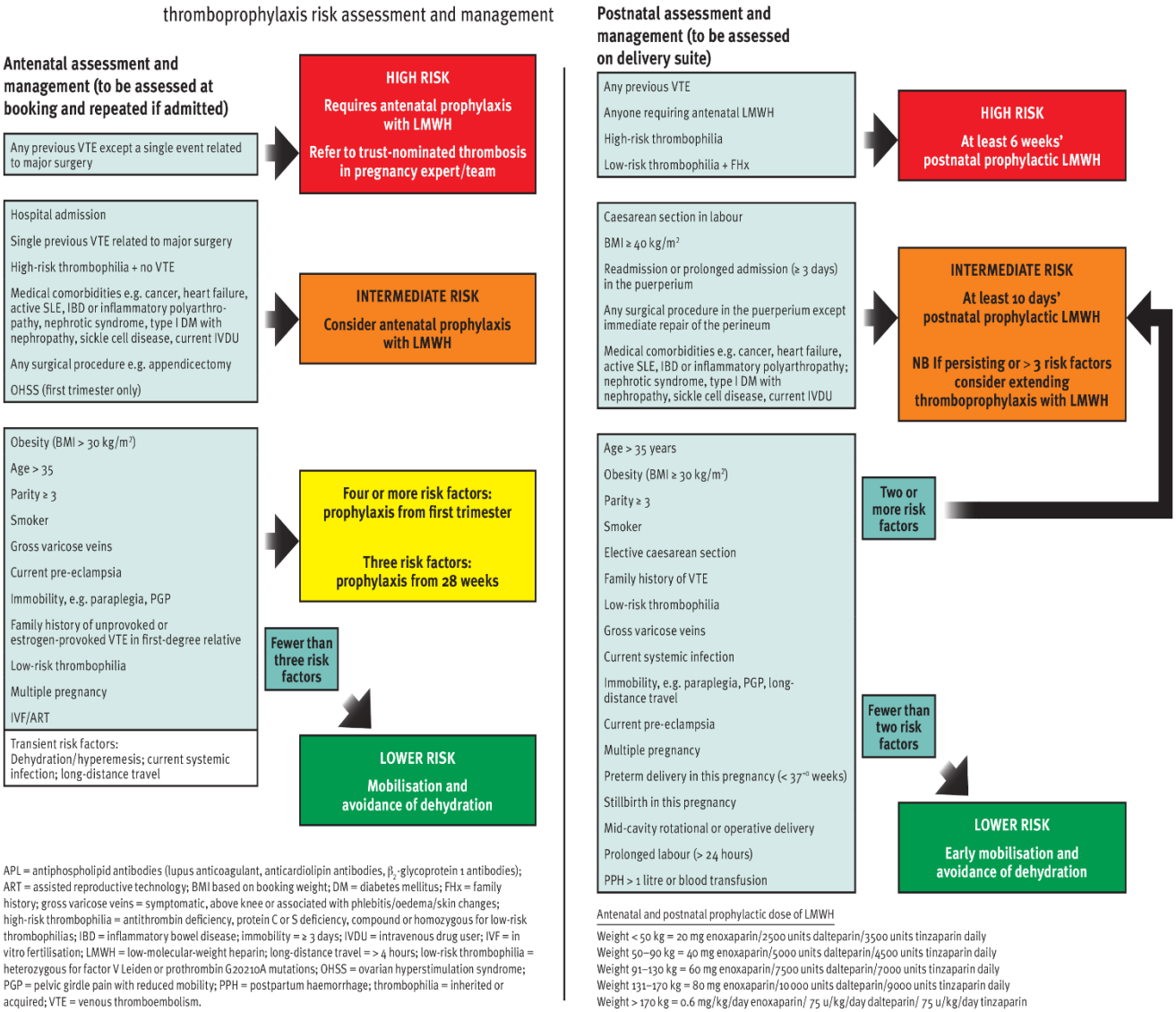
- ✓ Women with two or more risk factors should receive LMWH for seven days after delivery; women with three or more risk factors should be offered AES in addition to LMWH (177, 189).

D All women who have had an emergency Caesarean section and those who have an elective Caesarean section who have one or more additional risk factors for VTE, should receive thromboprophylaxis with LMWH for seven days (177, 189).

D Women with a previous VTE should receive LMWH for six weeks following delivery (177, 189).

- ✓ Women who are known to have an acquired or inherited thrombophilia should be considered for thromboprophylaxis for six weeks following delivery taking account of the family history, any personal risk factors and patient preference (177, 189).
- ✓ Women receiving prophylaxis antenatally should continue thromboprophylaxis doses for six weeks following delivery (177, 189). Warfarin is an alternative to LMWH in this situation.
- ✓ Women who are normally anticoagulated with warfarin out with pregnancy can recommence warfarin three days after delivery (177, 189).
- ✓ During lactation needs to be added and the drugs of choice NOACs not recommended either warfarin or LMWH (177, 189).

Figure 1: Obstetric thrombo-prophylaxis risk assessment and management



APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, β_2-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = > 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or acquired; VTE = venous thromboembolism.

Antenatal and postnatal prophylactic dose of LMWH

Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10 000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

RCOG Green-top Guideline No. 37a
33 of 40

Figure 2: Obstetric thromboprophylaxis risk assessment and management

Risk assessment for venous thromboembolism (VTE)

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

For patients with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed in consultation with a haematologist with expertise in thrombosis and bleeding in pregnancy.

Risk factors for VTE

Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1[a]
Age (> 35 years)		1
Obesity		1 or 2[b]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37[+0] weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS (first trimester only)		4
Current systemic infection		1
Immobility, dehydration		1
TOTAL		

Abbreviations: ART assisted reproductive technology; IVF in vitro fertilisation; OHSS ovarian hyperstimulation syndrome; VTE venous thromboembolism.

[a] If the known low-risk thrombophilia is in a woman with a family history of VTE in a first-degree relative postpartum thromboprophylaxis should be continued for 6 weeks.

[b] BMI ≥ 30 = 1; BMI ≥ 40 = 2

Travel related thrombosis:

- ✓ The risks and possible benefits of any intervention should always be discussed with the patient before travelling (190-197).

D Travelers should be advised to remain as ambulant as safely possible before, during and after journeys. Leg exercise whilst seated may be recommended (194, 198, 199).

D The use of AES for prevention of VTE during and after long-haul travel > 4 hours, is not routinely recommended. When used, care should be taken to ensure an appropriate fit (129, 200).

- ✓ Appropriate monitoring of the INR and dosage adjustment is recommended prior to travel for patients taking warfarin.
- ✓ In people deemed to be at especially high risk of travel related VTE, pharmacological prophylaxis can be considered. LMWH has been used for this purpose. Aspirin should not be used as a prophylactic measure in these cases (201).

Management of venous thromboembolism:

Ambulatory /outpatients care centers:

A Patients with suspected acute DVT or PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely (202, 203).

D Patients with intermediate-risk PE should not routinely receive thrombolytic therapy (204).

- ✓ Patients with intermediate-risk PE should be monitored in hospital and be considered for thrombolysis should they deteriorate (205).
- ✓ Patients with low-risk PE can be considered for outpatient management or early discharge.
- ✓ Patients with high-risk PE should be managed in a coronary care unit, intensive care unit or high dependency unit.

D Once confirmed, heparin or fondaparinux should be continued until the INR is at least 2.0 for at least 2 days if the patient will be treated with a vitamin K antagonist (warfarin). There is no need to monitor INR if patient will be started on Novel anticoagulants NOACs (204).

B Outpatient therapy of DVT may be considered for selected patients with appropriate support services in place (206-208).

- ✓ One general patient information leaflet should be available across hospitals/centers and paper copies of this leaflet made available in areas to which the general public have easy access.

Emergency Department:

C	Given the lack of evidence, anticoagulation treatment decisions for patients with sub-segmental PE without associated DVT should be guided by individual patient risk profiles and preferences (209-214). [Consensus recommendation]
D	Patients with intermediate-risk PE should not routinely receive thrombolytic therapy (204).
C	Selected patients with acute PE who are at low risk for adverse outcomes as determined by Pulmonary Embolism Severity Index **(**PESI), simplified PESI (sPESI) in (Table 9), or the Hestia criteria (215) (Table 10) may be safely discharged from the ED on anticoagulation, with close outpatient follow-up (215-234).
B	In selected patients diagnosed with acute DVT, a non–vitamin K antagonist oral anticoagulants (NOAC) may be used as a safe and effective treatment alternative to LMWH/VKA (206, 226, 235-247).
C	Selected patients with acute DVT may be safely treated with a NOAC and directly discharged from the ED (248-256).

Table 9: Pulmonary Embolism Severity Index (PESI) and simplified PESI

Original PESI (257)		Simplified PESI (258)	
Age	1 per year	Age >80 years	1
Male sex	10		
History of cancer	30	History of cancer	1
History of heart failure	10	History of heart failure or chronic lung disease	1
History of chronic lung disease	10		
Pulse rate >110 beats per min	20	Pulse rate >110 beats per min	1
Systolic blood pressure <100 mmHg	30	Systolic blood pressure <100 mmHg	1
Respiratory rate ≥30 breaths per min	20		
Body temperature <36° C	20		
Altered mental status#	60		
SaO_2 <90%	20	SaO_2 <90%	1
Risk classification"		Risk classification	
Class I (<65 points): very low risk		0 points: low risk	
Class II (66–85 points): low risk		≥1 point: high risk	
Class III (86–105 points): intermediate risk			
Class IV (106–125 points): high risk			
Class V (.125 points): very high risk			

SaO_2: arterial oxygen saturation. **#**: disorientation, confusion or somnolence;

Patients in PESI classes I and II are collectively referred to as low-risk patients

Table 10: Hestia criteria

1. Hemodynamically unstable?*
2. Thrombolysis or embolectomy necessary?
3. Active bleeding or high risk of bleeding?†
4. Oxygen supply to maintain oxygen saturation > 90% > 24 h?
5. Pulmonary embolism diagnosed during anticoagulant treatment?
6. Intravenous pain medication > 24 h?
7. Medical or social reason for treatment in the hospital > 24 h?
8. Creatinine clearance of less than 30 mL/min?‡
9. Severe liver impairment?§
10. Pregnant?
11. Documented history of heparin-induced thrombocytopenia?
If one of the questions is answered with YES, The patient can NOT be treated at home
*Include the following criteria but are left to the discretion of the investigator: systolic blood pressure < 100 mmHg with heart rate > 100 beats per minute; condition requiring admission to an intensive care unit. †Gastrointestinal bleeding in the preceding 14 days, recent stroke (less than 4 weeks ago), recent operation (less than 2 weeks ago), bleeding disorder or thrombocytopenia (platelet count < 75 9 109/L), uncontrolled hypertension (systolic blood pressure > 180 mm Hg or diastolic blood pressure > 110 mm Hg). ‡Calculated creatinine clearance according to the Cockroft-Gault formula. §Left to the discretion of the physician.

Deep vein thrombosis:

B Outpatient therapy of DVT may be considered for selected patients with appropriate support services in place (206-208).

Pulmonary Embolism:

B Validated prognostic models to identify patients at low risk of adverse outcomes may be incorporated into treatment algorithms for the management of patients with PE to identify those suitable for outpatient management or early discharge (259-265).

Pulmonary embolism:

A Patients with suspected PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely (202, 266, 267).

D Once confirmed the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist for at least 2 days. NOACS can be drug of choice for selected patients with no need to bridging with LMWH or INR monitoring (204).

D Patients with intermediate-risk PE should not routinely receive thrombolytic therapy (204).

- ✓ Patients with intermediate-risk PE should be monitored in hospital and be considered for thrombolysis should they deteriorate.
- ✓ Patients with low-risk PE can be considered for outpatient management or early discharge.
- ✓ Patients with high-risk PE should be managed in a coronary care unit or high dependency unit (268).
- ✓ If a device is used, retrievable Inferior Vena Cava (IVC) filters should be used although successful retrieval cannot be guaranteed (259, 269)

D Where IVC filters have been fitted because of an existing contraindication to anticoagulants at the time of presentation, anticoagulation may be introduced when the contraindication is resolved (270).

IVC filters significantly reduce the number of PEs suffered by patients who present with proximal DVT (1.1% v 4.8%, OR 0.22, 95% CI 0.05 to 0.90) but they are associated with an increase in the development of recurrent DVT (20.8% v 11.6%, OR 1.87, 95% CI 1.10 to 3.20) at two years follow up (270). This is the major complication of IVC filter insertion in patients with proximal DVT.

Other complications are shown in (Table 11) (269). Hence, the insertion of temporary/ retrievable rather than permanent IVC filters is preferred. Temporary IVC filters should be routinely removed within 25-54 days after insertion (271), unless there is a persistent indication for them.

Table 2: Complications of IVC filter insertion:

Immediate	
Misplacement	1.3%
Hematoma	0.6%
Pneumothorax	0.02%
Air embolus	0.2%
Carotid artery puncture	0.04%
Atrioventricular fistula	0.02%
Early	
Insertion site thrombosis	8.5%
Infection	(rare but documented)
Late	
DVT	21%
IVC thrombosis	2-10%
Post-thrombotic syndrome	15-40%
IVC penetration	0.3%
Filter migration	0.3%
Entrapment of guidewires	(rare but documented)
Filter tilting	(rare but documented)
Fracture	(rare but documented)

Lower limb DVT

A	Patients with suspected DVT should be treated with therapeutic doses of LMWH or fondaparinux until the diagnosis has been deemed very unlikely or confirmed (267, 272-274).
D	In confirmed DVT, LMWH or fondaparinux should be continued until the INR is at least 2.0 for at least 2 days on a vitamin K antagonist (Warfarin). NOACS can be drug of choice for selected patients with no need to bridging with LMWH or INR monitoring (204).
B	Intravenous UFH may be an appropriate alternative in certain circumstances, e.g. if thrombolysis is being considered, in the immediate postoperative period or where there is particular risk of bleeding (202).
A	Patients with cancer and VTE should be offered treatment with LMWH (rather than vitamin K antagonist) for three to six months and reviewed thereafter (275, 276).

Thrombolysis and Pharmaco-mechanical Therapy

D	Thrombolysis is not routinely recommended for patients with lower limb DVT (259, 277, 278).
D	Thrombolysis, preferably catheter-directed, or catheter-directed thrombolysis with percutaneous mechanical thrombectomy can be considered on an individual basis, particularly in patients at low bleeding risk with limb threatening or massive iliofemoral DVT (279, 280).

Superficial Thrombophlebitis

D	Patients with clinical signs of superficial thrombophlebitis affecting the proximal long saphenous vein should have an ultrasound scan to exclude concurrent DVT (204, 281).
B	Patients with superficial thrombophlebitis should have anti-embolism stockings and can be considered for treatment with prophylactic doses of LMWH for up to 30 days or fondaparinux for 45 days (281, 282).
B	If LMWH is contraindicated, 8-12 days of oral NSAIDs should be offered (283, 284).

- ✓ Patients with superficial thrombophlebitis at, or extending towards, the sapheno-femoral junction can be considered for therapeutic anticoagulation for 6-12 weeks (284).

Upper Extremity DVT

- ✓ Management of upper extremity DVT needs to be on an individual patient basis and should include management of any underlying condition (285).

D Patients with upper extremity DVT without underlying risk factors (*such as antiphospholipid antibodies*) do not require prolonged (more than 3-6 months) anticoagulant treatment (286).

Splanchnic Vein Thrombosis:

D Patients with acute splanchnic vein thrombosis should have treatment for any underlying disease and be considered on an individual basis for anticoagulation after careful assessment of individual risks and benefits (287, 288).

Incidental VTE

D In patients with incidental VTE detected by imaging, treatment decisions should be made on an individual basis taking account of the thrombus burden and the presence of additional risk factors for VTE as well as bleeding risk (289-291).

Further Management of venous thromboembolism:

Choice of anticoagulant:

A After a first episode of limb DVT or PE, treatment with a VKA or NOACs should be initiated (292-294).

D A higher target INR (3.5) may be considered if there is recurrent VTE whilst in the target range (293, 295-298).

B In patients with antiphospholipid syndrome and VTE, anticoagulation with a VKA, target INR 2.5, should be implemented. After a first episode of proximal limb DVT or PE, treatment with a VKA should be continued for at least three months (299, 300).

- ✓ Uninterrupted, long term continuation of VKA therapy after a first episode of VTE may be appropriate in some patients and can be based on individual assessment of risk factors, including:
  - An unprovoked first event
  - The site and severity of the first event
  - The presence of persistent comorbidities, e.g. cancer
  - The presence of persistent antiphospholipid antibodies
  - Male sex
  - Bleeding risk on anticoagulant treatment
  - Patient compliance and preference.

A Use of NOACs/LMWH/fondaparinux is an alternative and can be considered if VKA therapy is problematic, for example due to poor compliance/erratic intensity of anticoagulation (301, 302).

A LMWH rather than VKA should be considered in VTE associated with cancer (145).

C Neither aspirin nor statin is recommended for the prevention of recurrent VTE after discontinuation of VKA therapy (245, 303).

A Measurement of D-dimer concentration one month after discontinuation of a course of VKA therapy after a first episode of unprovoked VTE can be considered for the identification of patients who may benefit from resumption of VKA therapy and continuation in the long term (299, 300).

- ✓ After recurrent VTE, long term treatment with a VKA or DOACS is recommended but the nature of the recurrence (provoked or unprovoked), the elapsed time between episodes and risk of bleeding should be considered in reaching this decision (304).
- ✓ The use of long term VKA such as warfarin, or direct-acting oral anticoagulants (DOACs), should be subjected to periodic review, to include anticoagulant control, bleeding episodes and altered risk of bleeding (87, 305).

Graduated Elastic Compression Stockings:

A After DVT affecting a lower limb, the use of well fitted below-knee graduated elastic compression stockings for two years should be encouraged to reduce the risk of post-phlebitis syndrome (306).

Monitoring the anticoagulant effect:

1- *unfractionated heparin:*

D Therapeutic dosing of UFH should be monitored by use of a locally calibrated APTT assay using APTT ratio or APTT level in absence of ratio. Calibrated Anti Xa level for UFH is the gold standard if available (307).

2- *low molecular weight heparin:*

C Routine laboratory monitoring of LMWH is not recommended. Calibrated Anti Xa level for LMWH is the gold standard if available and can be used for special situations (307).

3- *VKA: INR control*

- ✓ There are several models of care for management of VKA therapy. The optimal approach suitable for local conditions and which provides the most precise INR control should be selected (308, 309).

A Computer-assisted dosing algorithms are recommended (310).

D Patient self-testing and self-management supported by a dedicated and well-trained anticoagulant team may be considered for selected patients on VKA (308, 311).

Adverse effects of venous thromboembolism prophylaxis and treatment:

Bleeding

D In choosing pharmacological thromboprophylaxis the risks of bleeding and other complications need to be considered alongside the likely benefits (104, 294, 312-314).

D Major bleeding in patients who are receiving warfarin or other VKAs should be treated by immediate reversal of anticoagulation. This is best achieved by administration of intravenous vitamin K and prothrombin complex concentrate (315, 316).

D Minor bleeding in patients who are anticoagulated with warfarin should be reversed using low doses of vitamin K (1-2.5 mg) given either intravenously or orally depending on the clinical circumstances and assessment of the bleeding (317, 318).

- ✓ In patients who are over anticoagulated, warfarin therapy should be temporarily discontinued and restarted at a decreased dose.
- ✓ Monitoring of patients should be more intensive during the first months of treatment when anticoagulant control tends to be less stable.
- ✓ Monitoring bleeding tendency during anticoagulation control is highly recommended.

Consensus guidelines on the risks of regional anaesthesia in the anticoagulated patient have been published by the American Society of Regional Anaesthesia and Pain Medicine (319). Modified consensus guidance based on these guidelines is shown in (Table 12).

Table 12: Guidance for central neural axial block in patients taking drugs affecting hemostasis:

Aspirin and NSAIDS	Clopidogrel	Unfractionated heparin prophylaxis (subcutaneous)	Unfractionated heparin treatment (intravenous)	LMWH**	Warfarin	Rivaroxaban Dabigatran
No issue	Stop 7 days Pre-operation if possible. If not, proceed with caution	Wait at least 4hr after a dose before block or catheter removal. Wait at least 1hr before dosing after procedure (catheter insertion or withdrawal)	Stop infusion 2-4 hr before block. Start infusion >1 hr after block. Remove epidural catheter no sooner than 2-4 hr after discontinuation of infusion	Wait at least 12 hrs after a prophylactic dose and 24 hr after a therapeutic dose before block.* Wait at least 10 hours after dose before removing catheter. After catheter removal wait 2-4 hr before next dose	Proceed if INR ≤1.5	These are started postoperatively. Wait 12-18 hrs after dose for epidural catheter removal. Wait 6 hrs before next dose

** Adapted from the American Society of Regional Anesthesia and Pain Medicine guidelines on the risks of regional anesthesia in the anticoagulated patient (319).*

*** With fondaparinux the period between administration and procedure should be greater than for LMWH due to its longer half-life.*

Heparin induced thrombocytopenia

A To minimise the incidence of HIT, LMWH should be used in preference to UFH.

- ✓ All Patients on heparin can developing HIT, and should be monitored by serial platelet counts between days 4–14 and during long term use of LMWH including:
  - All post-operative patients receiving UFH.
  - Patients post-cardiopulmonary bypass receiving UFH or LMWH (320).
- ✓ The following patients are at low risk of developing HIT and do not require routine platelet monitoring:
  - Post-operative patients (other than post-cardiopulmonary bypass) receiving LMWH
  - All medical and obstetric patients receiving any heparin for prophylaxis or treatment (320).

D All patients who are to receive UFH or LMWH for prophylaxis or treatment of VTE should have a platelet count performed in the 24 hours before receiving treatment (321).

D Monitoring patients for the development of HIT should be by performing serial platelet counts (322).

D Patients who have previously received UFH or LMWH within 100 days or in whom the history of recent exposure to heparins is not clear should have a platelet count performed within 24 hours of receiving the first dose of treatment (323).

D All other patients for whom monitoring is indicated should have platelet counts performed every two to three days from day four to day14 of exposure (324).

- ✓ HIT should be suspected if the platelet count falls by 30% or more or if there is thrombocytopenia (<150 x 109/l)
- ✓ 4T score can identify the patients with likelihood of HIT (321, 325).
- ✓ HIT should be considered in patients who develop a new thrombosis or in whom thrombosis extends and in patients who develop typical skin lesions or features of a systemic response such as fever, chills or shivering whilst receiving any form of heparin.

D	In cases where HIT is suspected the patient should be evaluated using a clinical scoring system to assess the pre-test probability of having the condition (324).
D	This should be followed, where appropriate, by laboratory testing for anti-HIT antibodies (ELISA or functional tests). The combined information should be used to assess the probability of having HIT (324, 326).
D	Whether or not there is evidence of a new thrombotic episode related to HIT, patients should receive therapeutic, as opposed to prophylactic, doses of NON Heparin products like (Argatroban, Liprudin or Danaparoid). Fondaparienoux can be used as alternative. (327)
D	Where warfarin therapy is proposed, it should not be introduced until the platelet count has risen into the normal range (150–400 x109/l).
D	When warfarin therapy is introduced it should be at a low dose (5 mg daily) and Danaparoid or Argatroban should be withdrawn only after the INR has been >2 on two consecutive days for patients on Danaparoid and >4 on two days in patients on Argatroban (326).

- ✓ A history of HIT should be carefully documented in the clinical record.

Reduced bone mineral density:

C	Monitoring of bone density in pregnant women exposed to LMWHs is not recommended (175, 328).

Implementation Considerations and Tools

Implementation of guidelines is intended to improve the quality of care and to promote patient safety, by presenting the current evidence base and translating it into clinical practice. The publication and dissemination of guidelines do not automatically result in their use. Therefore, some kind of implementation is needed. Implementation efforts should use a combined approach of strategies as multifaceted interventions are more likely to be effective than single intervention. The Focus should be on a specific level of implementation, such as system, organization, innovation, provider and patient, educational outreach visits, reminders, audit and feedback, and provider incentives for improving process of care and clinical out-comes. The central elements of successful strategies for guideline implementation include dissemination, education and training, social interaction, decision support systems and standing orders.

The guidelines should be as short and user-friendly as possible to reduce complexity. Suitable strategies to improve accessibility might include: checklists and further tools, such as the inclusion of tablets, smartphones and mobiles as platforms for the dissemination of guidelines (329). Hence, we decided to adopt NICE pathways and tools in the current guideline. NICE Pathways are interactive and designed to be used online (https://pathways.nice.org.uk/pathways/venous-thromboembolism#content=view-info-category%3Aview-about-menu). Additionally, the supply of educational materials (including written materials, didactic presentations and interactive conferences) is absolutely essential to raise awareness and increase familiarity and agreement with a guideline and its recommendations. For that reason, we advised to use simple instruction and patients' information in Arabic which is available in the Ministry of Health Website(https://www.moh.gov.sa/HealthAwareness/EducationalContent/Diseases/Heartcirculatory/Pages/012.aspx). Moreover, improvements in the organization of care are necessary, which may be promoted by the standardization of policies and procedures and the development of clinical protocols distribution of a referral form to general practitioners/Family physicians, for patients/public, counseling on lifestyle issues or self-management and print material such as guideline summaries. Moreover, electronic guidelines version using decision support systems (manual or automated) and reminders also will prompt health professionals to perform clinical actions according to the current state of evidence. For example, standing

'orders and standardized documentation are strategies to facilitate guideline adherence to eliminate variations in practice. Therefore, we recommend to enforce this current adapted guideline recommendations tools and pathways in the electronic health records at several health organizations in Saudi Arabia. At policy levels some strategies could be of use to ensure implementation of CPG, such as providers' incentives (pay for performance) and key performance indicators (KPIs). Therefore. we recommend using NICE audit recourse to help clinicians and organizations improve the quality of care (https://www.nice.org.uk/guidance/qs3/resources). We also strongly recommend the current guideline to be part of the requirements by the local Saudi accreditation body (CBAHI) as essential standards for accreditation of all the National Healthcare hospitals and agencies in Saudi Arabia.

Plan for Scheduled Review and Update

The panel has been decided to review this adapted CPG for updates after 3 years from publication date (2020) which should be on 2023 after checking for updates in the source guidelines, consultation of expert opinion on the changes needed for updating according to the newest evidence and recommendations published in this area and the clinical audit and feedback from implementation efforts in relevant healthcare sectors in collaboration with The National Center for Evidence Based Health Practice, Saudi Health Council.

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List of Appendices

Appendix 1: Inclusion / Exclusion CPGs Selection Criteria

1. **Methods of Development:** Evidence-Based CPGs: (Detailed Methodology of Development Documented; link Recommendations with Evidence; link to Systematic Reviews) rather than Consensus-based CPGs (Expert opinion)
2. **Authors' Organization** (CPG development group) from CPGs Database (Producer or Finder) and Specialized Society (clinical specialty) rather than single authors.
3. **Country:** International and national CPGs.
4. **Date of Publication:** Search within the last 5 years
5. **Language:** English CPGs only
6. **Status:** original source CPG (de novo developed) only.

Appendix 2: Key terms

Venous Thromboembolism (VTE), Deep Vein thrombosis (DVT), screening, Pulmonary embolism (PE), Clinical practice Guidelines (CPG), Guideline, Risk Assessment, Prophylaxis, treatment, management and adverse events. Thrombosis', 'Thromb*', 'Venous Thrombosis', 'Coagulation', 'Cancer', 'Tumor', 'Treatment', 'Prophylaxis*', 'Therapy', 'Surgery', 'Chemotherapy', 'Prognosis', 'Survival', 'Heparin', 'Coumarin', 'Warfarin*', 'Low molecular weight heparin*'and 'LMWH'

Appendix 3: Matrix of recommendations

Clinical area	Recommendation 1	Recommendation 2
Screening of venous thromboembolism:		
	NICE 2018	***SIGN 2014***
All Patients	Assess all patients to identify the risk of venous thromboembolism (VTE) and bleeding for all medical patients, for all surgical patients, for all pregnant women and all women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks, for all people admitted to the critical care unit and for all acute psychiatric patients).	D: - All patients admitted to hospital or presenting acutely to hospital should be individually assessed for risk of VTE and bleeding. The risks and benefits of prophylaxis should be discussed with the patient. - The use of a risk assessment method checklist is recommended for this purpose. - The assessment should be repeated regularly and at least every 48 hours. ✓ All patients should be assessed for their individual risk of thrombosis versus increased risk of bleeding with pharmacological prophylaxis. ✓ The risk assessment should be shared with the patient/career and the outcome of that discussion formally recorded as part of the routine process of informed consent to treatment.
Ambulatory/ Outpatient care centers		B: A validated clinical decision rule should be used in the initial assessment of outpatients presenting with suspected deep vein thrombosis or pulmonary embolism. ✓ The results of the initial assessment should be used to determine the diagnostic strategy.
Emergency Department	***The American College of Emergency Physicians (ACEP) 2018***	
	B: For adult patients with suspected acute PE and who are at low risk for acute PE, use the Pulmonary Embolism Rule-out Criteria PERC to exclude the diagnosis without further diagnostic testing. B: In patients older than 50 years deemed to be low or intermediate risk for acute PE, clinicians may use a negative age-adjusted D-dimer* result to exclude the diagnosis of PE.	

	NICE 2018	SIGN 2014
Medical patients	- Assess all medical patients to identify the risk of VTE and bleeding: • as soon as possible after admission to hospital or by the time of the first consultant review • using a tool published by a national UK body, professional network or peer-reviewed journal. The most commonly used risk assessment tool for medical patients is the Department of Health VTE risk assessment tool. - Balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis to medical patients. - If using pharmacological VTE prophylaxis for medical patients, start it as soon as possible and within 14 hours of admission, unless otherwise stated in the population-specific recommendations	
Surgical and trauma patients	- Assess all surgical and trauma patients to identify the risk of VTE and bleeding: • as soon as possible after admission to hospital or by the time of the first consultant review • using a tool published by a national UK body, professional network or peer-reviewed journal. The most commonly used risk assessment tool for surgical patients is the Department of Health VTE risk assessment tool. - Balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis to surgical and trauma patients. - If using pharmacological VTE prophylaxis for surgical and trauma patients, start it as soon as possible and within 14 hours of admission, unless otherwise stated in the population-specific recommendations. - Reassess all medical, surgical and trauma patients for risk of VTE and bleeding at the point of consultant review or if their clinical condition changes.	

Pregnant women and women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks	- Assess all women on admission to hospital or a midwife-led unit if they are pregnant or gave birth, had a miscarriage or had a termination of pregnancy in the past 6 weeks, to identify their risk of VTE and bleeding. Use a tool published by a national UK body, professional network or peer-reviewed journal. The most commonly used risk assessment tool was developed by the Royal College of Obstetricians and Gynecologists. Reassess risk of VTE and bleeding, and assess the need for thromboprophylaxis for all women: • within 6 hours of giving birth, having a miscarriage or having a termination of pregnancy **or** • if their clinical condition changes **and** they: - are pregnant **or** - gave birth, had a miscarriage or had a termination of pregnancy within the past 6 weeks.	
Prophylaxis and management of venous thromboembolism:		
Ambulatory/ Outpatients care centers		***SIGN 2014***
		A: Patients with suspected PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely. D: Once confirmed the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist, and for at least 5 days. D: Patients with intermediate-risk PE should not routinely receive thrombolytic therapy. - Patients with intermediate-risk PE should be monitored in hospital and be considered for thrombolysis should they deteriorate. - Patients with low-risk PE can be considered for outpatient management or early discharge. B: Outpatient therapy of DVT may be considered for selected patients with appropriate support services in place. - One general patient information leaflet should be available across hospitals/centers and paper copies of this leaflet made available in areas to which the general public have easy access.

Emergency Department	*The American College of Emergency Physicians (ACEP) 2018*	
	- In adult patients with sub segmental PE, is it safe to withhold anticoagulation? Level C recommendations. Given the lack of evidence, anticoagulation treatment decisions for patients with sub segmental PE without associated DVT should be guided by individual patient risk profiles and preferences. [Consensus recommendation] - In adult patients diagnosed with acute PE, is initiation of anticoagulation and discharge from the ED safe? C: Selected patients with acute PE who are at low risk for adverse outcomes as determined by PESI, simplified PESI (sPESI), or the Hestia criteria may be safely discharged from the ED on anticoagulation, with close outpatient follow-up. - In adult patients diagnosed with acute lower extremity DVT who are discharged from the ED, is treatment with a NOAC safe and effective compared with treatment with LMWH and VKA? B: In selected patients diagnosed with acute DVT, a NOAC may be used as a safe and effective treatment alternative to LMWH/VKA. C: Selected patients with acute DVT may be safely treated with a NOAC and directly discharged from the ED.	
Medical patients	NICE 2018	SIGN 2014
General measures	Assess all medical patients to identify the risk of VTE and bleeding	- Early mobilization and leg exercises should be encouraged in patients recently immobilized. - Adequate hydration should be ensured in immobilized patients.
Mechanical Prophylaxis	- Do not offer anti-embolism stockings to people who have: suspected or proven peripheral arterial disease peripheral arterial bypass grafting peripheral neuropathy or other causes of sensory impairment any local conditions in which anti-embolism stockings may cause damage – for example, fragile 'tissue paper' skin, dermatitis, gangrene or recent skin graft known allergy to material of manufacture severe leg oedema major limb	Mechanical methods of thromboprophylaxis work by increasing mean blood flow velocity in leg veins and reducing venous stasis. They include: - anti-embolism stockings (AES) - Intermittent pneumatic compression (IPC) devices pneumatic foot pumps.

	deformity or unusual leg size or shape preventing correct fit. - Use caution and clinical judgement when applying anti-embolism stockings over venous ulcers or wounds. - Ensure that people who need anti-embolism stockings have their legs measured and that they are provided with the correct size of stocking. Anti-embolism stockings should be fitted, and patients shown how to use them by staff trained in their use. -If arterial disease is suspected, seek expert opinion before fitting anti-embolism stockings. - Use anti-embolism stockings that provide graduated compression and produce a calf pressure of 14–15 mmHg. (This relates to a pressure of 14–18 mmHg at the ankle and is in line with British Standards BS 6612:1985 Specification for graduated compression hosiery and BS 7672:1993 Specification for compression, stiffness and labelling of anti-embolism hosiery.) Encourage people to wear their anti-embolism stockings day and night until they no longer have significantly reduced mobility. -Remove anti-embolism stockings daily for hygiene purposes and to inspect skin condition. In people with a significant reduction in mobility, poor skin integrity or any sensory loss, inspect the skin 2 or 3 times a day, particularly over the heels and bony prominences. - Monitor the use of anti-embolism stockings and offer assistance if they are not being worn correctly. -Stop the use of anti-embolism stockings if there is marking, blistering or discoloration of the skin, particularly over the heels and bony prominences, or if the person experiences pain or discomfort. If suitable, offer intermittent pneumatic compression as an alternative. Do not offer intermittent pneumatic compression to people with a known allergy to the material of manufacture. Advise the person to wear their device for as much time as possible.	

Pharmacological prophylaxis	Offer pharmacological VTE prophylaxis for a minimum of 7 days to acutely ill medical patients whose risk of VTE outweighs their risk of bleeding: Use LMWH as first-line treatment. If LMWH is contraindicated, use fondaparinux sodium	A: When the assessment of risk favors use of thromboprophylaxis, UFH, LMWH or fondaparinux should be administered. C: Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in medical patients.
Malignant diseases	- Do not offer VTE prophylaxis to people with cancer who are receiving cancer modifying treatments such as radiotherapy, chemotherapy or immunotherapy and who are mobile, unless they are also at increased risk of VTE because of something other than the cancer. - Consider pharmacological VTE prophylaxis for people with myeloma who are receiving chemotherapy with thalidomide, pomalidomide or lenalidomide with steroids. Choose either: aspirin (75 or 150mg) or LMWH. - Consider pharmacological VTE prophylaxis with LMWH for people with pancreatic cancer who are receiving chemotherapy. - If giving VTE prophylaxis to people with cancer continue for as long as they are receiving chemotherapy.	A: Patients with cancer are generally at high risk of VTE and should be considered for prophylaxis with LMWH, UFH or fondaparinux whilst hospitalized. A: Neither heparin nor vitamin K antagonists are indicated for prolongation of survival in cancer. A: Neither warfarin nor heparin should be used to prevent catheter-related deep vein thrombosis in cancer patients.
palliative care	- Consider pharmacological VTE prophylaxis for people who are having palliative care. Take into account temporary increases in thrombotic risk factors, risk of bleeding, likely life expectancy and the views of the person and their family members or careers (as appropriate): Use LMWH as first-line treatment. If LMWH is contraindicated, use fondaparinux sodium. - Do not offer VTE prophylaxis to people in the last days of life. - For recommendations on shared decision-making in the last days of life, see the NICE guideline on care of dying adults in the last days of life. - Review VTE prophylaxis daily for people who are having palliative care, taking into account the views of the person, their family members or careers (as appropriate) and the multidisciplinary team.	
Coronary Syndromes	Be aware that people receiving anticoagulant drugs as part of their	- In acute coronary syndromes, patients in whom there is electrocardiogram (ECG)

	treatment for an acute coronary syndrome do not usually need VTE prophylaxis	indication of ischemia and/or elevation of cardiac markers should receive therapeutic doses of LMWH or fondaparinux as part of the management of cardiac ischemia
Stroke / paralysis	- Do not offer anti-embolism stockings for VTE prophylaxis to people who are admitted for acute stroke. - Consider intermittent pneumatic compression for VTE prophylaxis for people who are immobile and admitted with acute stroke. If using, start it within 3 days of acute stroke. - Explain to the person admitted with acute stroke and their family members or careers (as appropriate) that intermittent pneumatic compression: • reduces the risk of DVT and may increase their chances of survival • will not help them recover from stroke, and there may be an associated increased risk of surviving with severe disability. - When using intermittent pneumatic compression for people who are admitted with acute stroke, provide it for 30 days or until the person is mobile or discharged, whichever is sooner.	A: AES should not be used routinely in stroke patients. A: Use of IPC should be considered during hospitalization in patients with acute stroke, if tolerated. A: In patients with non-hemorrhagic stroke at high risk of VTE, LMWH can be considered in addition to IPC.
Renal impairment	- If using pharmacological VTE prophylaxis for people with renal impairment, choose either LMWH or unfractionated heparin (UFH). - If needed, reduce the dose of LMWH and UFH for people with renal impairment. Base the decision on multidisciplinary or senior opinion, or locally agreed protocols.	
psychiatric illness	- Assess all acute psychiatric patients to identify their risk of VTE and bleeding: As soon as possible after admission to hospital or by the time of the first consultant review, using a tool published by an international body, professional network or peer-reviewed journal. The most commonly used risk assessment tool for hospital patients is the Department of Health VTE risk assessment tool (Table 8). Reassess all people admitted to an acute psychiatric ward for risk of VTE and bleeding at the point of consultant review or if their clinical condition changes.	

	- Consider pharmacological VTE prophylaxis with LMWH for people admitted to an acute psychiatric ward whose risk of VTE outweighs their risk of bleeding. - Consider pharmacological VTE prophylaxis with fondaparinux sodium, if LMWH is contraindicated for people admitted to an acute psychiatric ward whose risk of VTE outweighs their risk of bleeding. - Continue pharmacological VTE prophylaxis for people admitted to an acute psychiatric ward until the person is no longer at increased risk of VTE.	
intensive Care	NICE	SIGN
	- Assess all people admitted to the critical care unit for risk of VTE and bleeding. - Provide LMWH to people admitted to the critical care unit if pharmacological VTE prophylaxis is not contraindicated. - Consider mechanical VTE prophylaxis for people admitted to the critical care unit if pharmacological prophylaxis is contraindicated based on their condition or procedure. - If using mechanical VTE prophylaxis for people admitted to the critical care unit, start it on admission and continue until the person no longer has reduced mobility relative to their normal or anticipated mobility. - Reassess VTE and bleeding risk daily for people in critical care units. - Assess VTE and bleeding risk more than once a day in people admitted to the critical care unit if the person's condition is changing rapidly.	- Medical and surgical patients in intensive care units frequently have multiple risk factors for both thrombosis and bleeding. - Other forms of thromboprophylaxis, including mechanical measures, have not been adequately studied in the ICU setting.
Surgical and trauma patients	NICE 2018	SIGN 2014
General and abdominal Surgery	Advise people to consider stopping estrogen-containing oral contraceptives or hormone replacement therapy 4 weeks before elective surgery. If stopped, provide advice on alternative contraceptive methods. <u>Nursing care:</u> early mobilization and hydration encourage people to mobilize as soon as possible. Do not allow people to	<u>A</u>: Patients undergoing abdominal surgery who are at risk due to the procedure or personal risk factors should receive thromboprophylaxis with mechanical methods unless contraindicated and either subcutaneous LMWH, UFH or fondaparinux. <u>A</u>: AES are recommended for prophylaxis in surgical patients, in the absence of contraindications.

	become dehydrated unless clinically indicated. People using antiplatelet agents: Consider VTE prophylaxis for people who are having antiplatelet agents for other conditions and whose risk of VTE outweighs their risk of bleeding. Take into account the risk of bleeding and of comorbidities such as arterial thrombosis. If the risk of VTE outweighs the risk of bleeding, consider pharmacological VTE prophylaxis based on their condition or procedure. If the risk of bleeding outweighs the risk of VTE, consider mechanical VTE prophylaxis. People using anticoagulation therapy Consider VTE prophylaxis for people at increased risk of VTE who are interrupting anticoagulant therapy. Offer VTE prophylaxis to people undergoing abdominal (gastrointestinal, gynecological, urological) surgery who are at increased risk of VTE. Start mechanical VTE prophylaxis on admission for people undergoing abdominal surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. Add pharmacological VTE prophylaxis for a minimum of 7 days for people undergoing abdominal surgery whose risk of VTE outweighs their risk of bleeding, taking into account individual patient factors and according to clinical judgement. Choose either: Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism LMWH or fondaparinux sodium. Consider extending pharmacological VTE prophylaxis to 28 days postoperatively for people who have had major cancer surgery in the abdomen.	D: IPC devices are recommended for prophylaxis of DVT in surgical patients. A: In patients undergoing abdominal surgery AES can be used alone when pharmacological agents are contraindicated, for example due to high bleeding risk. C: Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in surgical patients, as other available agents are more effective. -Pharmacological thromboprophylaxis is typically continued until discharge. Extended prophylaxis should be considered on a case-by-case basis, for example when multiple thrombosis risk factors are present. -The use of AES should continue until there is a return to the pre-morbid level of mobility.
Cardiac Surgery	Consider mechanical VTE prophylaxis on admission for people who are undergoing cardiac surgery who are at increased risk of VTE. Choose either: anti-embolism stockings or intermittent pneumatic compression.	D: Patients undergoing CABG surgery should be offered mechanical thromboprophylaxis where feasible. D: Patients undergoing CABG surgery who are not at high risk of bleeding can be offered pharmacological thromboprophylaxis with

	Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. Consider adding pharmacological VTE prophylaxis for a minimum of 7 days for people who are undergoing cardiac surgery and are not having other anticoagulation therapy: Use LMWH as first-line treatment. If LMWH is contraindicated, use fondaparinux sodium	UFH or LMWH in addition to mechanical thromboprophylaxis.
Thoracic Surgery	Consider VTE prophylaxis for people undergoing thoracic surgery who are at increased risk of VTE. Start mechanical VTE prophylaxis on admission for people undergoing thoracic surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. Consider adding pharmacological VTE prophylaxis for people undergoing thoracic surgery for a minimum of 7 days to people whose risk of VTE outweighs their risk of bleeding: Use LMWH as first-line treatment. If LMWH is contraindicated, use fondaparinux sodium	D: Patients undergoing thoracic surgery should be offered mechanical prophylaxis with IPC or AES. D: Patients undergoing thoracic surgery who are not at high risk of bleeding should be offered pharmacological thromboprophylaxis with UFH or LMWH in addition to mechanical thromboprophylaxis
Craniotomy, Neurosurgery or Traumatic brain Surgery	Offer mechanical VTE prophylaxis on admission to people undergoing elective spinal surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue for 30 days or until the person is mobile or discharged, whichever is sooner. Consider adding pharmacological VTE prophylaxis with LMWH for people undergoing elective spinal surgery whose risk of VTE outweighs their risk of bleeding, taking into account individual patient and surgical factors (major or complex surgery) and according to clinical judgement. If using LMWH for people undergoing elective spinal surgery, start giving it 24–48 hours postoperatively according to clinical judgement, taking into account patient characteristics and surgical procedure. Continue for 30 days or until the person is mobile or discharged, whichever is sooner. If needed, start LMWH earlier than 24 hours after the operation for people	A: Neurosurgical patients should routinely be offered mechanical prophylaxis (with AES or IPC). B: Combining LMWH with mechanical prophylaxis may be considered in patients with additional risk factors for VTE, such as patients with intracranial neoplasm.

	undergoing elective spinal surgery. Base the decision on multidisciplinary or senior opinion, or a locally agreed protocol. Consider mechanical VTE prophylaxis for people undergoing cranial surgery. If using mechanical VTE prophylaxis for people undergoing cranial surgery, start it on admission. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue for 30 days or until the person is mobile or discharged, whichever is sooner. Consider adding pre-operative pharmacological VTE prophylaxis with LMWH. Give the last dose no less than 24 hours before surgery for people undergoing cranial surgery whose risk of VTE outweighs their risk of bleeding. Consider adding pharmacological VTE prophylaxis with LMWH, starting 24–48 hours after surgery for people undergoing cranial surgery whose risk of VTE outweighs their risk of bleeding. Continue for a minimum of 7 days. If needed, start LMWH earlier than 24 hours after the operation for people undergoing cranial surgery. Base the decision on multidisciplinary or senior opinion, or a locally agreed protocol. Do not offer pharmacological VTE prophylaxis to people with ruptured cranial vascular malformations (for example, brain aneurysms) or people with intracranial hemorrhage (spontaneous or traumatic) until the lesion has been secured or the condition has stabilized.	
Spinal Surgery	Offer mechanical VTE prophylaxis on admission to people undergoing elective spinal surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Consider adding pharmacological VTE prophylaxis with LMWH, for people undergoing elective spinal surgery whose risk of VTE outweighs their risk of bleeding, taking into account individual patient and surgical factors (major or complex surgery) and according to clinical judgement. If using LMWH for people undergoing elective spinal surgery, start giving it 24–48 hours postoperatively according to clinical judgement, taking into	A: Neurosurgical patients should routinely be offered mechanical prophylaxis (with AES or IPC). B: Combining LMWH with mechanical prophylaxis may be considered in patients with additional risk factors for VTE, such as patients with intracranial neoplasm.

	account patient characteristics and surgical procedure. Continue for 30 days or until the person is mobile or discharged, whichever is sooner. If needed, start LMWH earlier than 24 hours after the operation for people undergoing elective spinal surgery. Base the decision on multidisciplinary or senior opinion, or a locally agreed protocol.	
Orthopedic Surgery	Offer VTE prophylaxis to people undergoing elective knee replacement surgery whose VTE risk outweighs their risk of bleeding. Consider VTE prophylaxis for people undergoing other knee surgery (for example, osteotomy or fracture surgery) whose risk of VTE outweighs their risk of bleeding. Consider pharmacological VTE prophylaxis for people undergoing foot or ankle surgery. Be aware that VTE prophylaxis is generally not needed if giving local or regional anesthetic for upper limb surgery. Consider VTE prophylaxis for people undergoing upper limb surgery if the person's total time under general anesthetic is over 90 minutes or where their operation is likely to make it difficult for them to mobilize.	A: Patients undergoing THR or TKR surgery should receive pharmacological prophylaxis *(With LMWH, fondaparinux, rivaroxaban or dabigatran)* combined with mechanical prophylaxis unless contraindicated. A: Extended prophylaxis should be given. D: As other agents are more effective for prevention of DVT, aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in orthopedic patients. C: Patients with increased risk of bleeding should be given mechanical prophylaxis alone. C: If the bleeding risk has become acceptable then pharmacological prophylaxis should be added. A: Pneumatic foot pumps can be considered for prophylaxis as an alternative to IPC in Orthopedic surgery patients.
Urological Surgery	Offer VTE prophylaxis to people undergoing abdominal (gastrointestinal, gynecological, urological) surgery who are at increased risk of VTE. For people undergoing bariatric surgery, Start mechanical VTE prophylaxis on admission for people undergoing abdominal surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. Add pharmacological VTE prophylaxis for a minimum of 7 days for people undergoing abdominal surgery whose risk of VTE outweighs their risk of bleeding, taking into account individual patient factors and according to clinical judgement. Choose LMWH or fondaparinux sodium	D: Patients having urological surgery should be offered mechanical prophylaxis with IPC or AES. D: Patients having urological surgery who have any additional risk factors for VTE should be offered mechanical prophylaxis and LMWH.
Vascular Surgery	Consider pharmacological VTE prophylaxis with LMWH for a minimum of 7 days for people who are undergoing open vascular	D: Patients with critical limb ischemia or who are undergoing major abdominal or peripheral vascular surgery *(including*

	surgery or major endovascular procedures, including endovascular aneurysm repair whose risk of VTE outweighs their risk of bleeding. Consider mechanical VTE prophylaxis on admission for people who are undergoing open vascular surgery or major endovascular procedures, including endovascular aneurysm repair, if pharmacological prophylaxis is contraindicated. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility	*amputation),* should be considered for thromboprophylaxis. D: In patients undergoing varicose vein surgery who have no additional risk factors for VTE postoperative AES are recommended. D: In the presence of additional risk factors the addition of UFH or LMWH is recommended.
Plastic and reconstructive surgery		- Patients scheduled for plastic and reconstructive surgery should be considered for mechanical prophylaxis and pharmacological thromboprophylaxis with LMWH.
Bariatric surgery	Offer VTE prophylaxis to people undergoing bariatric surgery. Start mechanical VTE prophylaxis on admission for people undergoing bariatric surgery. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. Add pharmacological VTE prophylaxis for people undergoing bariatric surgery for a minimum of 7 days for people whose risk of VTE outweighs their risk of bleeding. Choose either: LMWH or fondaparinux sodium	- Patients undergoing bariatric surgery should receive thromboprophylaxis as recommended for those undergoing general surgery. - The dosages of heparin may need to be increased in patients who are obese.
ENT surgery	Consider pharmacological VTE prophylaxis with LMWH for a minimum of 7 days for people undergoing ears, nose or throat (ENT) surgery whose risk of VTE outweighs their risk of bleeding. Consider mechanical VTE prophylaxis on admission for people undergoing ENT surgery who are at increased risk of VTE and high risk of bleeding. Choose either: anti-embolism stockings or intermittent pneumatic compression. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility	- Mechanical methods and pharmacological prophylaxis with LMWH may be considered for patients undergoing high-risk ENT surgery.

Obstetrics / gynecology	NICE	SIGN
Antenatal/Obstetrics	Consider LMWH for all women who are admitted to hospital or a midwife-led unit if they are pregnant or gave birth, had a miscarriage or had a termination of pregnancy in the past 6 weeks, and whose risk of VTE outweighs their risk of bleeding. Do not offer VTE prophylaxis to women admitted to hospital or a midwife-led unit who are in active labor. Stop pharmacological VTE prophylaxis when women are in labor. If using LMWH in pregnant women, start it as soon as possible and within 14 hours of the risk assessment being completed and continue until the woman is no longer at increased risk of VTE or until discharge from hospital or the midwife-led unit. If using LMWH in women who gave birth or had a miscarriage or termination of pregnancy, start 4–8 hours after the event unless contraindicated and continue for a minimum of 7 days. Consider combined prophylaxis with LMWH plus mechanical prophylaxis for pregnant women or women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks and who are likely to be immobilized, or have significantly reduced mobility relative to their normal or anticipated mobility for 3 or more days after surgery, including caesarean section: Use intermittent pneumatic compression as first-line treatment. If intermittent pneumatic compression is contraindicated, use anti-embolism stockings. Continue until the woman no longer has significantly reduced mobility relative to her normal or anticipated mobility or until discharge from hospital.	D: All women should be assessed for risk factors for VTE when booking for antenatal care and at each subsequent maternity contact. - Women should be asked about a personal and family history of VTE and whether an objective diagnosis was made. D: Routine testing for thrombophilia in pregnancy is not indicated. C: Low molecular weight heparins are the agents of choice for antenatal thromboprophylaxis. D: Antenatal thromboprophylaxis should generally be commenced in the first trimester of pregnancy. C:-Vitamin K antagonists have adverse fetal effects and should generally be avoided in pregnancy. In women with mechanical heart valves, however, the risks and benefits of VKA and heparin should be assessed on an individual basis. C: Women of childbearing age using VKA should be clearly informed of the risk of keratogenesis associated with these agents and should be advised to seek appropriate medical advice if they are planning to become pregnant or as soon as possible *(and within two weeks following a first missed period)* if they suspect that they may be pregnant. D: Pregnant women considered to be at increased risk of VTE should be advised to wear AES when immobile/hospitalized. D: All women should be assessed after delivery for risk factors for VTE. D: Women with multiple risk factors for VTE should be considered for postnatal thromboprophylaxis. -Women with two or more risk factors should receive LMWH for seven days after delivery; women with three or more risk factors should be offered AES in addition to LMWH. D: All women who have had an emergency Caesarean section and those who have an elective Caesarean section who have one or more additional risk factors for VTE, should

		receive thromboprophylaxis with LMWH for seven days. D: Women with a previous VTE should receive LMWH for six weeks following delivery. -Women who are known to have an acquired or inherited thrombophilia should be considered for thromboprophylaxis for six weeks following delivery taking account of the family history, any personal risk factors and patient preference. -Women receiving prophylaxis antenatally should continue thromboprophylaxis doses for six weeks following delivery. Warfarin is an alternative to LMWH in this situation. -Women who are normally anticoagulated with warfarin out with pregnancy can recommence warfarin three days after delivery.
Travel related thrombosis		SIGN
		- The risks and possible benefits of any intervention should always be discussed with the patient before travelling. D: Travelers should be advised to remain as ambulant as safely possible before, during and after journeys. Leg exercise whilst seated may be recommended. D: The use of AES for prevention of VTE during and after long-haul travel is not routinely recommended. When used, care should be taken to ensure an appropriate fit. - Appropriate monitoring of the INR and dosage adjustment is recommended prior to travel for patients taking warfarin. - In people deemed to be at especially high risk of travel-related VTE, pharmacological prophylaxis can be considered. LMWH has been used for this purpose.
Managing venous thromboembolism		
	NICE 2018	***SIGN 2014***
Outpatient management of acute VTE	- Consider outpatient treatment for suspected or confirmed low-risk PE, using a validated risk stratification tool to determine the suitability of outpatient treatment. - When offering outpatient treatment to people with suspected PE, follow	***1. Deep vein thrombosis*** B: Outpatient therapy of DVT may be considered for selected patients with appropriate support services in place. ***2.*** **Pulmonary Embolism** B: Validated prognostic models to identify patients at low risk of adverse outcomes may

	recommendations on diagnosis and initial management. When offering outpatient treatment to people with confirmed PE, follow the recommendations in the section on anticoagulation treatment for confirmed DVT or PE. - Agree a plan for monitoring and follow-up with people having outpatient treatment for suspected or confirmed low-risk PE. Give them: written information on symptoms and signs to look out for, including the potential complications of thrombosis and of treatment direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns information about out-of-hours services they can contact when their healthcare team is not available.	be incorporated into treatment algorithms for the management of patients with PE to identify those suitable for outpatient management or early discharge.
Pulmonary embolism	Venous thromboembolism: diagnosis and anticoagulation treatment in algorithm visual summary: https://pathways.nice.org.uk/pathways/venous-thromboembolism/managing-venous-thromboembolism	A: Patients with suspected PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely. D: Once confirmed the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist, and for at least 5 days D: Patients with intermediate-risk PE should not routinely receive thrombolytic therapy. - Patients with intermediate-risk PE should be monitored in hospital and be considered for thrombolysis should they deteriorate. - Patients with low-risk PE can be considered for outpatient management or early discharge. - Patients with high-risk PE should be managed in a coronary care unit or high dependency
Lower limb DVT		A: Patients with suspected DVT should be treated with therapeutic doses of LMWH or fondaparinux until the diagnosis has been deemed very unlikely or confirmed. D: In confirmed DVT the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist, and for at least 5 days. B: Intravenous UFH may be an appropriate alternative in certain circumstances, e.g. if

		thrombolysis is being considered, in the immediate postoperative period or where there is particular risk of bleeding. A: Patients with cancer and VTE should be offered treatment with LMWH (rather than vitamin K antagonist) for three to six months and reviewed thereafter. D: Thrombolysis is not routinely recommended for patients with lower limb DVT. D: Thrombolysis, preferably catheter-directed thrombolysis or catheter-directed thrombolysis with percutaneous mechanical thrombectomy, can be considered on an individual basis, particularly in patients at low bleeding risk with limb threatening or massive tibiofemoral DVT.
Superficial Thrombophlebitis:		D: Patients with clinical signs of superficial thrombophlebitis affecting the proximal long saphenous vein should have an ultrasound scan to exclude concurrent DVT. B: Patients with superficial thrombophlebitis should have anti-embolism stockings and can be considered for treatment with prophylactic doses of LMWH for up to 30 days or fondaparinux for 45 days. B: If LMWH is contraindicated, 8-12 days of oral NSAIDs should be offered. - Patients with superficial thrombophlebitis at, or extending towards, the saphenous-femoral junction can be considered for therapeutic anticoagulation for 6-12 weeks.
Upper Extremity DVT		- Management of upper extremity DVT needs to be on an individual patient basis and should include management of any underlying condition. D: Patients with upper extremity DVT without underlying risk factors *(such as antiphospholipid antibodies)* do not require prolonged *(more than 3-6 months)* anticoagulant treatment.
Splanchnic Vein Thrombosis		D: Patients with acute splanchnic vein thrombosis should have treatment for any underlying disease and be considered on an individual basis for anticoagulation after careful assessment of individual risks and benefits.
Incidental VTE		D: In patients with incidental VTE detected by imaging, treatment decisions should be made on an individual basis taking account of the thrombus burden and the presence of additional risk factors for VTE as well as bleeding risk.

Further Management of venous thromboembolism	NICE 2018	SIGN 2014
Choice of anticoagulant	- Offer anticoagulation treatment for at least 3 months to people with confirmed proximal DVT or PE. For recommendations on treatment after 3 months see the section on long-term anticoagulation for secondary prevention. - If not already done, carry out baseline blood tests, when starting anticoagulation treatment. - When offering anticoagulation treatment, take into account comorbidities, contraindications and the person's preferences. - Offer either apixaban or rivaroxaban to people with confirmed proximal DVT or PE. If neither apixaban nor rivaroxaban is suitable offer: low molecular weight heparin (LMWH) for at least 5 days followed by dabigatran or edoxaban or LMWH concurrently with a vitamin K antagonist (VKA) for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. - Do not routinely offer unfractionated heparin (UFH) with a VKA to treat confirmed proximal DVT or PE unless the person has renal impairment or established renal failure or an increased risk of bleeding. - Do not routinely offer self-management or self-monitoring of INR to people who have had DVT or PE and are having treatment with a VKA.	A: After a first episode of limb deep vein thrombosis or pulmonary embolism, treatment with a VKA should be initiated. A: Use of LMWH is an alternative and can be considered if VKA therapy is problematic, for example due to poor compliance/erratic intensity of anticoagulation. A: LMWH rather than warfarin should be considered in VTE associated with cancer. C: Neither aspirin nor statin is recommended for the prevention of recurrent VTE after discontinuation of VKA therapy. B: After a first episode of limb deep vein thrombosis or pulmonary embolism the target INR should be 2.5. D: A higher target INR (3.5) may be considered if there is recurrent VTE whilst in the target range. B: In patients with antiphospholipid syndrome and VTE, anticoagulation with a VKA, target INR 2.5, should be implemented. After a first episode of proximal limb deep vein thrombosis or pulmonary embolism, treatment with a VKA should be continued for at least three months. - Uninterrupted, long term continuation of VKA therapy after a first episode of VTE may be appropriate in some patients and can be based on individual assessment of risk factors, including: - an unprovoked first event - the site and severity of the first event - the presence of persistent comorbidities, e.g. cancer - the presence of persistent antiphospholipid antibodies - male sex - bleeding risk on anticoagulant treatment - Patient compliance and preference. A: Measurement of D-dimer concentration one month after discontinuation of a course of VKA therapy after a first episode of unprovoked VTE can be considered for the identification of patients who may benefit

		from resumption of VKA therapy and continuation in the long term. - After recurrent VTE, long term treatment with a VKA is recommended but the nature of the recurrence (provoked or unprovoked), the elapsed time between episodes and risk of bleeding should be considered in reaching this decision. - The use of long term VKA should be subjected to periodic review, to include anticoagulant control, bleeding episodes and altered risk of bleeding.
Graduated Elastic Compression Stockings	- Do not offer elastic graduated compression stockings to prevent post-thrombotic syndrome or VTE recurrence after a DVT. This recommendation does not cover the use of elastic stockings for the management of leg symptoms after DVT. - If offering elastic graduated compression stockings to manage leg symptoms after DVT, explain how to apply and use them, how long they should be worn and when they should be replaced.	A: After deep vein thrombosis affecting a lower limb, the use of well fitted below-knee graduated elastic compression stockings for two years should be encouraged to reduce the risk of post-phlebitis syndrome.
Monitoring the anticoagulant effect	- Assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with people who have had anticoagulation treatment for 3 months (3 to 6 months for people with active cancer) after a proximal DVT or PE. Follow the recommendations on shared decision making, supporting adherence and medication review in the NICE guidelines on: medicines optimization medicines adherence patient experience in adult NHS services. - Consider stopping anticoagulation treatment 3 months (3 to 6 months for people with active cancer) after a provoked DVT or PE if the provoking factor is no longer present and the clinical course has been uncomplicated. If anticoagulation treatment is stopped, give advice about the risk of recurrence and provide: written information on symptoms and signs to look out for direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns information about out-of-hours services they can contact when their healthcare team is not available.	***1-*** unfractionated heparin: D: Therapeutic dosing of UFH should be monitored by use of a locally calibrated APTT assay. ***2-*** low molecular weight heparin: C: Routine laboratory monitoring of LMWH is not recommended. ***3-*** Warfarin: INR control: - There are several models of care for management of VKA therapy. The optimal approach suitable for local conditions and which provides the most precise INR control should be selected. A: Computer-assisted dosing algorithms are recommended. D: Patient self-testing and self-management supported by a dedicated and well-trained anticoagulant team may be considered for selected patients.

	- Consider continuing anticoagulation beyond 3 months (6 months for people with active cancer) after an unprovoked DVT or PE. Base the decision on the balance between the person's risk of venous thromboembolism (VTE) recurrence and their risk of bleeding. Discuss the risks and benefits of long-term anticoagulation with the person and take their preferences into account. - Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks. - Do not rely solely on predictive risk tools to assess the need for long-term anticoagulation treatment. - Consider using the HAS-BLED score to assess the risk of major bleeding in people having anticoagulation treatment for unprovoked proximal DVT or PE. Discuss stopping anticoagulation if the HAS-BLED score is 4 or more and cannot be modified. - Take into account the person's preferences and their clinical situation when selecting an anticoagulant for long-term treatment. - For people who do not have renal impairment, active cancer, established triple positive antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg): offer continued treatment with the current anticoagulant if it is well tolerated or if the current treatment is not well tolerated, or the clinical situation or person's preferences have changed, consider switching to apixaban if the current treatment is a direct-acting anticoagulant other than apixaban. - For people with renal impairment, active cancer, established triple positive antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg), consider carrying on with the current treatment if it is well tolerated. - If anticoagulation treatment fails follow the recommendation on treatment failure. - For people who decline continued anticoagulation treatment, consider aspirin 75 mg or 150 mg daily. - Review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people taking long-term anticoagulation treatment or aspirin.	

Adverse effects of venous thromboembolism prophylaxis and treatment		D: In choosing pharmacological thromboprophylaxis the risks of bleeding and other complications need to be considered alongside the likely benefits. D: Major bleeding in patients who are receiving warfarin or other VKAs should be treated by immediate reversal of anticoagulation. This is best achieved by administration of intravenous vitamin K and prothrombin complex concentrate. D: Minor bleeding in patients who are anticoagulated with warfarin should be reversed using low doses of vitamin K (1-2.5 mg) given either intravenously or orally depending on the clinical circumstances and assessment of the bleeding. - In patients who are over anticoagulated warfarin therapy should be temporarily discontinued continued at a decreased dose. - Monitoring of patients should be more intensive during the first months of treatment when anticoagulant control tends to be less stable.
Heparin induced thrombocytopenia		A: To minimise the incidence of HIT, LMWH should be used in preference to UFH. • Patients at high risk of developing HIT, and who should be monitored by serial platelet counts between days 4–14 are: - all post-operative patients receiving UFH - Patients post-cardiopulmonary bypass receiving LMWH. • The following patients are at low risk of developing HIT and do not require routine platelet monitoring: - post-operative patients (other than post-cardiopulmonary bypass) receiving LMWH - All medical and obstetric patients receiving any heparin for prophylaxis or treatment. D: All patients who are to receive UFH or LMWH for prophylaxis or treatment of VTE should have a platelet count performed in the 24 hours before receiving treatment. D: Monitoring patients for the development of HIT should be by performing serial platelet counts. D: Patients who have previously received UFH or LMWH within 100 days or in whom the history of recent exposure to heparins is not clear should have a platelet count performed within 24 hours of receiving the first dose of treatment.

		D: All other patients for whom monitoring is indicated should have platelet counts performed every two to three days from day four to day14 of exposure. - HIT should be suspected if the platelet count falls by 30% or more or if there is thrombocytopenia (<150 x 109/l). - HIT should be considered in patients who develop a new thrombosis or in whom thrombosis extends and in patients who develop typical skin lesions or features of a systemic response such as fever, chills or shivering whilst receiving any form of heparin. D: In cases where HIT is suspected the patient should be evaluated using a clinical scoring system to assess the pre-test probability of having the condition. D: This should be followed, where appropriate, by laboratory testing for anti-HIT antibodies. The combined information should be used to assess the probability of having HIT. D: Whether or not there is evidence of a new thrombotic episode related to HIT, patients should receive therapeutic, as opposed to prophylactic, doses of argatroban or danaparoid. D: Where warfarin therapy is proposed it should not be introduced until the platelet count has risen into the normal range (150–400 x109/l). D: When warfarin therapy is introduced it should be at a low dose (5 mg daily) and danaparoid or argatroban should be withdrawn only after the INR has been >2 on two consecutive days for patients on danaparoid and >4 on two days in patients on argatroban. - A history of HIT should be carefully documented in the clinical record.
Reduced bone mineral density		C: Monitoring of bone density in pregnant women exposed to LMWHs is not recommended.

Appendix 4: AGREE II Instrument Domain Scores of the included guidelines:

CPGs AGREE II DOMAINS	SIGN 2010 (UPDATED 2014)	NICE 2018	*The American College of Emergency Physicians 2018*
D1: Scope and Purpose	**92%**	**89%**	**96%**
D2: Stakeholder Involvement	**96%**	**85%**	**69%**
D3: Rigour of Development	**77%**	**81%**	**92%**
D4: Clarity and Presentation	**94%**	**82%**	**88%**
D5: Applicability	**73%**	**75%**	**83%**
D6: Editorial Independence	**67%**	**98%**	**71%**
This table uses the AGREE II Domain Score Color Coding (< 40% red > 41 – 70% yellow > 71 % green)			
Therefore, the panel decided to select the _____.			

Appendix 5: Decision Support tool

Decision Support tool for the Adaptation Working Panel for CPGs for 'Evidence-Based Clinical Practice Guideline for Screening, Prophylaxis and Management of Venous Thromboembolism'

Chairperson: Dr. Samia Alhabib

PHASE	MODULE	STEP	TOOL	DECISION		REASON *(if not utilized)*
				Utilized	Not utilized	
ONE: SET-UP	1.1. Preparation	1	1	√		
			2	√		
		2		√		
		3		√		
		4		√		
		5	3	√		
			4	√		
			1	√		

		6	5	√		
TWO: ADAPTATION	2.1. Scope and Purpose	7	6	√		
	2.2. Search and Screen	8	2	√		
			7	√		
		9	8	√		
		10	9		√	Decided to rely on inclusion/ exclusion criteria (filters) and PIPOH compatibility.
			10		√	
	2.3. Assessment	11	9	√		
			10	√		
		12	11	√		
		13	12		√	Decided to select all recommendations from SIGN, NICE, ACEP
		14	13		√	Decided to rely on D3 Scores of AGREE II
			14		√	
		15	15		√	Decided to rely on D5, D2 Scores of AGREE II
	2.4. Decision and Selection	16	Table (?)	√		
		17	Decision making and selection (? options)	√		The panel modified the options to be two (Accept or Reject) rather than five according to recommendation of CPG Committee
	2.5. Customization	18	16	√		
THREE: FINALIZATION	3.1. External Review and Acknowledgment Module	19	17			
		20				
		21				
		22				
	3.2. Aftercare Planning	23	18			
	3.3. Final Production	24				

Appendix 6: Reviewers comments on included CPGs

Guideline	*NICE*	*SIGN*	*ACEP*
Domain 1. Scope and Purpose			
Item 1: The overall objective(s) of the guideline is (are) specifically described.	Appraiser 1: The objectives are only summarized, and potential impact of following guidelines are not stated. In addition, Limitations of the usefulness of the guidelines based on paucity of data and ability to apply clinical judgement are not stated.	Appraiser 10: The current guideline provides comprehensive advice on prevention and management of VTE based on the evidence available to answer a set of key questions. The guidelines apply to all adult patients at risk of VTE and to patients with specific conditions who are also at risk of developing VTE. Health intent: prevention and management of VTE. Expected benefit or outcome: better application of prophylactic, diagnostic and treatment methods of VTE by health practitioners in different specialties. Targets: all hospitalized patients at risk of VTE and especially the ones with medical illnesses. The items are well written within the guidelines and could be easily located in the two subsections, The need for a guideline and the remit of the guideline. Under the introduction section of the guideline. Appraiser 2: The guideline defines VTE-risk adult patient groups and explains the prophylaxis procedures available. Appropriate methods of prophylaxis are regarded in later sections of the guidelines for specific patient groups. Page 2. Appraiser 16: This was clearly indicated in 1.2.1 and 1.2.2.	
Item 2: The health question(s) covered by the	Appraiser 1: No specific timing mentioned for applying the risk assessment and no	Appraiser 10: The health questions are separately listed in Annex 1 of the guidelines, thus, could be easily located. A set of different health	

guideline is (are) specifically described.	support or weight of evidence stated. Frequently, statements such as \"Balance the person\'s individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis\". How? DOH-VTE assessment tool does not allow for risk scoring.	questions covering different domains are written i.e. Risk factors, prevention, adverse effects, investigation, and management of VTE. Examples, specific considerations, precise and detailed explanations are included under each question. Such a description easily enables anyone to initiate the development of the guidelines. Appraiser 2: On page 2, the rationale for prophylaxis states the target population. diagnostic and treatment option Appraiser 16: The health questions were specified in Annex1 (page69 - 71) Appraiser 17: The target population are well defined and intervention with comparisons between different modalities are stated for the well-defined subpopulations. Generally, the guidelines and guidance are well written. There are limited references, yet what is stated is clearly adequate.	
Item 3: The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Appraiser 4: 16 years and above Appraiser 1: Not all potential adult patient populations are covered. Also, this guideline does not cover patients with suspected or confirmed DVT.	Appraiser 10: Target population: all adult patients at risk of VTE. The guideline includes a comprehensive, detailed list of all patients at risk of VTE as it provides a risk assessment tool that describes and groups patients into different categories. Some of these include surgical patients/ any patient undergoing an invasive procedure, medical patients, pregnancy and puerperium. This target population is specifically described in the risk factors for venous thromboembolism subsection of section2, key recommendations, as well as in the key questions of the guideline. The description is specific enough for health practitioners to deliver the actions recommended in the guidelines to the correct and eligible patients.	Appraiser 3: This guideline is not intended to address the care of pediatric patients, or those with VTE in the setting of cardiac arrest or pregnancy.

		Appraiser 2: The guideline identifies adult patient groups at risk of VTE Appraiser 16: The specific population was mentioned under the Overall Objectives (1.2.1). There were no specific labeled sections for the target patient population. Appraiser 17: Almost all possible populations are covered. One large group is the outpatients though this was stated early on that the focus are inpatients.	
Domain 2. Stakeholder Involvement			
Item 4: The guideline development group includes individuals from all relevant professional groups**.**	Appraiser 3: There are some specialized professional groups not included like: adult ICU consultant, clinical pharmacist, Public, Oncology consultant, health educators…. Appraiser 4: some important specialties are not included like cardiologist, oncologists...etc. Appraiser 1: All important and relevant specialties are represented.	Appraiser 10: The acknowledgment section of the guideline introduced the development committee as follows: “SIGN is a collaborative network of clinicians….etc. Appraiser 2: A Guideline Developer’s Handbook’, available at www.sign.ac.ukpage 64 Appraiser 16: The development group is stated in section 19 (page 64). There was no description of each member’s role in the guideline development group. Appraiser 17: All important subspecialties are included in the main group, including members of the public (lay individuals).	Appraiser 3: There are some specialized professional groups not included like: clinical pharmacist, patient, Public, health educators, only 1 nurse…. Appraiser 2: I could not see any hematologist or clinical pharmacist Appraiser 4: Not clearly stated.
Item 5: The views and preferences of the target population (patients, public, etc.) have been sought.	Appraiser 3: Patient preferences was not discussed (e.g. selection of location of mechanical garments, in addition; cultural acceptance of some medication content that carries some special concerns like pork origin. Appraiser 1: Not evident, though the summary of the guidelines is recommended for informing the patients and their families.	Appraiser 10: The acknowledgments section has addressed patient involvement in the guideline development as follows: “PATIENT INVOLVEMENT" Appraiser 2: The risk of VTE is significantly increased in patients who are hospitalized after trauma, surgery or immobilizing medical illness, and also in pregnant and puerperal women, page 2 Appraiser 16: This was specified in details in page 65.	Appraiser 3: Patient were not involved in the developmental group, so their preferences was not discussed Appraiser 4: No clear participation of patients on this guideline

Item 6: The target users of the guideline are clearly defined.	Appraiser 1: Yes. With subsequent definition and guidance on the role of healthcare providers involved.	Appraiser 10: The target users of the guideline are explicitly described in the introduction of the guideline under the remit of the guideline subsection as follows: “TARGET USERS OF THE GUIDELINE" Appraiser 2: target users of the guideline. This guideline will be of particular interest to medical practitioners in a wide range of Specialties including general practitioners, nurses, pharmacists and dentists page 2 Appraiser 16: Although the different categories of target users of the guideline were stated in section 1.2.2 (page 2), there was no description of how the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care). Appraiser 17: Yes. With definition and guidance on the role of healthcare providers involved.	
Domain 3. Rigor of Development			
Item 7: Systematic methods were used to search for evidence.	Appraiser 1: Yes, but the definitions are not	Appraiser 10: This domain questions the degree to which a systematic methodology was used in the search for evidence, taking into account a clear description of search terms used, sources consulted, and dates of the literature covered. On the basis of the above criteria it was noted that the guideline adequately presented the search methods. The current guideline provides a details systematic method was used in search for evidence, taking into account a clear description of sources consulted and time period searched. However, there was no clear description of search terms used. Appraiser 16: The systematic literature review was stated on page 63. It stated the databases and the time periods searched. However, it did not specify the search terms, or the full search strategy included. Appraiser 17: Yes, very well systematized.	Appraiser 4: Limited to English literature only

Item 8: The criteria for selecting the evidence are clearly described.	Appraiser 2: Yes, based on best available evidence and by experts, people using services, careers and the public. Appraiser 4: It was included in separate appendix Appraiser 1: Levels of evidence and grades of recommendations are not as clearly defined as other guidelines.	Appraiser 10: The criteria for inclusion and exclusion in this guideline did not addressed, thus, there was no clear inclusion and exclusion criteria described and rationale. However, IDENTIFYING AND SELECTING THE EVIDENCE was explicitly described in sign55 separate file. Appraiser 2: SIGN guidelines are developed by multidisciplinary groups of practicing clinicians using a standard methodology based on a systematic review of the evidence. Appraiser 16: The criteria for including/excluding evidence identified by the search were not provided. Appraiser 17: Yes, though they are not using an agreed on, well-defined scale for assessment of the level of evidence.	
Item 9: The strengths and limitations of the body of evidence are clearly described.	Appraiser 3: level of evidence and limitations was not clarified well Appraiser 2: I could not find it Appraiser 4: The level of evidence is not clearly explained in several situations Appraiser 1: To a large extent this is done but, in the guidelines,' "Methods, evidence and recommendations"	Appraiser 10: The guideline document has graded the level of evidence based on their strength and limitation and they were included in a table titled 'Key to evidence statements and grades of recommendations' Appraiser 16: There were no statements highlighting the strengths and limitations of the evidence. Appraiser 17: Yes, but the discussion is abbreviated.	
Item 10: The methods for formulating the recommendations are clearly described.	Appraiser 1: Strength of the recommendation and level of evidence are not stated. Delphi technique not used.	Appraiser 10: The guideline document described its process of formulating the recommendations in three stages under the 'consultation and peer review section'. The first one being the national open meeting during which the following takes place: A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time.	

		The national open meeting for this guideline was held on 29th September 2009 and was attended by 118 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline. A specialist committee of external reviewers also review a draft of the recommendations and their evidence. Any comments made by this committee is addressed again and justified by the guideline group. A final check is then made by an editorial group. Appraiser 16: There was no description of the methods used to formulate the recommendations and how final decisions were arrived. However, there is a reference to 'SIGN 50: A Guideline Developer's Handbook'. Appraiser 17: The recommendation development process was discussed in clear details.	
Item 11: The health benefits, side effects, and risks have been considered in formulating the recommendations.	Appraiser 4: True, however cost effectiveness was another factor mentioned in the guidelines Appraiser 1: Not written in the guidelines but in the "Methods, evidence and recommendations". It is still not detailed and not enough to support developing strength of recommendations.	Appraiser 10: The guideline considers the health benefit and risk/side effects in formulating recommendation and have precisely discussed the overall effects of different management method. These aspects were discussed in detail relating to specific patient populations and conditions. Specific patient conditions in which the recommendations do not apply were also provided. Appraiser 16: The risks of bleeding were stated in different recommendation statements. However, there was no evidence that this was planned a priori. There was no supporting data when reporting harms/risks. Appraiser 17: The health benefits, side effects, and risks have been considered but not clear how it affected the strength of recommendations.	

Item 12: There is an explicit link between the recommendations and the supporting evidence.	Appraiser 1: Not written in the guidelines but in the "Methods, evidence and recommendations"	Appraiser 10: The guideline mentioned the link between guideline development group and using the evidence to inform recommendation in section 18 and Annex 1, taking into account that the guideline development group was failed to recognize sufficient evidence in order to answer all of the key questions asked in this guideline. However, it was easy to define the link between the recommendation and supporting evidence in the key recommendation section. It was summarized clearly. Appraiser 16: Each recommendation is linked to a key evidence description and reference list. However, the recommendations were not linked to evidence summaries/tables. Appraiser 17: Yes	
Item 13: The guideline has been externally reviewed by experts prior to its publication.	Appraiser 3: There are some subspecialties not involved in the review process like: adult ICU consultant, clinical pharmacist, Public, Oncology consultant, health educators…. Appraiser 4: Not clearly stated. Appraiser 1: There were 3 expert advisers but the purpose, intent, and methodology are not documented in the guidelines. It is written on the NICE general methodology web site.	Appraiser 10: The external review by experts of the guideline are explicitly described in the Consultation and Peer review section of the guideline under the remit of the guideline subsection as follows: 'This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer and must justify any disagreement with the reviewers' comments.' The Consultation and Peer review section continues by providing a comprehensive list of each member of the developing group that includes the titles, names, disciplines, expertise, institutions, and geographical location of each member. The means by which the guideline was developed and	Appraiser 2: It was mentioned that it was externally reviewed but did not details who are the external reviewers

		reviewed internally and externally are provided including all personnel involved in these processes. Finally, members of the editorial group involved in the final quality control step were also comprehensively acknowledged. The Consultation and Peer review section provided a precise description of each member's role/ contribution to the guideline development. This has demonstrated the appropriateness and relevance of each member to their chosen roles in the guideline development. This has also conveyed the wide variety of expertise of the involved committee members. Appraiser 16: The details of peer review were stated on pages 65-66. Appraiser 17: Yes, from different set of experts than the developers, though the methods taken to undertake the external review was not described in detail.	
Item 14: A procedure for updating the guideline is provided.	Appraiser 1: It is only stated that "All NICE guidance is subject to regular review and AGREE Advancing the science of practice guidelines. may be updated or withdrawn". And "Following publication, and in accordance with the NICE guideline manual, NICE will undertake a review of whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update" No clear timeline or criteria were mentioned. No methodology stated.	Appraiser 10: The guideline had a clear statement in the introduction section with regards to updating the guideline which stated that last update done was in 2014 and they will consider reviewing the guideline every three year, moreover, there was an explicit time interval to guide decisions about when an update will occur and methodology for the updating procedure is reported. Appraiser 16: In section 18.23, it was stated that this guideline was issued in 2010 and will be considered for review in three years. However, it was updated in November 2011 and October 2014. This information was stated on the front page of the guideline. This was not stated in the update section. The methodology for updating the guideline was not reported. Appraiser 17: Methodology for the updates are not described in detail.	

Domain 4. Clarity of Presentation			
Item 15: The recommendations are specific and unambiguous	Appraiser 4: In some conditions it was very concise and not clear e.g. for cancer patients Appraiser 1: The recommendations are written in a very general format and risk benefit calculation is not clear either. Strength of the recommendation is missing. Recommendations are made for every sub-population. I like the fact that they state the responsibility of individual healthcare workers.	Appraiser 10: The recommendations of the guideline have precisely described all aspects of VTE including patients' assessments for risk factors, VTE prophylaxis, diagnosis and management. These aspects were discussed in detail relating to specific patient populations and conditions. Specific patient conditions in which the recommendations do not apply were also provided. Appraiser 16: The recommendations did not include the dosage or duration of the medications for VTE prophylaxis. Appraiser 17: All the criteria listed below are included.	Appraiser 3: 5 Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department with Suspected acute Venous Thromboembolic Disease was examined and have the recommendations. The recommendations are still have an area for further research to cover the defects that raised from the reviewed studies.
Item 16: The different options for management of the condition or health issue are clearly presented.	Appraiser 3: There are some situations not clarified like: - Head trauma - Patient with invasive lines (CVP, Al) - Bed redden patents sent home - Hospitalized long-term patients - Patient in critical care units and on CRRT (dialysis) Appraiser 1: To some extent it is clear which options are preferable but not as well as other guidelines	Appraiser 10: The recommendations section of the guideline listed a number of different options for prophylaxis, diagnosis, and management of patients at risk of VTE. These were described in relation to specific patient population and clinical conditions in which they are most appropriate. Appraiser 2: SIGN guidelines are developed by multidisciplinary groups of practicing clinicians using a standard methodology based on a systematic review of the evidence. Appraiser 17: Yes. They are clear and well written	Appraiser 3: The different options for management of the condition or health issue were not clearly presented.
Item 17: Key recommendations are easily identifiable.	Appraiser 1: Yes, they are but perhaps a bit too summarized.	Appraiser 10: The key recommendations in sign guideline were easy to identify. These recommendations answer the main question(s) that have been identified in different ways. For example, typed in bold, underlined or presented as flow charts or	

		algorithms. The recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritized for implementation are: risk factors for venous thromboembolism, thrombo Prophylaxis in surgical Patients, thromboprophylaxis in medical Patients, Pregnancy and the Puerperium, diagnosis of venous thromboembolism, Preliminary assessment, initial management of venous thromboembolism, further management of venous thromboembolism, adverse effects of venous thromboembolism Prophylaxis and treatment. Appraiser 16: Key recommendations were stated on pages 4-6. Appraiser 17: Yes. Recommendations are clear and well described. The recommendation strength is also easily identified.	
Domain 5. Applicability			
Item 18: The guideline describes facilitators and barriers to its application.	Appraiser 3: There are some situations not clarified like: - Head trauma - Patient with invasive lines (CVP, Al, … - Bed redden patents sent home - Hospitalized long-term patients - Patient in critical care units and on CRRT (dialysis) Appraiser 2: There are footprints identify the limitations and more information. Appraiser 4: Did not provide a clear guide on how to apply it Appraiser 1: To some extent facilitators and	Appraiser 10: The guideline provides the existing facilitator and barriers that could impact the application of the recommendation, in implementation section, it was clearly identified the facilitator and barrier by understanding the current practice as a first step in implementation the guideline, method was sought by designed audit tool which could assist in this process. The guideline also identifies the key information in order to successfully implement this tool. Appraiser 2: Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working barriers not explore?	

	barriers are stated but embedded within the guidelines and not distinguished clearly.	Appraiser 16: There were no statements of the facilitators and barriers to the guideline application. Appraiser 17: To some extent facilitators and barriers are stated but embedded within the guidelines and not distinguished clearly.	
Item 19: The guideline provides advice and/or tools on how the recommendations can be put into practice.	Appraiser 4: In concise way. Appraiser 1: NICE though limited tools are provided. On the positive side they are easy, but on the downside, they come a bit short on clear benefit/risk assessment.	Appraiser 10: Tools and resources to facilitate application was provided in this guideline in Provision of information section which was included: Patient leaflet and checklist. It was easy to find and clearly presented. Appraiser 2: The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline. -Compliance with and recording of risk assessment in all patients admitted to or presenting acutely at hospital. -Compliance with appropriate prescription of mechanical and pharmacological prophylaxis. -Percentage of time in range for INR for patients receiving VKA and percentage INR tests <1.5 and >4.5 as measures of likely poor efficacy and bleeding risk. -The rate of healthcare associated VTE should be recorded and monitored routinely to identify areas where the risk assessment policy may need to be reviewed. -National condition-specific audits should use available linked datasets to monitor readmission or death associated with a VTE episode. still need more elaboration. Appraiser 16: There were checklists and algorithms in the appendices. The guideline stated on page 62 "The implementation strategy for this guideline is available on the SIGN website at www.sign.ac.uk.". I visited the website and couldn't find a specific implementation strategy for this guideline. Appraiser 17: Yes. There is a good Quick reference guide, Audit tools and mobile apps.	

Item 20: The potential resource implications of applying the recommendations have been considered.	Appraiser 1: Resource implications are not adequately stated and also are embedded within the guidelines and not distinguished clearly.	Appraiser 10: in the implementing the guideline section, it was stated that: resource implications of Key recommendations: No recommendations are considered likely to reach the £5 million threshold which warrants full cost impact analysis. Therefore, there was no clear identification of the types of cost, methods by which the cost information was sought and neither a description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations. Appraiser 2: Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Appraiser 16: Only the following statement was mentioned on page 62: 17.1 resource implications of key recommendations No recommendations are considered likely to reach the £5 million threshold which warrants full cost impact analysis. Appraiser 17: Full cost impact analysis was NOT done.	
Item 21: The guideline presents monitoring and/or auditing criteria.	Appraiser 3: It is not clarified Appraiser 2: there is monitoring but no clear auditing Appraiser 1: There is a very good audit tool that is provided on the web site.	Appraiser 10: The auditing criteria of the guideline have precisely described all aspects of defined criteria that are derived from the key recommendations in the guideline Appraiser 2: Auditing current practice. A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between	Appraiser 3: It is not clarified well. They declared that the clinical policies are scheduled for revision every 3 years.

		staff and multidisciplinary team working. Appraiser 16: 17.2 Auditing current practice. A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working. The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline. - Compliance with and recording of risk assessment in all patients admitted to or presenting acutely at hospital. - Compliance with appropriate prescription of mechanical and pharmacological prophylaxis. - Percentage of time in range for INR for patients receiving VKA and percentage INR tests <1.5 and >4.5 as measures of likely poor efficacy and bleeding risk. - The rate of healthcare associated VTE should be recorded and monitored routinely to identify areas where the risk assessment policy may need to be reviewed. - National condition-specific audits should use available linked datasets to monitor readmission or death associated with a VTE episode. Appraiser 17: Good audit tool is included	

Domain 6. Editorial Independence			
Item 22: The views of the funding body have not influenced the content of the guideline.	Appraiser 1: The guidelines were funded by a government agency. There is a very clear conflict of interest policy stated and it is quite comprehensive and adequate.	Appraiser 10: SIGN has a rather unusual status: although the running costs of the guideline development program are funded by the Clinical Resource and Audit Group of the Scottish Executive, it is a professionally led, multidisciplinary, independent organization. Appraiser 2: statement of funding was not mentioned clearly However. Further details about SIGN and the guideline development methodology is contained in 'SIGN 50: A Guideline Developer's Handbook', available at www.sign.ac.uk Appraiser 16: There were no statements on funding bodies or disclaimers. Appraiser 17: The guidelines were funded by a government agency. There is a conflict of interest policy stated.	
Item 23: Competing interests of guideline development group members have been recorded and addressed.	Appraiser 2: all committee members declared interests including consultancies, fee paid work, shareholdings, fellowships and support from the healthcare industry. Appraiser 1: There is a very clear conflict of interest policy stated and it is quite comprehensive and adequate.	Appraiser 10: All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive. Addressed and recorded. Appraiser 2: A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. Appraiser 16: The following statement is the only statement in the guideline regarding completing interests of guideline development group members. Appraiser 17: The guidelines were funded by a government agency. There is a conflict of interest policy stated.	Appraiser 3: There was no evidence found regarding recording or addressing of competing interest of the guideline development group members. Appraiser 2: They were not clear. Appraiser 4: Not in details in comparison to NICE

Overall Assessment			
	Appraiser 4: Some areas are not very well covered like patients with cancer and the use of DOAC. Also, the screening tool used in guidelines was not validated as mentioned by the authors. Appraiser 1: The background material are too comprehensive and length, but the summarized guidelines are too concise. IN addition, some non-standardized methodologies are used to present the guidelines, omitting the weight of evidence and impact of certain clinical influences on benefit and risk. The guidelines are fragmented into many documents though all are easily accessible on the web site.	Appraiser 16: We need access to the evidentiary tables to assess the appropriateness of the recommendation statements.	Appraiser 3: I suggest that we can get a lot of recommendations from this clinical policy regarding the 5 critical domains that were investigated. But still we need to have more to be used as an ER guideline. Appraiser 4: Better presentation of key messages and to include a guidance on how to implement these guidelines.

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