The Role of Physical Therapists in the Management of Individuals at Risk for or Diagnosed with Venous Thromboembolism – A 2021 Evidence-Based Clinical Practice Guideline

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Abstract

No matter the practice setting, physical therapists work with patients who are at risk for and/or have a history of VTE. In 2016, the first clinical practice guideline (CPG) addressing the physical therapy management of VTE was published with support of the APTA Academy of Cardiovascular and Pulmonary Physical Therapy and the Academy of Acute Care and focused primarily on lower extremity DVT. This CPG is an update of the 2016 CPG with the most current evidence available for the management of patients with LE DVT and added new key action statements to include guidance on UE DVT, PE and special populations. This document will guide physical therapy practice in the prevention of, screening for and management of patients at risk for or diagnosed with VTE.

Through a systematic review of published studies and structure appraisal process, key action statements were written to guide the physical therapist. The evidence supporting each action was rated and the strength of statement was determined. **Table 1** lists the 19 key action statements. Clinical practice algorithms (**Figures 1-3**) based upon the key action statements were developed that can assist with clinical decision making. Physical therapists, along with other members of the healthcare team, should work to implement these key action statements to decrease the incidence of VTE, improve the diagnosis and acute management of VTE, and reduce the long term complications of VTE.

Introduction

Purpose of the CPG

Venous thromboembolism (VTE) refers to the formation of a blood clot in a vein that can present as either a deep vein thrombosis (DVT), typical occurring in the lower extremity (LE) but can also be present in the upper extremity (UE), or as a pulmonary embolism (PE). It is estimated that VTE affects 1 to 2 people per 1000 each year in the United States.[1] and those with a diagnosis of pulmonary embolism have a mortality rate of 4.9% over the first 30 days post diagnosis.[2]

In addition to the acute risk of death, one third to one half will have long-term complications such as post-thrombotic syndrome (PTS) or chronic thromboembolic pulmonary hypertension (CTEPH).[1] The risk of recurrence is high after an episode of VTE. In those with an unprovoked VTE, 10% will have a recurrent VTE in the first year after treatment with 36% have a repeat VTE in the following 10 years.[3]

In 2016, the first clinical practice guideline (CPG) addressing the physical therapy management of VTE was published with support of the APTA Academy of Cardiovascular and Pulmonary Physical Therapy and the Academy of Acute Care and focused primarily on lower extremity DVT.[4] Beginning in 2019, the VTE Guideline Development Group (GDG) followed a systematic process to update the original 2016 CPG with the most current evidence available for the management of patients with LE DVT and added new key action statements to include guidance on UE DVT, PE and special populations.

This CPG is based on systematic reviews of published studies on the risks of early ambulation in patients with diagnosed VTE and on established clinical guidelines on prevention, risk factors, and screening for VTE and its secondary clinical consequences. The updated CPG contains 19 key action statements (**Table 1**), with 3 additional figures and 15 tables. This CPG is intended to be used as a reference document to

guide physical therapist (PT) practice in the prevention of, screening for, and treatment of adult patients in all practice settings at risk for any VTE. Specifically, this CPG will:

- Discuss the role of clinicians in identifying patients who are at risk for VTE and actions that can be taken to decrease the risk of a first or recurring VTE.
- Provide clinicians with tools to determine the risk of VTE in their patient populations and determine the likelihood of VTE when symptoms are present.
- Assist clinicians in decision-making regarding mobilization based on the chosen medical intervention for VTE as well as the clinical signs and severity of a VTE.
- Discuss current pharmacological and nonpharmacological treatment strategies and their impact on symptoms and prognosis of VTE.
- Describe recommendations for the physical therapy community when symptoms of PTS and CTEPH present themselves.
- Assist clinicians in making appropriate referrals for medical management of long-terms consequences of VTE and risk of recurrence

Although primarily written for physical therapists, other health care professionals should find this CPG helpful in their treatment of patients who are at risk for or have a diagnosed VTE. The CPG can also serve as a reference publication for health care providers, patients, families and caretakers, educators, policy makers, and payers on the best current practice of physical therapist management of patients at risk for and diagnosed with VTE

Background

Deep vein thrombosis is a serious, yet potentially preventable, medical condition that occurs when a thrombus forms in a deep vein, most commonly in the calf, thigh, or pelvis but can occur in veins of the upper extremity. Upper extremity DVT is included in the current update due to the rise in incidence; likely related to the increased use of central venous catheters (CVC), peripherally inserted central catheters (PICC) and cardiac pacemakers.[5] The risk factors for thrombosis formation are best described through Virchow's Triad of vascular stasis, endothelial injury, and/or hypercoagulability.[6] These factors can trigger the coagulation cascade and the formation of a blood clot.[7]

Evidence exists that the coagulation cascade is activated when injury to blood vessels occurs with surgery or other trauma and remains active for at least 5 to 6 weeks.[8-10] It has been shown that 45% to 80% of symptomatic VTE events occur after hospital discharge. Length of prophylaxis medication can vary based on the medical diagnosis. For example, according to the recommendations in the NICE Guidelines on reducing risk of hospital acquired VTE, prescription length for nonsurgical patients should be during periods of inactivity, seven days for acutely ill medical patients and 28 days for elective hip replacement surgery. Yet even if individuals are on anticoagulant medications, the clot can still progress and the process of breaking down the clot may take longer in some individuals. Given this timeline, it is vital that physical therapists in the outpatient setting be diligent in screening for VTE.

A life-threatening, acute complication of DVT is PE. This complication occurs when the clot dislodges, travels through the venous system, through the right heart and causes a blockage in the pulmonary circulatory system. Pulmonary embolism is classified by the American Heart Association based on clinical symptoms and degree of right ventricular involvement as massive, submassive, and non-massive[11] whereas the European Society classifies PE as high, intermediate (low and high intermediate) and low risk.[12] This CPG seeks to help clinicians navigate the diverse presentations and classifications of PE as it relates to clinical decision-making, specifically mobility decisions, for each subgroup of patients with PE.

Beyond the threat of PE and its sequelae, LE DVT may lead to long-term complications of post-thrombotic syndrome. Post-thrombotic syndrome (PTS) develops in 20% to 50% of patients presenting with a LE DVT even when an appropriate anticoagulant is used.[13, 14] The pathophysiology of PTS involves permanent damage to the valves of the veins and reflux of blood in the venous system. This then causes venous hypertension that reduces muscle perfusion, increases tissue permeability and leads to the symptoms of PTS.[15] These symptoms include chronic aching pain, intractable edema, limb heaviness, and leg ulcers.[16] This chronic pathology can cause serious long-term ill health, impaired functional mobility, poor quality of life, and increased costs for the patient and the health care system.[16]

In those who survive PE, significant cardiopulmonary morbidity can occur, most notably chronic thromboembolic pulmonary hypertension, but the incidence of CTEPH is relatively low (approximately 1-2%.[17] The ESC defines CTEPH as a disease caused by persistent obstruction of pulmonary arteries from organized thrombi which ultimately leads to a reduction of blood flow and a remodeling of the pulmonary vascular bed.[18] The clot(s) narrow the lumen of the vessels as does the microvascular remodeling and scarring from chronic inflammation which may lead to pulmonary hypertension and reduced systemic oxygenation.[19-21] Chronically, the vascular tissue becomes fibrotic which causes a fixed mechanical obstruction and results in reduced vascularization and concomitant pulmonary hypertension.[18] Over time, the workload imposed on the right heart increases and contributes to right heart dysfunction and then failure.[12, 16, 17] CTEPH involves symptoms of dyspnea/shortness of breath (especially with exertion), fatigue, swelling of legs, dizziness, fainting, chest tightness with exertion and sometimes palpitations.[12, 16, 19-21]

Across various practice settings, physical therapists encounter patients who are at risk for VTE, may have an undiagnosed UE or LE DVT or PE, or have recently been diagnosed with a UE or LE DVT or PE. The physical therapist's responsibility to every patient is 5-fold: (1) prevention of VTE, (2) assess for UE and LE DVT and PE, (3) contributing to the health care team in making prudent decisions regarding safe mobility for these patients, (4) patient education and shared decision making, and (5) prevention of long-term consequences of PE and DVT. Such decisions should always be made in collaboration with the referring physician and other members of the health care team. It is assumed that such decisions will not be made in isolation and that the physical therapist will communicate with the medical team. Due to the long-standing controversy regarding mobilization versus bed rest following VTE diagnosis and with the development of new anticoagulation medications, the physical therapy community needs evidence-based guidelines to assist in clinical decision making.

Scope of the Guideline

The 2016 VTE CPG used literature from 2003 through 2014 with a focus on prevention of VTE and physical therapy management of those with a lower extremity DVT. The GDG took multiple steps to determine the scope of the revised CPG. Following a presentation of the 2016 CPG at a 2018 national conference, guidance on the current revision was received from attendees who asked for the inclusion of special populations, including pediatrics, and management of pulmonary embolism and upper extremity DVT. In late 2018 the GDG conducted a survey on the 2016 VTE CPG to help guide the revision process. Surveys were sent to members of the following APTA sections/academies: Cardiovascular and Pulmonary, Oncologic, Acute Care, and Orthopedics. The survey was also sent to those who had previously provided the GDG with feedback. Sixty-four responses were received, and the key findings were that the CPG guided clinicians' practice (74.2% agreed and 21% said somewhat guided their practice). Respondents asked for more information on management of pulmonary embolism and upper extremity DVT, how the location of the VTE might affect decision making, exercise prescription and progression for those with VTE, clarification on compression and more guidance when the person is not anticoagulated.

Based on this feedback and the GDG's own analysis of new findings in the literature, including updated CPG addressing VTE by other organizations, and contemporary physical therapy practice, the GDG decided the revised CPG should focus on the following areas: (1) updating the previous key action statements in the 2016 VTE CPG by combining some of the statements as appropriate, (2) inclusion of screening and management of those with pulmonary embolism, (3) inclusion of screening and management of those with UE DVT, (4) provision of more guidance on management of those who are not prescribed anticoagulation and (5) inclusion of adult special populations, but not the pediatric population. Literature from 2015 to February 2021 was reviewed with an emphasis on other CPG, systematic reviews, meta-analyses, and randomized controlled trials.

Statement of Intent

The information in this CPG is written to inform the reader of the best information available at the time of publication. The key action statements are meant to provide guidance, but not mandates on clinical practice. This CPG is not intended to be construed or to serve as a legal standard of care. Each professional needs to use their expertise and experience, combined with the person's values to make decisions about the care plan. Clinicians do not practice in isolation, there needs to be a team approach in determining how a person will be screened for a potential VTE and managed after a diagnosis of a VTE. The information in this CPG should be part of the discussion on a system wide approach to serving these individuals but should not be the only document used.

Methods

The Guideline Development Group (GDG) was composed of physical therapists with special interest in acute care and cardiovascular and pulmonary practice and members of the Academy of Cardiovascular and Pulmonary Physical Therapy, two of whom were involved in the original guideline. This revision of the 2016 CPG includes an updated literature review of LE DVT since the publication date of 2015; as well as, a literature review of pulmonary embolism, upper extremity DVT, and special populations with coagulopathies.

Literature Search

This CPG update is based on the original foundation of physical therapy evidence gathered for the risk assessment, mobilization and treatment of LE DVT published in the 2016 VTE CPG.[4] The current update utilized a search strategy performed by a research librarian to identify new literature discussing LE DVT published between 2015 and 2020 and new search terms for UE DVT, PE, and special populations for all publication dates up to 2020. The current search utilized the following databases: PubMed, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), and the Physiotherapy Evidence Database (PEDro). Controlled vocabularies, such as MeSH and CINAHL headings, were used whenever possible in addition to key words. Results were limited to articles written in English. Case reports and pediatric literature were excluded. The search strategy by key words, MeSH terms, and databases is shown in **Table 2**. Using this search strategy within our appropriate timeline and after eliminating unrelated publications, the GDG initially reviewed 1,559 articles and ultimately sent 24 publications out for review. Most of these were systematic reviews, meta-analysis, and clinical practice guidelines.

Literature Review

The GDG followed the same process for the literature review as the original VTE CPG and the full description of literature review methods can be found the original document.[4] Briefly, the results of the literature and guideline search were distributed to the members of the GDG for appraisal and determination of inclusion in the update. The selected articles then went through an external review process whereby volunteer clinicians and academicians reviewed each article using an approved appraisal tool. Prior to review, reliability of the GDG and appraisers was established through the critical appraisal of test articles to establish interrater reliability. Volunteers qualified to be appraisers with agreement of 90% or more.

Selected articles were randomly paired to appraisers and reviewed by 3 individuals who used 1 of 3 critical appraisal tools: Assessment of Multiple Systematic Review (AMSTAR) tool for systematic reviews, Appraisal of Guidelines for Research and Evaluation (AGREE II) for clinical practice guidelines, and APTA Critical Appraisal Tool for Experimental Intervention Studies (CAT-EI) for intervention studies.

Levels of Evidence and Grades of Recommendations

The GDG followed a previously published process on developing physical therapy CPGs.[22] **Table 3** lists criteria used to determine the level of evidence associated with each practice statement, with level I as the highest level of evidence and level V as the lowest level of evidence. **Table 4** presents the criteria for the grades assigned to each action statement. The grade reflects the overall and highest levels of evidence available to support the action statement. The CPG lists each key action statement followed by rating of level of evidence and grade of the recommendation. Each action statement is also given a status definition to indicate changes made from the 2016 VTE CPG. **Table 5** provides explanations of each of these terms. Under each statement is a summary providing the supporting evidence and clinical interpretation. The statements are organized in **Table 1** according to the action statement number, the statement, and the key phrase or action statement.

Agree II Review

This CPG was evaluated by 3 GDG members using the AGREE II instrument to assess the methodological quality of the guideline. The 3 members scored this guideline as high quality according to the AGREE II tool (Appendix 2, available at ptjournal.apta.org).

External Review Process by Stakeholders

This CPG underwent 2 formal reviews. First, draft reviewers were invited stakeholders representing the American College of Chest Physicians, the European Society of Cardiology, and the National Association of Thrombosis Foundation. The second draft was posted for public comment on the APTA Academy of Cardiovascular & Pulmonary website; and notices were sent via email from the APTA to all members as well as a separate email to Academy of Cardiovascular & Pulmonary Physical Therapy members, literature appraisers, and clinicians who inquired about the CPG during its development.

Document Structure

The action statements organized in **Table 1** are introduced with their assigned recommendation grade, followed by a standardized content outline generated by BRIDGE-Wiz software (http://gem.med.yale.edu/BRIDGE-Wiz/BridgeWizOnLine/).[23] Each statement has a content title, a recommendation in the form of an observable action statement, indicators of the evidence quality, and the strength of the recommendation. The action statement profile describes the benefits, harms, and costs associated with the recommendation; a delineation of the assumptions or judgments made by the GDG in formatting the recommendation; reasons for any intentional vagueness in the recommendation; and a summary and clinical interpretation of the evidence supporting the recommendation. Each member of the GDG reviewed the supporting evidence for each key action statement.

Action Statement 1: Advocate for a Culture of Mobility and Physical Activity

Advocate for a culture of mobility and physical activity in all practice settings unless medical contraindications for mobility exist. (Evidence Quality I; Recommendation Strength: A – Strong)

Action Statement Profile

Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports rec
Status Definition: Reaffirmed, no new evidence
Aggregate Evidence Quality: Level I evidence based on the number of other CPG and systematic reviews that promote mobility as a preventive measure to decrease risk of VTE.
Benefits: Activity decreases likelihood of VTE
Risk, Harm Cost: Mobility could lead to a musculoskeletal injury or in rare incidences a cardiovascular event. Overreliance on activity could lead to an under prescription of pharmacological prophylaxis.
Benefit-Harm Assessment: Preponderance of Benefit
Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.
Intentional Vagueness: The exact amount of physical activity needed to lower VTE risk is not defined.

Role of Person/Patient Preferences: The individual should be educated regarding the benefits of mobility and encouraged to maintain mobility as much as possible to decrease the risk of adverse outcomes.
Exclusions: None
Quality Improvement: Implementation of an early mobilization program and promotion of activity can reduce the likelihood of VTE.
Implementation and Audit: Written, face to face, and electronic educational tools should be used to encourage physical activity.

Supporting Evidence and Clinical Interpretation:
Since the publication of the first CPG, the recommendations on mobility have not changed with further support published. The 2019 National Institute for Health and Care Excellence (NICE) Guidelines on reducing risk of hospital acquired VTE continue to support mobility and education on mobility as a preventive strategy.[24] Following surgical treatment, patients should be encouraged to mobilize as soon as possible and physical activity should be promoted as a way to reduce VTE both during hospitalization and after discharge from the hospital.[24] A 2020 systematic review found that ambulation decreased the rate of VTE in hospitalized patients, but acknowledged difference in how ambulation and mobility are defined and mixed results on the effectiveness of ambulation in in higher quality studies.[25] A 2016 quality improvement project found a progressive mobility protocol in the ICU reduced the incidence of VTE from 21% pre-protocol to 7.5% after implementation.[26] The study used a model where an individual is challenged to reach higher levels of mobility as they recover instead of aiming for a universal level or minimum threshold of activity. Based on these studies and recommendations, mobility continues to be viewed a way to decrease the risk of VTE.

While mobility has benefits, prophylaxis medication still has an important role in preventing VTE. In a systematic review of nine studies, 20,000 hospitalized patients, prophylaxis reduced the rate of symptomatic VTE in at-risk hospitalized medical patients without increasing major bleeding.[27] Best results are found when medication is combined with mobility. In a combined medication and ambulation study with over 800 adult acutely ill patients admitted to the hospital in which ambulation was indicated for VTE prevention, the incidence of VTE was significantly lower when patients received enoxaparin in comparison to a placebo medication.[28] The importance of combining medication with activity for hospitalized patients is also stressed in a 2020 systematic review.[25]

Based on the evidence in the 2016 CPG and a search for new literature, physical therapists should continue to advocate for a culture of mobility and activity across all practice settings. As movement specialists, physical therapists need to confront any unnecessary bedrest or forced immobility and promote activity. Mobility should be encouraged in patients while in the hospital and in the community to prevent the complications associated with immobility. Physical therapists should acknowledge differences in how immobility is defined[29] and that the exact amount of mobility needed to decrease the risk of VTE remains unknown.

Action Statements 2: Assess for Risk of VTE with reduced mobility.

During initial interview and physical examination assess risk of VTE in patients with reduced mobility (Evidence Quality: I; Recommendation Strength: A - Strong)

Action Statement Profile:

Level of Evidence Quality (I-V): Level I - High quality studies (> 50% of criteria)

Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports recommendation

Status Definition: Reaffirmed and updated

Aggregate Evidence Quality: Level I evidence based on the number of other CPGs and systematic reviews supporting the use of RAMs to assess risk.

Benefits: Risk assessment can guide prescription of preventive measures

Risk, Harm, and Cost: None.

Benefit-Harm Assessment: Preponderance of benefit over harm

Value Judgments: There are other tools to assess risk that may be preferred by other interprofessional teams.

Intentional Vagueness: None

Role of Patient Preferences: Some individuals may decline follow up screening or preventive interventions.

Exclusions: None

Quality Improvement: Implementation of risk assessment for VTE into the initial PT examination will improve patient care by identifying those patients that would benefit from additional information on risk mitigation, such as hydration and the benefit of mobility.

Implementation and Audit: Healthcare systems can implement risk assessment models across their system.

Supporting Evidence and Clinical Interpretation:

As stated in the original VTE CPG, the physical therapy examination includes comprehensive screening and specific testing leading to diagnostic classification or, as appropriate, a referral to another practitioner.[30] In the case of VTE, understanding the factors that place individuals at risk for a VTE allows a thorough review of medical history and specific questioning in the patient interview to determine risk level. Risk factors include previous venous thrombosis or embolism, increasing age, active cancer or cancer treatment, severe infection, estrogen-containing oral contraceptives, hormonal replacement therapy, pregnancy or given birth within the previous 6 weeks, immobility (bed rest, flight travel, fractures), surgery, anesthesia, critical care admission, central venous catheters, inherited thrombophilia, and obesity.[31] The relationship between particular risk factors and presence of VTE has been found through retrospective and prospective studies and identified as having support from level I evidence in systematic reviews and CPGs.[24, 32-36]

The NICE guidelines on VTE states all patients should be assessed for risk of VTE using a standardized tool.[24] Risk assessment models (RAM) use a checklist to determine whether risk factors for VTE are present and each risk factor is assigned a point value. If a set point level is reached, the patient is considered at an increased risk, and prophylactic interventions can be used. The original VTE CPG provided a number of

examples of RAMs including Department of Health VTE risk assessment tool,[24] IMPROVE VTE RAM,[37] the Autar DVT Risk Assessment Scale,[38] and the Geneva Risk Score[39] but did not recommend a single one. In the current update, the CPG committee has agreed on recommendations for specific RAM usage.

The Padua Prediction Score (PPS; **Table 6**) is favored for VTE risk assessment of all hospitalized patients based on recommendation in the American College of Chest Physicians (ACCP) guidelines.[33] The PPS is recommended because it includes minimal time to implement while still providing the best available risk assessment of hospitalized patients.[36] In this RAM, points are assigned to baseline features increasing the patient's risk of VTE categorizing a patient as either high (≥ 4 points) or low risk (< 4 points) of VTE.[40] The Padua Prediction Score has been validated in non-ambulatory patients and is appropriate for use with hospitalized patients. The risk of VTE when a patient is ambulatory is so low that it may not be appropriate to utilize a RAM in an outpatient setting without additional factors that raise their personal risk (see **Action Statement 3**).

Another RAM for therapists to consider is the Caprini score. The Caprini score is the most validated for a wide range of patients and considers a much longer list of predisposing conditions contributing to the risk of VTE.[41] There are 38 individual risk factors assigned between 1 to 5 points based on the likelihood of an individual factor to contribute to VTE. A final score of ≥ 10 points identifies a patient as high risk and ≤ 9 is considered low risk.[42] While this model may be cumbersome due to its length, the Caprini score has been validated as a patient-completed questionnaire which provides an excellent risk assessment tool in settings where patients are able to independently complete the questionnaire.[42, 43] Due to its length, the full Caprini model is not listed in this document. The tool can be found here: https://www.isms.org/dvt/.

In summary, given the risks and harms associated with a VTE and the relationship of VTE incidence to the presence of risk factors, physical therapists should assess risk of VTE in patient populations with reduced mobility. Physical therapists should utilize the recommended RAMs for risk assessment, unless another RAM is currently utilized with their health care system. It is important to use the agreed upon tool if one is already established within your institution to effectively communicate risk among the health care team.

Action Statement 3: Assess for Additional Risk Factors of VTE in all High-Risk Patients.

When a patient presents with conditions (i.e. cancer or inherited clotting disorder) that independently increase VTE risk, therapists should have a high index of suspicion for VTE and assess for additional risk factors. (Evidence Quality: I; Recommendation Strength: B - Moderate)

Action Statement Profile:

Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): B, Moderate - A preponderance of level II studies but at least 1 level I study
Status Definition: New; not in prior version
Aggregate Evidence Quality: Level I evidence including the ACCP guidelines and multiple systematic reviews validating that the conditions discussed in this section (except for COVID-19) have increased risk of VTE. Systematic reviews to support the use of the Khorana score for patients with cancer.

Benefits: Risk assessment can guide prescription of preventive measures
Risk, Harm Cost: None
Benefit-Harm Assessment: Preponderance of benefit
Value Judgments: There are other tools to evaluate risk that may be preferred by other interprofessional teams.
Intentional Vagueness: None
Role of Person/Patient Preferences: Some individuals may decline follow up screening or preventive interventions.
Exclusions: None
Quality Improvement: More comprehensive evaluation practices. Implementation of risk assessment for VTE into the initial PT examination for those with heightened risk of VTE will improve patient care by identifying those patients that would benefit from additional information on risk mitigation. Heightened awareness of the increased risk of VTE in these patient populations may allow a lower threshold of possible symptoms to elicit VTE screening.
Implementation and Audit: Healthcare systems can implement risk assessment models across their system. The Khorana RAM is published in this document (**Table 7**) and available in online calculator formats (i.e. https://www.mdcalc.com/khorana-risk-score-venous-thromboembolism-cancer-patients)

Supporting Evidence and Clinical Interpretation:
All patients with reduced mobility should be assessed for VTE risk during the initial interview and evaluation, but there are certain groups of patients (i.e. active cancer, thrombophillic conditions) that require additional discussion due to a higher occurrence of VTE.[35] People with an active form of cancer carry a four to eight times greater risk of developing a VTE than someone without cancer.[36, 44, 45] Furthermore, VTE remains the second leading cause of death for patients with cancer.[46] The overall prevalence of incidental PE is 5% for patients with cancer[47] and half of those with PEs are diagnosed from routine imaging.[48] Despite many patients receiving anticoagulants (89% on low molecular weight heparin; LMWH), the incidence of recurrent VTE at 12 months was 6.4% for patients with cancer.[49]

Depending on the type of cancer, disease progression, treatment provided, and patient status, the incidence of developing a VTE varies significantly, with rates ranging from 0.5% to as high as 20%.[44, 47, 49] Solid tumors and hematologic malignancies have the highest incidence of VTE, followed by lung and gastrointestinal cancers.[50, 51] Cancer treatment including chemotherapy and erythropoiesis-stimulating agents increase the risk of VTE.[36] The delivery of these treatments, including the use of indwelling central venous catheters, can further compound a patient's risk profile.[36, 51]

The Padua Prediction Score, recommended as the risk assessment model in **Action Statement 2** of this document, does account for the heightened risk of cancer conditions in its scoring system; however the Khorana risk stratification tool was developed in 2009 to identify high risk individuals within this group.[52] The Khorana score, shown in **Table 7**, allocates points based on five clinical and pre-chemotherapy laboratory values: primary tumor site, platelet count, hemoglobin concentration or the use of erythropoiesis-stimulating agents, leukocyte count, and BMI.[52, 53] Based on points accumulated, patients are put into a low risk, intermediate risk, or high risk. The Khorana score has been validated to identify

high risk ambulatory cancer patients in order to facilitate the initiation of thromboprophylaxis. Despite this validation, a 2019 systematic review and meta-analysis including data on >34,000 patients reports only 23.4% of the patients that developed a VTE were in the high-risk group.[53] This shows that while this score helps to identify those at the highest risk, individuals in the intermediate and low risk still require extra attention given the high rates of VTE in this patient population.

In addition to patients with cancer, there are other groups of patients that carry increased risk of VTE including inherited protein deficiencies (i.e. antithrombin, factor V Leiden, and others) and acquired thrombophilia (i.e. antiphospholipid syndrome).[31, 36] Factor V Leiden mutation, for example, is present in 5% of the population and carries a 3- to 8-fold increased risk of VTE.[50] While these groups are also represented in the Padua Prediction Score, this guideline does not have an additional risk assessment tool to specifically assess the risk of VTE in these patients. This information is presented here to highlight the need for heightened scrutiny for the signs and symptoms of VTE in patients with conditions causing coagulopathies. Patients that fall into this category may benefit from additional time spent on preventative measures (see **Action Statement 4**) and have a lower threshold of suspicion required for use of a VTE likelihood tool (see **Action Statements 5, 6, and 7**).

Finally, the coronavirus disease of 2019 (COVID-19) is a novel, inflammatory condition not accounted for in previously validated risk assessment models because it was not a clinical condition at the time of their development. COVID-19 patients have an increased risk of VTE (most commonly as a PE)[54] likely due to the cytokine storm from a hyperactive immune response and profound systemic inflammation.[55-57] Even with the use of prophylactic anticoagulation, VTE has been reported in 27% of patients hospitalized with severe COVID-19.[58] In addition, the risk of PE in hospitalized patients with COVID-19 has been reported to be more than double compared to patients in the ICU with influenza.[59] Given the extremely high risk, physical therapists should advocate for early mobility and physical activity unless medical contraindications for mobility exists. As mentioned above for the other patient groups at high risk of VTE, physical therapists should be cognizant of the risk and prioritize routine screening for signs and symptoms of VTE in patients suffering and recovering from COVID-19.[54]

While most of this CPG has excluded the pediatric population, it is important to note that COVID-19 can lead to endothelial injury and hypercoagulability in children, placing them at risk for VTE [60, 61]. Though multiple agencies have published guidelines on recommendations for anticoagulant use with COVID-19, there is a resultant post-infectious immune dysregulation called Multi-System Inflammatory Syndrome in Children (MIS-C) that further places children at risk for VTE. MIS-C cases can occur weeks after a patient tests positive for COVID-19. Children with MIS-C have activation of hypercoagulation, widespread inflammation, and multi-system organ dysfunction.[62] Hispanic and African American children under the age of 21 are at highest risk, with most cases falling between the ages of 3-12 years old.[63] MIS-C should be managed in an intensive care unit as deterioration of medical status can occur rapidly. Initial signs and symptoms of MIS-C are similar to Kawasaki Disease and can progress to myocarditis, cardiogenic shock, toxic shock syndrome, and macrophage activation syndrome.[64] Physical therapists should be aware of the risk factors for VTE in children who have COVID-19 and those at risk for developing MIS-C.

Action Statement 4: Provide Preventive Measures for Those Who are High Risk for VTE.
When a patient is identified as high risk for VTE, provide preventive measures including education on the signs and symptoms of VTE, activity, hydration, mechanical compression and referral for medical treatment. (Evidence Quality: I; Recommendation Strength: B - Moderate)

Action Statement Profile:
Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports rec
Status Definition: Revised and updated -
Aggregate Evidence Quality: Level I evidence based on the number of other CPG stress the importance education in the prevention of VTE.
Benefits: Preventive measures can decrease rate of VTE
Risk, Harm Cost: Small risk of adverse effects from interventions
Benefit-Harm Assessment: Preponderance of Benefit
Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.
Intentional Vagueness: Specifics on medications are not provided in these guidelines because the selection can be population specific and prescription is outside the physical therapist's scope of practice.
Role of Person/Patient Preferences: Some individuals may choose to decline preventive measures or discontinue measures.
Exclusions: None
Quality Improvement: Preventive actions can reduce the likelihood of VTE.
Implementation and Audit: Systems can be developed to provide preventive care at hospital admission and discharge and during physical therapy management outside of the hospital setting.

Supporting Evidence and Clinical Interpretation:
This key action statement maintains the same level of evidence and strength with additional support from other updated CPGs. In the updated ACCP Guidelines[33] there were no changes from their 2012[65] recommendation on prevention. The 2018 NICE Guideline[66] established guidance on reducing the risk of hospital acquired VTE that was then updated again in 2019.[24] They added statements on the importance of providing education on admission and discharge to patients and family members about correct use of anti-embolism stockings, compression, risks and possible consequences of VTE, possible prophylaxis side effects, and how people can reduce their risk of VTE through hydration, exercise, and mobility. These guidelines also provide additional information on recommendations for prophylactic medications and specific recommendations for some special populations such as people with cancer, CAD, renal impairment, and undergoing orthopedic procedures.

The 2016 VTE CPG included a separate key action statement that physical therapists should recommend mechanical compression for individuals at a high risk for VTE. This statement was combined with the overall statement on preventive measures. Since the 2016 guidelines, the 2019 NICE Guidelines state that anti-embolism stockings and/or intermittent pneumatic compression are recommended for those hospitalized and at an increased risk of VTE, especially those who are immobile. The guidelines also

provide reasons to stop wearing stockings such as blistering, pain, and when mobility is no longer significantly reduced. The guidelines stress the prescription of the correct size of stocking to maintain appropriate pressures. Given the evidence reviewed in the original 2016 CPG and the additional evidence included in the 2019 NICE Guideline, compression therapy, either through stockings or intermittent pneumatic compression, should continue to be recommended as part of the preventive plan for those at high risk for VTE.[24]

For individuals who are at risk for VTE, preventive measures should be initiated immediately, including education regarding leg exercises, ambulation, proper hydration, mechanical compression, and assessment regarding the need for medication referral. Physical therapists can play a large role in providing and reinforcing these preventive measures.

Action Statement 5: Establish Likelihood of LE DVT When a Patient Presents with Symptoms.
Establish the likelihood of a LE DVT if the patient presents with pain, tenderness, swelling, warmth and/or discoloration in the lower extremity and take appropriate action based on results.
(Evidence Quality I; Recommendation Strength: A – Strong)

Action Statement Profile:
Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports rec
Status Definition: Reaffirmed; no new evidence
Aggregate Evidence Quality: Level I evidence based on the recommendation of the Wells criteria in the ACCP guidelines and high-quality cohort studies.
Benefits: Lead to early intervention for LE DVT and decrease risk of adverse effects. DVT.
Risk, Harm Cost: Assessment can lead to additional diagnostic tests and the prescription of interventions that have some risk for adverse side effects.
Benefit-Harm Assessment: Preponderance of benefit over harm.
Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.
Intentional Vagueness: None
Role of Person/Patient Preferences: Some individuals may decline further medical testing.
Exclusions: None
Quality Improvement: Assist the physical therapist in a more accurate screening tool for appropriate referral.
Implementation and Audit: Healthcare systems can implement likelihood assessment tools across their system. The screening tool is published in this document (**Table 8**) and available in online calculator formats (i.e. https://www.mdcalc.com/wells-criteria-dvt)

Supporting Evidence and Clinical Interpretation:
The recommendation for screening of LE DVT has not changed from the original VTE CPG published in 2016.[4] There has been no new level I studies on clinical probability tools used to identify patients with LE DVT. It continues to be true that the presence of signs and symptoms of LE DVT including pitting edema,

pain, tenderness, swelling, warmth, redness or discoloration of superficial veins should raise suspicion of LE DVT but are insufficient for diagnosis.[67-69] The ACCP Guidelines[68] recommend the use of a standardized tool to take the clinical features indicative of LE DVT and determine the likelihood of the VTE and the Wells criteria continues to be the most well-studied prediction tool.[68, 70-72] For these reasons, the GDG recommends the use of the Wells criteria **(Table 8)** as the standardized tool for physical therapists to use during their examination process when signs and symptoms of VTE are present. The Wells criteria score combines clinical symptoms of DVT with risk factors to stratify the patients into DVT likely or DVT unlikely.[68] This process helps to ensure that diagnostic tests are ordered when appropriate and seeks to limit the cost and complications of unnecessary tests. The results of the assessment should then be communicated to the medical team. **Figure 1** diagrams the decision tree to follow when a therapist encounters signs and symptoms of a DVT.

There are other clinical prediction tools published, including the Oudega rule designed for the needs of the primary care provider. There has been no other tool developed that has been shown to be more effective when compared to the Wells Criteria score.[72, 73] The I-DVT has recently been developed as a simplified likelihood tool including only 4 of the clinical features from the original Wells score. While initial studies show similar diagnostic accuracy, larger studies are required before this tool could be recommended above the Wells criteria.[74]

Based on the evidence procured in the 2016 VTE CPG and a thorough review of the current body of literature, the Wells criteria for LE DVT continues to be the most reliable at determining likelihood of LE DVT across patient populations and practice settings. The current CPG maintains the original recommendation for physical therapists to use the Wells criteria in their clinical practice, to advocate for its use with their interdisciplinary team, and communicate the results appropriately to facilitate the diagnosis of LE DVT.

Action Statement 6: Establish the Likelihood of UE DVT When Patient Presents with Symptoms.
Establish the likelihood of UE DVT if patients present with clinical symptoms including swelling, pain, edema, cyanosis and/or dilation of superficial veins and take appropriate action based on results.
(Evidence Quality II; Recommendation Strength: B – Moderate))

Action Statement Profile:
Level of Evidence (I-V): Level II - Lesser quality study due low critical appraisal score of systematic review
Recommended Grades (A-R): B, Moderate - at least one level I cohort study on topic supports recommendation
Status Definition: New; not in prior version
Aggregate Evidence Quality: Level II based on a high-quality cohort study and a lower quality systematic review.
Benefits: Lead to early intervention for UE DVT and decrease risk of adverse effects.
Risk, Harm Cost: Assessment can lead to additional diagnostic tests and the prescription of interventions that have some risk for adverse side effects

Benefit-Harm Assessment: Preponderance of benefit over harm
Value Judgments: There are other tools to evaluate likelihood that may be preferred by other interprofessional teams.
Intentional Vagueness: None
Role of Person/Patient Preferences: Some individuals may decline further medical testing.
Exclusions: None
Quality Improvement: Assist the physical therapist in a more accurate screening tool for appropriate referral.
Implementation and Audit: Healthcare systems can implement likelihood assessment tools across their system. The screening tool is published in this document (**Figure 2**).

Supporting Evidence and Clinical Interpretation:
Deep vein thrombosis of the upper extremity can develop in any of the deep veins of the upper extremity including both proximal (i.e. subclavian, axillary) and distal (i.e. brachial, ulnar and radial) veins.[5] Historically, upper extremity DVT are less common than lower extremity DVT, but the prevalence is increasing related to the frequent use of indwelling central venous catheters.[5] In addition, the coagulopathies associated with active cancer contribute to the increased incidence with a diagnosis of cancer found in approximately 40% of patients with UE DVT.[75] Similar to LE DVT, a DVT in the upper extremity carries the risk of traveling to the lungs. Constans et al reports approximately 20% of patients diagnosed with UE DVT are complicated by pulmonary embolism.[75] In addition to the acute risk of PE, approximately 25% of patients with upper extremity DVT will develop post-thrombotic syndrome.[75] The major signs and symptoms of UE DVT are due to the venous congestion and include swelling, pain, edema, cyanosis, and dilation of superficial veins.[5] These clinical signs are not always present and many cases (33% to 60%) of UE DVT are asymptomatic and can go undetected.[5]

When physical therapists encounter clinical evidence of UE DVT, there is a clinical scoring system developed by Constans et al to calculate the overall likelihood of UE DVT from four points of evidence: presence of central venous catheter or pacemaker, localized pain, unilateral edema, and whether another diagnosis is at least plausible (**Figure 2**).[76] Kleinjan et al added determination of D-dimers to increase the negative predictive accuracy of an "unlikely" categorization by Constans criteria. In a multi-center prospective cohort study, 87 out of 406 patients with suspected UE DVT were categorized as "UE DVT unlikely" by Constans criteria with D-dimer testing and there were no incidence of UE DVT during the 3 months of follow-up in this cohort.[77] **Figure 1** diagrams the decision tree to follow when a therapist encounters signs and symptoms of an UE DVT.

If UE DVT is suspected, the patient will require further diagnosis testing for accurate diagnosis. Currently, contrast medium enhanced ultrasonography is recommended with compression sonography due to the high sensitivity (97%) and specificity (96%) in detecting UE DVT in the distal veins. The anatomic positioning of proximal veins may limit accessibility for compression ultrasonography requiring contrast-enhanced computed tomography (CT) or magnetic resonance phlebography for accurate diagnosis.[5]

For these reasons, the GDG recommends the utilization of Constans criteria with D-dimer to assess likelihood of UE DVT. If Constans Criteria determines UE DVT to be unlikely and D-dimer is < 500 µg/L, physical therapists should feel confident that a UE DVT is largely excluded. However, if the D-dimer is > 500 µg/L then sonography should be performed. If the Constans criteria indicates that an UE DVT is likely, the D-dimer should be skipped and sonography should be performed prior to mobility.

Action Statement 7: Establish the Likelihood of PE When a Patient Presents with Symptoms.
When a patient presents with dyspnea, chest pain, presyncope or syncope, and/or hemoptysis, evaluate the likelihood of PE and take appropriate action based on results.
(Evidence Quality I; Recommendation Strength: A – Strong)

Action Statement Profile:
Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports recommendation.
Status Definition: New; not in prior version
Aggregate Evidence Quality: Level I evidence based on multiple systematic reviews and the ESC guidelines.
Benefits: Lead to early intervention for PE and decrease risk of adverse effects.
Risk, Harm Cost: Assessment can lead to additional diagnostic tests and the prescription of interventions that have some risk for adverse side effects.
Benefit-Harm Assessment: Preponderance of benefit over harm
Value Judgments: There are other tools to evaluate likelihood that may be preferred by other interprofessional teams.
Intentional Vagueness: None
Role of Person/Patient Preferences: There are other tools to evaluate likelihood that may be preferred by other interprofessional teams.
Exclusions: None
Quality Improvement: Assist the physical therapist in a more accurate screening tool for appropriate referral.
Implementation and Audit: Healthcare systems can implement likelihood assessment tools across their system. The screening tool is published in this document (**Table 9**) and available in online calculator formats (i.e. https://www.mdcalc.com/geneva-score-revised-pulmonary-embolism).

Supporting Evidence and Clinical Interpretation:
The clinical presentation of pulmonary embolism can be evasive because the symptoms can be variable and non-specific, but accurate diagnosis is critical given the risk of death.[12] Long et al reported mortality rates of missed, untreated PE as high as 26%.[78] The most common symptoms of acute PE include dyspnea, chest pain, pre-syncope or syncope, or hemoptysis.[12, 79, 80] The presence of these symptoms should raise the suspicion of PE especially when they occur in conjunction with known risk factors such as surgery, trauma, immobility, cancer, and hormone therapy.[79]

Assessment of PE likelihood allows symptomatic patients to be categorized by the probability of an actual, confirmed PE. Historically, clinical judgement was the primary approach to assessing the probability of PE in patients presenting with symptoms.[12, 81] Despite reports of the accuracy of implicit clinician opinion, this process lacks standardization leading to the development of clinical prediction rules for PE.[81, 82] Clinical prediction rules allow clinicians to determine pretest probability of PE, but these scores do not diagnose or rule in the condition alone. A high probability of PE determined by a clinician requires imaging (i.e. computed tomographic pulmonary angiography) to confirm PE.[83]

There are several clinical prediction rules that have been utilized and validated to determine the probably of PE including Wells score, Geneva score, YEARS rule, Miniati score, and Charlotte rule.[84, 85] The 2019 European Society of Cardiology (ESC) Guidelines for the Diagnosis and Management of Acute Pulmonary Embolism states that the Wells Criteria for Pulmonary Embolism and revised Geneva score are the most frequently used and share similar effectiveness for identifying high risk individuals. Despite their common effectiveness, the Wells score includes the subjective assessment of whether or not an alternative diagnosis is more likely than PE. The Geneva score lacks this subjective element and relies only on objective and reproducible findings making it the recommended prediction rule of the GDG.[12]

The revised Geneva score used 8 weighted variables representing either risk or clinical evidence of VTE to identify patients as low probability, intermediate probability, or high probability **(Table 9)**. Individually weighted variables can cause miscalculation and difficulty in the clinical application leading to the development of the revised Geneva score with each variable weighted equally (1 point per variable). The revised Geneva score identifies low probability of PE as 0 – 1 point, intermediate probability as 2 – 4 points, and high probability as ≥ 5 points. In two large prospective diagnostic trials of 1049 patients, confirmed PE was found in 7% of the 378 low-probability patients, 29.4% of the 629 intermediate-probability patients and 64.3% of the 42 high-probability patients. The revised Geneva score improved the clinical utility and, despite its simplification of scoring, maintained the diagnostic accuracy of the original score.[86, 87] From these data, they concluded that the revised Geneva score can safely rule out PE when combined with a normal D-dimer test.

The Pulmonary Embolism Rule-out Criteria (PERC) was developed originally for emergency room patients to quickly rule out PE to avoid unnecessary diagnostic testing.[88] The PERC utilizes eight clinical features highly associated with the absence of PE including age < 50 years, pulse < 100 bpm, SaO_2 > 94%, no unilateral leg swelling, no hemoptysis, no recent trauma or surgery, no history of VTE, and no oral hormone use.[12, 89] When all eight of these clinical variables are negative, the pretest probability of PE becomes so low that PE can be ruled out and no additional tests are needed.[89] Physical therapists who find themselves questioning the possibility of a PE in a patient categorized as low probability should utilize the PERC rule to safely exclude the possibility of PE.

The effective implementation of clinical prediction rules reduces the need for expensive and invasive diagnostic imaging procedures and can assist the physical therapist in clinical decision-making to facilitate the continued implementation of physical therapy services.[12, 87] For these reasons, the GDG recommends

the use of a standardized screening tool. While both the Wells score and the revised Geneva score are useful tools, the GDG recommends the use of the revised Geneva score which lacks the subjectivity of the Wells score to assess the probability of PE when signs and symptoms are observed. Physical therapists should advocate for its use with their interdisciplinary team and determine the best way to communicate the results and risks.

Action Statement 8: Assess Medical Intervention

When a patient presents with a recently diagnosed provoked or unprovoked VTE, assess medical intervention.

(Evidence Quality: V; Recommendation Strength: P – Best Practice)

Level of Evidence (I-V): V - Expert opinion
Recommended Grades (A-R): P, Best Practice - Current clinical practice norms
Status Definition: New; not in prior version
Aggregate Evidence Quality: Level V based on the expert opinion of the GDG and standard practice in the clinical setting. No studies exist that address this specific action statement.
Benefits: Provides therapists with information on actions of the medical team to enhance decision making on safe mobilization by the physical therapist.
Risk, Harm Cost: No risk, harm or cost in assessing medical intervention
Benefit-Harm Assessment: Preponderance of Benefit
Value Judgments: None
Intentional Vagueness: Specific guidance on physical therapy management for each intervention is not provided. Numerous factors beyond medical intervention will affect patient management.
Role of Person/Patient Preferences: None
Exclusions: None
Quality Improvement: Confirming medical intervention will improve the interprofessional health team communication, improve patient safety, and provide the physical therapist with guidance on when it is appropriate to begin physical therapy management.
Implementation and Audit: A review of medical interventions should be a standard part of physical therapy management.

Supporting Evidence and Clinical Interpretation:

Following the diagnosis of a VTE, there are multiple medical interventions that can address the clot and decrease the risk of further complications. This action statement provides a summary of basic medical interventions to ensure therapists review and consider the intervention after the diagnosis of a VTE. The evidence of one intervention over another will not be shared here but can be found in the references used throughout this statement.

The primary pharmacological intervention for a VTE is the prescription of anticoagulants. They are recommended for proximal and in some cases distal LE DVT.[33] They are also commonly prescribed for UE DVT and PE.[18, 33, 90, 91] Anticoagulants help lower the risk of future clots and can stop the growth of the present thrombus. The specific medication, delivery method, therapeutic levels, and therapy

considerations including mobilization are described in **Action Statement 9**. Systemic thrombolytic therapy can also be used to actively break down the clots. Thrombolytics carry greater risk for bleeding and tend to be used in life threatening situations such when hypotension is present during a massive pulmonary embolism.[33]

Catheter-directed thrombolysis involves using a catheter placed in the vessel to administer a thrombolytic agent at the site of the clot. It is not the first consideration for a DVT but can be an option for those at higher risk for PTS.[33] It can also be used with an UE DVT or PE when severe symptoms are present.[18, 91] Catheter-based thrombus removal can also be used to aspirate or fragment the clot. When a life-threatening PE is present, surgical embolectomy with cardiopulmonary bypass can be an option.[18, 33] If the person shows signs of right ventricular failure, mechanical ventilation, ECMO, volume optimization, vasopressors, and inotropes may be needed.

If a person cannot be on certain medications, placement of an inferior vena cava (IVC) filter can be used to capture clots and limit their ability to travel to the heart, lungs and brain. The clot stays in the filter until the body is able to break it down. IVC filters are not typically recommended, but might be used in unique situations.[18] More details on IVC filters and mobilization are in **Action Statement 13**.

In summary, it is key for the physical therapist to take the time to review medical interventions used or planned after the diagnosis of a VTE. The intervention will provide guidance on when physical therapy can be initiated with individuals and provide insight into the severity of the VTE.

Action Statement 9: Confirm Pharmacological Management

With a recently diagnosed VTE treated pharmacologically, confirm medication class and date/time initiated prior to mobilizing the patient. (Evidence Quality IV; Recommendation Strength: D – theoretical/foundational)

Action Statement Profile

Level of Evidence (I-V): IV
Recommended Grades (A-R): D– (theoretical/foundational)
Status Definition: Revised and updated
Aggregate Evidence Quality: Level IV evidence based on lack of evidence other than case studies and manufacturers' information which is based upon evidence from therapeutic range of medications.
Benefits: Provides therapists with information on actions of the medical team to enhance decision making on safe mobilization by the physical therapist.
Risk, Harm Cost: No risk, harm or cost in confirming medical intervention.
Benefit-Harm Assessment: Preponderance of Benefit over Harm.
Value Judgments: The GDG recommends following FDA approved drug-label recommendations regarding time to achieve therapeutic levels
Intentional Vagueness: None
Role of Person/Patient Preferences: None

Exclusions: None
Quality Improvement: Identifying an individual's medication used for anticoagulation and the time to achieve therapeutic effectiveness can decrease the bedrest time following a VTE and provide guidance for mobility.
Implementation and Audit: Algorithms in the CPG can be used as a platform to develop institutional-based mobility protocols between therapists and other departments (see **Figures 1 and 3**).

Supporting Evidence and Clinical Interpretation:
When a patient is diagnosed with an UE or LE DVT, there is a risk of developing a PE when treatment has not been initiated; therefore, mobility is not indicated unless a medical intervention to reduce the chance of emboli traveling to the lungs is initiated. Medical interventions for an existing DVT include anticoagulation (**Action Statements 10 & 11**), or IVC filter (**Action Statement 13**). According to the American College of Chest Physicians Guidelines on Antithrombotic Therapy, anticoagulation is the main intervention unless the patient is at a high risk of bleeding which would be the primary contraindication to anticoagulation.[33] Anticoagulation should be initiated as soon as possible.[24, 33, 92-95]

Anticoagulants are the primary defense used to prevent and treat a VTE by suppressing the function of various circulating clotting factors. They are used to prevent the formation of thrombi and the enlargement of a clot that is circulating in the blood.[96-98] Anticoagulants do not actively degrade the clot, but rather allow the body's natural clot lysis mechanisms to break down the thrombus. For example, LMWH has been shown to stabilize an existing clot and resolve symptoms through the drug's anti-inflammatory properties, making a clot less likely to migrate as an embolus.[96-98]

Therefore, prior to initiating mobility out of bed, a physical therapist should review all medications each patient is prescribed. In addition to consulting with the medical team regarding appropriateness of mobility, PTs should verify if a patient is taking an anticoagulant prior to mobilization. There are multiple anticoagulant medications available and drug choice may be dependent upon the patient's renal function and risk of bleeding. Although PTs do not play a role in recommending the anticoagulant of choice, PTs should initiate mobility when the anticoagulant that is prescribed has achieved therapeutic level based on the time since initiation.[42]

The current options for anticoagulation include unfractionated heparin (UFH), LMWH, direct oral Xa inhibitors (DOACs), Fondaparinux (Arixtra; an indirect inhibitor of factor Xa), and warfarin (Coumadin; which is a vitamin K antagonist) (See **Table 10**).[96] Individuals should continue with their anticoagulant for 3-6 months following the first episode of diagnosed thrombosis.[18, 24, 33] LMWH or DOACs are the primary choice of anticoagulation by physicians for treatment of DVT in the outpatient or home setting due to ease of use and low incidence of side effects.[93, 94, 99] Due to the fact LMWH is excreted primarily by the kidneys, increased bleeding complications have been reported when LMWH is used in patients with renal insufficiency and other populations.

PTs should also observe for signs of increased bleeding or bruising in patients who are taking anticoagulants, as well as risk stratify patients for bleeding complications utilizing the HAS-BLED bleeding

score.[100] Risk of bleeding complications decreases after 6 months of taking an anticoagulant. The 2018 National Institute for Health and Care Excellence (NICE) VTE guideline[66] recommends using the HAS-BLED score to assess the risk of major bleeding in people on anticoagulation for unprovoked proximal DVT or PE, and advises stopping anticoagulation if the HAS-BLED score is 4 or more and cannot be modified. These risk factors include, among others, thrombocytopenia or concomitant use of antiplatelet agents; anemia; concomitant treatment with nonsteroidal anti-inflammatory drugs; hypertension; and poor adherence to the prescribed anticoagulant regimen or poor INR control (on VKA treatment).[101]

Unfractionated heparin is indicated for individuals with high bleeding risk (see **Table 10**) and/or renal disease who are hospitalized as it is a slower anticoagulant with a shorter half-life.[102] The initial dose of heparin is particularly critical when heparin is administered by subcutaneous (SC) injection, because an adequate anticoagulant response is not achieved in the first 24 hours unless a high starting dose is used.[102] Therapeutic heparin levels and aPTT ratios were achieved at 24 hours in only 37% of patients given SC heparin compared with 71% of those given the same total dose by continuous IV infusion.[102] Because the anticoagulant response to heparin varies among patients with thromboembolic disorders, it is standard practice to adjust the dose of heparin and monitor its effect, usually by measurement of the aPTT. In patients with venous thromboembolism the dose of heparin is usually adjusted to maintain aPTT at an intensity equivalent to a heparin level of 0.2 to 0.4 U/mL as measured by protamine titration or an anti-factor Xa level of 0.30 to 0.7 U/mL.[102] Heparin is considered in the therapeutic range when the aPTT is equivalent to 1.5 to 2.5 times the control value (in seconds).[102] Therefore, the GDG recommends waiting to mobilize a patient started on UFH at least 24 hours if IV infusion of heparin is used. PTs can assess therapeutic level of UFH by assessing the most current aPTT levels and mobilize patients when they achieve a therapeutic level.

Both UFH and LMWH can cause heparin-induced thrombocytopenia (HIT) which is an immune mediated reaction to heparins. HIT can occur in 2-3% of patients treated with UFH and approximately 1% of patients treated with LMWH.[93, 103] HIT will result in a paradoxical increased risk for venous and arterial thrombosis and this risk lasts approximately 100 days following initial reaction. Fondaparinux (Arixtra) is similar to LMWH and is often used when individuals need treatment or prophylaxis for VTE but have a history of heparin-induced thrombocytopenia (HIT).[93, 103] Fondaparinux is also used for thromboprophylaxis in medical and surgical patients as is LMWH. Therefore, patients with a history of HIT should not receive either LMWH or UFH with subsequent VTE.[93, 103] DOACs or Fondaparinux are choices of treatment for individuals with a history of HIT.

Direct oral anticoagulant drugs (direct thrombin inhibitors and direct factor Xa inhibitors) have been growing in popularity due to their ease of use (no laboratory monitoring, no adverse dietary or drug interactions) and their rapid time to peak therapeutic levels. In addition, there appears to be less risk of cerebral hemorrhage compared to vitamin K antagonists.[104] Current oral anticoagulation drugs include rivaroxaban (Xarelto), dabigitran (Pradaxa), apixaban (Eliquis) and edoxaban (Savaysa) and are discussed in **Table 10**. Direct oral anticoagulant drugs are recommended by the American Association of Orthopedic Surgeons (AAOS) for hip and knee arthroplasty, but have not been recommended for individuals who have cancer and/or are undergoing treatment for cancer as well as those who are pregnant due to lack of

evidence of their use.[105] In addition, due to lack of evidence on drug-drug interaction with new medications and experimental treatments, DOACs have not been recommended at this time for patients with COVID-19.[106, 107]

Warfarin (Coumadin) is usually not the first choice of medication for anticoagulation due to the length of time to achieve peak therapeutic levels (days). If warfarin is the chosen medication for the patient to remain on after discharge, the drug is usually introduced on day one during administration of another loading anticoagulant (usually with LMWH or UFH).[94] Warfarin is continued for at least 5 days until an INR > 2 is achieved for at least 24 hours, prior to discontinuing the loading anticoagulant.[24, 33, 92] Currently, warfarin has been used less often due to the popularity of the DOACs; as well as, the fact that warfarin crosses the blood brain barrier and can be responsible for brain bleeds, particularly in individuals who fall.[108-111]

Mobility concerns in the acute setting with an individual receiving warfarin are made based upon the loading anticoagulant and not the INR associated with warfarin. Elevated INR (i.e. > 4) should raise concern regarding exercise and out of bed activity when patients are taking warfarin.[112] According to expert opinion, if INR is between 4.0 and 5.0, resistive exercises should be held and participation in light exercise (RPE ≤ 11) should be performed.[112] If gait is unsteady, ambulation should be restricted when the INR is elevated > 3.9 due to risk of bleeding if a fall or injury occurs.[112] The likelihood of bleeding is reported to rise steeply as INR increases above 5.0.[108-112] If INR is > 5.0, discussions should be held with the referring physician regarding patient safety. When an INR > 6.0, the medical team should consider bedrest until INR is corrected.[104, 112] INRs can usually be corrected within 2 days.[112] When reversal of anticoagulation is needed for a patient on warfarin requiring surgery, fresh frozen plasma is used to replace the anticoagulation.[108] Long term management of venous thromboembolism with anticoagulation is presented in **Table 11** including the considerations for their use.

With all anticoagulants there is a risk of bleeding; therefore, in addition to the risk of venous thromboembolism, physical therapists should be aware of and assess the risk of bleeding in all patients. See **Table 12** for factors associated with high risk of bleeding. In addition, updated guidelines have extended the length of time on anticoagulants to 3 - 6 months following diagnosis of DVT or PE.[24, 33, 92] Those at greatest need for extended treatment include those with cancer and genetic clotting disorders.[18, 65, 66]

Physical therapists should confirm the medication class and the date/time medication was initiated prior to mobilizing the patient. In addition, PTs should assess the patient's knowledge of the medication and risk of bleeding, as well as importance of compliance with taking the medication for the full amount of time prescribed.[24, 92]

Action Statement 10: Mobilize Patients with LE DVT when Therapeutic Level of Anticoagulation is Achieved

When a patient with a recently diagnosed LE DVT reaches the therapeutic threshold of anticoagulant medication, physical therapists should mobilize the patient. (Evidence Quality I; Recommendation Strength: A-Strong)

Action Statement Profile

Level of Evidence (I-V) Level I

Recommended Grades (A-R): A–Strong

Status Definition: Reaffirmed and updated

Aggregate Evidence Quality: Level I evidence based upon multiple systematic reviews demonstrating the safety of mobility following anticoagulation

Benefits: Mobility will limit the negative effects of bedrest, decrease risk of another VTE, and improve function and quality of life.

Risk, Harm Cost: Risks associated with use of anticoagulants include increased risk of bleeding. If an anticoagulant is not at a therapeutic level, there may be an increased risk of PE with mobilization.

Benefit-Harm Assessment: Benefits outweigh the risks

Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.

Intentional Vagueness: Specific anticoagulants, their dosage or therapeutic levels are not recommended in this document. Physical therapists should work within their health care system to develop institution specific protocols for mobility post VTE.

Role of Person/Patient Preferences: Patients should be informed regarding the risk of immobility for developing further VTE and the benefit of mobility.

Exclusions: Patients with other medical conditions preventing or limiting mobility.

Quality Improvement: Mobilization will decrease adverse effects of bedrest and can reduce the likelihood of further adverse effects of the DVT.

Implementation and Audit: Mobilization protocols can be developed based on the recommendations in the CPG. By providing a clinical decision algorithm for decision making with the use of anticoagulants, individuals should be able to implement the recommendations with. greater ease.

Supporting Evidence and Clinical Interpretation:

Patients who have a documented LE DVT and have reached therapeutic levels of the prescribed anticoagulant should mobilize out of bed and be encouraged to ambulate in order to prevent venous stasis. In doing so, deconditioning is minimized, length of hospital stay may be shortened,[113] and other adverse effects of prolonged bed rest, such as pressure ulcers can be avoided. A common concern for mobilizing a patient with an LE DVT is that the clot will dislodge and embolize to the lungs, causing a potentially fatal PE. However, early ambulation has been shown to lead to no greater risk of PE than bed rest for people with a diagnosed LE DVT who have been treated with anticoagulants.[114, 115]

Two meta-analyses showed no increased risk of PE, progression of DVT or DVT-related deaths with ambulation compared to bed rest once patients were anticoagulated.[114, 115] The studies included in these meta-analyses have great heterogeneity including differences in the timing of ambulation following initiation of anticoagulation. Nevertheless, the conclusion was that “early” ambulation was safe as soon

as the level of effective anticoagulation had been reached.[33, 114, 115] In addition, patients experiencing moderate or severe pain from the DVT had better outcomes in the affected limb if early mobility was implemented.[115] Similar conclusions were reported in 2 earlier systematic reviews, 1 with 3 studies totaling 300 patients[116] and 1 with 9 studies.[117]

Early mobilization can benefit the patient with LE DVT by potentially reducing the risk for extension of a proximal LE DVT and reducing long-term symptoms of PTS.[118, 119] The 2016 ACCP Guidelines provides a moderate strength recommendation that patients with an acute LE DVT should receive early ambulation over initial bed rest because of the potential to decrease PTS[120] and improve quality of life.[116] In summary, early mobilization of patients with an LE DVT who are anticoagulated does not put the patient at increased risk of PE and provides the added benefits of mobility. The GDG recommends mobilizing patients with a LE DVT once anticoagulation is initiated and therapeutic levels achieved.

Based on the evidence that exists on time to peak therapeutic levels of the anticoagulants discussed in key **Action Statement 9** and found in **Figure 3,** expert consensus recommends early ambulation of individuals with a LE DVT who are receiving anticoagulation and have reached their peak therapeutic levels based on the specific anticoagulation medication they are prescribed.

Action Statement 11: Mobilize Patients with UE DVT when Therapeutic Level of Anticoagulation is Achieved.

When a patient with a recently diagnosed upper extremity DVT reaches the therapeutic threshold of anticoagulant medication, mobilize the patient. (Evidence Quality: V; Recommendation Strength: R – Absence of research on topic)

Action Statement Profile

Level of Evidence (I-V): V - Expert opinion
Recommended Grades (A-R): R, Research - Absence of research on topic, conflicting or absent studies
Status Definition: New; not in prior version
Aggregate Evidence Quality: There are no studies or reports that look at the safety of mobilization for those with an upper extremity DVT. This action statement is applying information from the studies examining mobilization of those with a lower extremity DVT.
Benefits: Mobility will limit the negative effects of bedrest, decrease risk of another DVT, and improve function and quality of life.
Risk, Harm Cost: Risks associated with use of anticoagulants include increased risk of bleeding. If an anticoagulant is not at a therapeutic level, there may be an increased risk of PE with mobilization.
Benefit-Harm Assessment: Preponderance of benefit
Value Judgments: The GDG is making a judgment that the evidence on mobility after a LE DVT can be applied to UE DVT.
Intentional Vagueness: Specific anticoagulants, their dosage or therapeutic levels are not recommended in this document. Physical therapists should work within their health care system to develop institution specific protocols for mobility post VTE

Role of Person/Patient Preferences: Patients should be informed regarding the risk of immobility in developing further VTE and the benefit of mobility.
Exclusions: Patients with other medical conditions preventing or limiting mobility.
Quality Improvement: Mobilization will decrease adverse effects of bedrest and can reduce the likelihood of further adverse effects of the DVT.
Implementation and Audit: Mobilization protocols can be developed based on the recommendations in the CPG Given that there is no research surrounding mobilization of those with an upper extremity DVT, clinicians should contribute to data collection surrounding this topic.

Supporting Evidence and Clinical Interpretation:
A thorough review of clinical practice guidelines, systematic reviews, meta-analyses and research studies found no studies or even guidance on mobilizing individuals with an UE DVT. All of the studies surrounding management of those with an UE DVT address medications or interventional procedures. Because of the lack of information on mobilization after an UE DVT, the GDG decided to apply best evidence from LE DVT. Based on similar rates of PE and complications between those with UE and LE DVT and some commonalities in risk factors[91, 121] it would seem that a person with an UE DVT could be treated similarly post medical intervention. According to the results from two meta-analyses and a separate systematic review, mobilization for those with a LE DVT is safe once therapeutic levels of anticoagulants are met.[114, 115, 118] Based on this information, the GDG felt that as long as therapeutic levels of anticoagulants are met, those with an UE DVT should be safe for mobilization and general activity.

There is the question of what kind of mobilization is safe for those with an UE DVT. How does movement, intensity of the activity, gravity and clot location affect risk of PE? Is UE movement the same as general mobility such as transfers and walking? Again, there are no studies or published guidelines in these areas. When a person has a clot in their lower extremity, movement and intensity are not limited, but the leg typically stays below the level of the heart and lungs. For individuals with an UE DVT, it may be wise to avoid strenuous and overhead activities out of concern for a clot traveling to the lungs. This may not be a major concern given that most functional activities can be completed with the shoulder below 90 degrees and do not require strenuous efforts. For those with a central venous catheter, they may be limited by pain and discomfort and naturally avoid overhead and strenuous activities.

The recommendation by the GDG, based on expert opinion, is that general mobility such as walking and upper extremity motion during activities such as activities of daily living and transfers is safe once therapeutic levels of medications are reached. Patients should also be encouraged to use their arm to avoid development of restrictions in range of motion. Limitations due to any catheters or invasive lines should be taken into consideration with activity recommendations. Future research and inquiry are needed on appropriate upper extremity activity post UE DVT diagnosis.

Action Statement 12: Do Not Routinely Recommend Mechanical Compression for those with a New DVT.

When a patient has a newly diagnosed LE DVT, do not routinely recommend mechanical compression (e.g. intermittent pneumatic compression &/or graduate compression stockings). (Evidence Quality: II; Recommendation Strength: B - Moderate)

Action Statement Profile

Level of Evidence (I-V): Level II - Lesser quality studies (< 50% of criteria)

Recommended Grades (A-R): B, Moderate - Level II studies, at least one II directly on topic supports recommendation

Status Definition: Revised and updated

Aggregate Evidence Quality: Earlier lower quality studies found a benefit with compression while more recent, higher quality studies have called into question the effectiveness of compression to lower the risk of PTS.

Benefits: Not using compression with every patient will decrease unneeded medical expenses and limit exposure to adverse effect of compression such as skin irritation and ulceration due to improper fit.

Risk, Harm Cost: Some individuals may find benefit and pain relief with compression.

Benefit-Harm Assessment: Equilibrium

Value Judgments: None

Intentional Vagueness: Compression cannot be recommended for all individuals but cannot be excluded completely in some situations.

Role of Person/Patient Preferences: Some people may want to use compression for pain relief or perceived benefits. Patients should be educated in proper usage of compression.

Exclusions: None

Quality Improvement: Decrease unnecessary prescription of mechanical compression.

Implementation and Audit: Given that compression is no longer recommended for most patients, education on this change needs to be implemented. While not recommended for most patients, some may benefit from compression.

Supporting Evidence and Clinical Interpretation:

In 2016, the GDG recommended mechanical compression after a LE DVT diagnosis to lower the risk of PTS. This statement was in line with recommendations in other CPGs at the time.[65] Since that time, the SOX Trial, a large RCT including over 800 participants, was completed showing that elastic compression stockings (30-40 mm Hg graduated pressure) worn for 6 months did not prevent PTS or reduce leg pain in individuals with a first episode acute proximal DVT.[122, 123] Smaller studies have also questioned the value of compression after a diagnosis of DVT to prevent PTS.[124] Based on the inclusion of the SOX Trial in data analysis, the NICE guideline on VTE Management no longer recommend compression stockings to prevent PTS.[66] The Guidelines on VTE Management[33] suggest not using compression stockings routinely to prevent PTS, but do state a trial of compression may be appropriate for those with acute or chronic symptoms.

Given multiple earlier and lesser quality research studies supporting compression, recent systematic reviews and meta-analyses done on the role of compression post DVT have led to mixed recommendations based on conflicting information and study design. In a 2017 Cochrane systematic review[125], compression therapy post DVT led to a reduction in PTS (RR = 0.62, 95% CI 0.38-1.01) but

compression did not affect the severity of PTS. The authors stated the evidence was low quality and that the pooled results should be interpreted with caution. Burgstaller et al[126] concluded in their systematic review that based on mixed results and the inability to pool data from the RCT due to differences in follow up time, compression stockings cannot be justified, but they cannot be excluded completely. Jin et al[127] found no difference in the incidence of PTS between compression and control groups as part of their review. The authors did draw attention to the different diagnostic criteria across studies and the low numbers of studies to make a strong conclusion on the role of compression.

Based on the recent SOX Trial, recently updated CPGs, and systematic reviews the GDG recommends that compression is not routinely recommended for individuals post DVT diagnosis. If the individual has unresolved pain, swelling or a preference to try compression, this option can be considered. If compression is prescribed, the therapist should provide education on proper fitting to decrease risk of skin breakdown and discomfort.

Action Statement 13: Mobilize Individuals with an Inferior Vena Cava Filter

When a patient has an inferior vena cava (IVC) filter implanted, mobilize the patient once they are hemodynamically stable and there is no bleeding at the puncture site.

(Evidence Quality: V; Recommendation Strength: P-Best Practice)

Action Statement Profile

Level of Evidence (I-V): V - Expert opinion

Recommended Grades (A-R): P, Best Practice - Current clinical practice norms

Status Definition: Reaffirmed and updated

Aggregate Evidence Quality: Level V based upon expert opinion and evidence of mobility with LE DVT and anticoagulation. There is high level of evidence supporting use of IVF when anticoagulation is contraindicated, but there is a lack of evidence of mobility post IVC filter placement.

Benefits: Mobility will limit the negative effects of bedrest, decrease risk of another VTE, and improve function and quality of life.

Risk, Harm Cost: If filter not properly place, there may be an increased risk of PE with mobilization.

Benefit-Harm Assessment: Preponderance of Benefit

Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.

Intentional Vagueness: None

Role of Person/Patient Preferences: Discomfort post-op of IVC filter placement should be discussed prior to mobility as well as importance of mobility for circulation and decreased VTE risk.

Exclusions: Patients with other medical conditions preventing or limiting mobility.

Quality Improvement: Mobilization will decrease adverse effects of bedrest and can reduce the likelihood of further adverse effects of the DVT.

Implementation and Audit: Mobilization protocols can be developed based on the recommendations in the CPG. Activity needs to be promoted by the full medical team. Written, face to face, and electronic educational tools should be used to encourage physical activity.

Supporting Evidence and Clinical Interpretation:
Inferior vena cava filter placement is a type of percutaneous endovascular intervention for venous thromboembolic disease and is usually performed by an interventional radiologist. Venous access is via the right internal jugular or right femoral veins. The best placement location for the IVC filter to prevent lower extremity and pelvic VTE is just inferior to the renal artery access veins.[128]

Routine use of IVC filters is not recommended, however there are a few populations that are indicated to have an IVC filter placed temporarily or long term. Indications for IVC filter include individuals with recent proximal DVT with an absolute contraindication to anticoagulation treatment or who are at a decidedly high risk of PE and not anticoagulated.[33, 92] An IVC filter is indicated in these patients to decrease the risk of recurrent PE when there is a lack of other treatment options. In addition, an IVC filter may be utilized in patients receiving anticoagulation if they have had recurrent PEs.[92] There are risks associated with IVC filter placement including penetration of the venous wall (up to 19% in one study)[129] and adjacent organ involvement with symptoms in 8% of the population provided an IVC filter.[129] Up to 5% of the patients with IVC filters require surgical removal of the permanent filter.[129] Additional complications include fracture of the filter while in place and/or relocation/movement of the filter. One last complication of grave concern is the occasional extension of a LE DVT progressing and extending up to the filter and/or filter thrombosis in patients due to their inability to be anticoagulated.[130, 131]

Two RCTs[132, 133] and a systematic review combined with a meta-analysis[134] evaluated anticoagulation with and without IVC filters. Recurrent VTE was low in both groups in the meta-analysis. These studies reported a 50% lower incidence of PE when an IVC filter was used. For those with a IVC filter, there was a 70% increase in risk of DVT over those with no filter. Despite the presence of an IVC filter, the two groups had no difference in all-cause mortality or PE related mortality.

Following placement of an IVC filter, patients should be mobilized once he or she is hemodynamically stable and there is no bleeding at the puncture site as mobility carries the same risk of dislodging an existing clot, but the presence of the filter would prevent a catastrophic PE.[128] Physical therapists should monitor ambulation and mobility to ensure patient safety and to determine the appropriate level of required assistance prior to the patient being discharged.[128] In patients who have an IVC filter not recently inserted, assessment should be made of the LE vascular system as well as identifying the time frame since IVC filter placement. The longer the IVC remains in place, the higher the risk of complications from filters.[92]

Action Statement 14: Consult the Medical Team to Safely Mobilize a Patient with LE DVT Not Treated with IVC Filter or Anticoagulant

Consult with the medical team when a patient presents with a documented LE DVT below the knee, is not anticoagulated, does not have an IVC filter and patient is prescribed out of bed mobility by the physician. (Evidence Quality: V; Recommendation Strength: P-Best Practice)

Action Statement Profile

Level of Evidence (I-V): V
Recommended Grades (A-R): P, Best Practice
Status Definition: Reaffirmed and **u**pdated
Aggregate Evidence Quality: Level V evidence from expert opinion based on lack of existence of evidence and guidance on mobility for this population. Since there is a lack of strong evidence, this is considered to be an expert opinion recommendation.
Benefits: Mobility will limit the negative effects of bedrest, decrease risk of another VTE, and improve function and quality of life.
Risk, Harm Cost: Mobilization could lead to a potential increased risk of PE should the LE DVT embolize when not treated.
Benefit-Harm Assessment: Preponderance of benefit over harm
Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.
Intentional Vagueness: Specific guidelines are not provided because it is rare that a patient will not have anticoagulants prescribed or an IVC filter in this country. Each patient should be considered individually.
Role of Person/Patient Preferences: Patients should be informed of the risks and benefits bed rest versus mobilization.
Exclusions: None
Quality Improvement: Mobilization will decrease adverse effects of bedrest and can reduce the likelihood of further adverse effects of the DVT.
Implementation and Audit: Specifically identifying patients who would be appropriate in this category might help health care providers understand the importance of mobility and become more aware that the location of the DVT is significant for prognosis and risk.

Supporting Evidence and Clinical Interpretation:
There may be times when a patient has been diagnosed with an isolated, below the knee LE DVT but no medical intervention is initiated. The patient may have a contraindication for receiving anticoagulant medications such as increased risk of bleeding or presence of a recent bleeding event (i.e. post-acute subdural hematoma) or they do not meet the criteria for an IVC filter (i.e. a patient in palliative or hospice care). The ACCP guidelines report that thromboses confined to the muscular veins of the calf (soleus, gastrocnemius) that have not extended beyond the popliteal have a lower risk of extension beyond the calf and should be followed with serial imaging of the deep veins for 2 consecutive weeks if not given medications for anticoagulation.[33] In these situations, a consult with the primary physician or medical team should guide the decision to mobilize the patient. In cases where the patient has an isolated distal DVT of the leg and has severe symptoms or risk factors for extension, the ACCP recommends anticoagulation over serial imaging.[135]

It should be noted, controversy exists between guidelines regarding the medical intervention for the isolated distal calf DVT. The 2018 NICE guidelines recommend treating distal (calf vein) DVT with anticoagulation versus observation, unless there are contraindications to anticoagulation. These guidelines recommend anticoagulation therapy to continue for 3 months. In contrast, the ACCP 2021 antithrombotic guidelines update recommend compression ultrasound imaging for two weeks rather than

treatment with anticoagulation.[33] Therefore, isolated calf DVTs may or may not be medically managed with anticoagulation but require follow-up re-evaluation and possibly referral for medical management.

Continuing to remain on bed rest will only increase the risk of additional VTE and other adverse effects of immobilization.[4, 114, 115] At some point, the patient needs to return to daily activities, and it might be appropriate to begin mobilization even though an untreated LE DVT is present. In other situations, the reason for not addressing the LE DVT may be short term. It may be wise to wait until anticoagulation can begin. The physical therapist needs to discuss all of these factors with the interprofessional team and the patient when making a clinical judgment about mobilization. Although a physician may order physical therapy to increase the physical activity level of a patient, it is the physical therapist's clinical decision whether to mobilize the patient based on the available information about the patient's LE DVT and risk status.

Action Statement 15: Mobilize Patient with Non-massive (low risk) PE when Therapeutic Level of Anticoagulation is Achieved

When a patient with a non-massive, low risk PE reaches the therapeutic threshold of anticoagulant medication, physical therapists may mobilize the patient. (Evidence Quality: I; Recommendation Strength: A - Strong)

Action Statement Profile

Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)

Recommended Grades (A-R): A, Strong - Level I studies, at least one level I on topic supports recommendation

Status Definition: New; not in prior version

Aggregate Evidence Quality: **Level I evidence based on ESC guidelines which describe the population at low risk as those with nonmassive PEs.**

Benefits: Mobility will limit the negative effects of bedrest, decrease risk of another VTE, and improve function and quality of life.

Risk, Harm Cost: Risks associated with use of anticoagulants include increased risk of bleeding. If an anticoagulant is not at a therapeutic level, there may be an increased risk of PE with mobilization.

Benefit-Harm Assessment: Preponderance of Benefit

Value Judgments: As movement specialists, physical therapists place emphasis on mobility and exercise.

Intentional Vagueness: Specific anticoagulants, their dosage or therapeutic levels are not recommended in this document. Physical therapists should work within their health care system to develop institution specific protocols for mobility post VTE.

Role of Person/Patient Preferences: Patients should be informed of the risks and benefits bed rest versus mobilization

Exclusions: Patients with other medical conditions preventing or limiting mobility. Also, excludes intermediate (submassive) and high risk (massive) PE as diagnosed from right ventricular involvement from Echocardiography or other diagnostic tests.

Quality Improvement: Mobilization will decrease adverse effects of bedrest and can reduce the likelihood of further adverse effects of the DVT.
Implementation and Audit: Mobilization protocols can be developed based on the recommendations in the CPG. Clinicians should contribute to the collection of data regarding the safety of mobilization of these low risk for morbidity and mortality patients and contribute to the evidence.

Supporting Evidence and Clinical Interpretation:
Acute pulmonary embolism has an annual incidence of 100,000 cases in the United States and can result in severe dyspnea, chronic thromboembolic pulmonary hypertension and even death. Pulmonary embolism is classified based on the severity and risk for early (< 30 day) mortality (See **Table 13**).[18, 92] Selected patients with a proven PE may be determined stable and low risk to be treated on an outpatient basis determined by the use of the Hestia criteria.[136] There are two classification systems: one from the European Society of Cardiology which uses high, intermediate (subdivided into intermediate-high and intermediate-low) and low risk.[18] The ESC system is equivalent to the classification system used by the ACCP who use massive (high risk), submassive (includes intermediate-high and intermediate-low risk) and non-massive (low risk).[11, 33]

Non-massive pulmonary embolism, otherwise described as low risk PE, is defined as a PE without signs of right ventricular strain on echocardiogram and/or without biomarker elevation in the presence of hemodynamic stability.[92] Hemodynamic stability alone does not accurately classify PE, but absence of right ventricular involvement and other comorbidities also assist in determining improved prognosis post PE. Therefore, assessment of risk should be performed using Pulmonary Embolism Severity Index (PESI) or simple PESI (sPESI). A score of I or II on PESI or 0 on simple PESI defines low risk PE,[137] as well as determination of right ventricular function post PE. In a meta-analysis of 21 cohort studies and over 3,000 patients, 34% of patients identified with I or II on PESI or 0 on sPESI were diagnosed with right ventricular dysfunction placing them in the intermediate risk category. Assessment of the RV by imaging methods or laboratory biomarkers should be performed, even in the presence of a low PESI or a negative sPESI.[138] Individuals with an acute PE and without right ventricular dysfunction should be considered low risk for mortality, and therefore should be considered appropriate candidates for early mobility following appropriate anticoagulation.[33, 92]

If the PE is classified as low risk, the ESC guidelines recommend early discharge from the hospital in addition to continuation of anticoagulation treatment.[92] The British medical society further recommends individuals diagnosed with a low risk PE be treated in the outpatient setting with continuous follow-up.[139] Based on these recommendations, mobility should be encouraged once the therapeutic level of anticoagulation is achieved to prevent adverse effects of bed rest, deconditioning, and venous stasis. Early ambulation does not increase the risk of additional PEs compared to bedrest in individuals treated with anticoagulants.[114, 115] A meta-analysis showed the absence of a higher risk of new PE or other adverse clinical events when individuals were ambulated compared to bed rest.[114]

Therefore, the recommendation is for individuals with a non-massive PE to be active once anticoagulation is initiated and therapeutic levels have been achieved.[140] Monitoring of vital signs and signs and symptoms

of worsening PE should be performed during initial mobilization of these patients. Monitoring for evidence of instability should be performed with these individuals including abnormal HR response, decreases in SpO_2, hypotension, as well as any signs of abnormal dyspnea, or chest pain. Physical therapists should promote mobility and provide therapeutic interventions as needed to encourage activity.

Action Statement 16: Do Not Mobilize Massive PE or Submassive/Intermediate High-Risk PE until Low Risk and Hemodynamically Stable

When a patient presents with a massive or submassive PE categorized as high or intermediate risk, do not mobilize patient until criteria are met for low risk PE and the patient is hemodynamically stable.

(Evidence Quality: V; Recommendation Strength: P – Best Practice)

Action Statement Profile

Level of Evidence (I-V): V - Expert opinion

Recommended Grades (A-R): P, Best Practice - Current clinical practice norms

Status Definition: New; not in prior version

Aggregate Evidence Quality: **Level** V expert opinion based on the lack of evidence of safety mobilizing these high-risk patients. As these patients are defined as unstable, best practice would be to await patient stability prior to mobility.

Benefits: Limiting mobility in these patients is critical for patient safety.

Risk, Harm Cost: Immobility can lead to adverse effects if over an extended time.

Benefit-Harm Assessment: Preponderance of Benefit

Value Judgments: None H

Intentional Vagueness: Guidance is not given if right ventricular function testing is not repeated (usually with echocardiogram)

Role of Person/Patient Preferences: Patients may prefer to be mobile, however it is necessary for patients to be hemodynamically stable for purposes of mobility.

Exclusions: Those with non-massive (low risk) PE

Quality Improvement: Identification of the high risk, hemodynamically unstable patient is important to streamline the appropriate use of physical therapy service.

Implementation and Audit: Mobilization protocols can be developed based on the recommendations in the CPG. Given that there is no research addressing mobilization of those with a pulmonary embolism, clinicians should contribute to data collection addressing this topic including the frequency of hemodynamically unstable PEs as well as length of time to achieve stability prior to mobilization.

Supporting Evidence and Clinical Interpretation:

Pulmonary embolism is classified based on the severity and risk for early (< 30 day) mortality (see **Table 13**).[92] Massive PE or high risk PE is characterized as overt hemodynamic instability and requires immediate advanced therapy including anything from thrombolysis, fibrinolysis, catheter ablation, surgical embolectomy or even extracorporeal membrane oxygenation (ECMO).[92, 141] Hemodynamic instability in

the presence of PE often indicates a central or extensive PE.[142] Syncope may also occur and has been associated with higher prevalence of instability including right ventricular dysfunction.[142] See **Table 14** for the definition of hemodynamic instability. Individuals who present with a massive PE require stabilization and monitoring until they demonstrate hemodynamic stability and improvement in right heart function, usually defined by repeated echocardiograms. These patients are not candidates for physical therapy and mobility until hemodynamic stability is achieved.

Individuals with a PE who are hemodynamically stable and without systemic hypotension, but with presence of acute right ventricular dysfunction and myocardial injury (including elevated troponin or NTproBNP) are at intermediate-high risk for adverse outcomes. Acute right ventricular pressure overload at the time of PE diagnosis is an important determinant of the severity; as well as, the early clinical outcomes of PE.[11, 92, 143, 144] Individuals defined as intermediate high risk for adverse outcomes may also benefit from more advanced treatments including reperfusion therapy.[92, 141] For individuals who do not present with hemodynamic compromise or systemic hypotension, protocols utilizing anticoagulation are considered standard treatment except in those who have right ventricular dysfunction and myocardial injury. Therefore, recommendations for early discharge post PE include ruling out right ventricular dysfunction as well as right heart thrombi (within the first 24-48 hours).[138]

Patients in the PEITHO trial identified as intermediate-high risk PE required 2 - 3 days of anticoagulation to ensure they were stable due to the mean time identified before hemodynamic decompensation or death (1.79+/- 1.6 days).[145] A systematic review and meta-analysis that contained only cohort studies suggests predictive value of morbidity and mortality improved when utilizing clinical criteria as well as image findings and/or laboratory biomarkers[138] A prospective trial found that ruling out right ventricular dysfunction and/or thrombi early after hospital admission decreases risk for recurrent VTE within three months following the initial event.[138] Hemodynamic stability and lack of RV dysfunction defines low risk PE and therefore, candidacy for mobility.

Therefore, physical therapists should review the patient's admitting and subsequent medical information to identify hemodynamic status, presence of a normal BP, as well as evaluate for right ventricular involvement with the PE by reviewing echocardiogram results. In the presence of hemodynamic instability, persistent hypotension, and right ventricular involvement with concomitant residual DVT the physical therapist should not mobilize individuals with the presence of any of these signs of instability.[92, 140, 146] Once hemodynamic stability is attained, blood pressure normalized, and treatment initiated, mobility may be indicated. According to the ESC guidelines, after reperfusion treatment and hemodynamic stabilization, high-risk PE patients can be switched to oral anticoagulation at which time mobility could be initiated following therapeutic levels of the anticoagulant achieved.[12] Right ventricular function and/or normalization of biomarkers may not return to normal in high-risk or intermediate-high risk patients for weeks, therefore these individuals should be monitored closely for hemodynamic stability with activity and PTs working with these patients should continue monitoring due to the potential stresses on the right ventricle.[12]

Action Statement 17: Refer Patient for Medical Re-Evaluation if No Improvement in Signs and Symptoms of VTE after One to Two Weeks

When a patient with a documented VTE does not show improvement in signs/symptoms of VTE after one to two weeks of medical treatment (anticoagulation, IVC filter, catheter or surgical intervention), refer the patient for medical re-evaluation. (Evidence Quality: V, Recommendation Strength: P - Best Practice)

Action Statement Profile

Level of Evidence (I-V): Level V – Expert Opinion

Recommended Grades (A-R): Recommendation Strength: P – Best Practice)

Aggregate Evidence Quality: Level V. Expert opinion due to the presence of best practice information to continue to monitor/follow a patient with a documented VTE and no improvement in signs and symptoms.

Status Definition: New; not in prior version

Benefits: Re-evaluation can lead to improved medical care and decrease risk of adverse events.

Risk, Harm, Cost: No risk or harm with a medical consult, increased cost of diagnostic testing and/or physician consult

Benefit-Harm Assessment: Preponderance of Benefit

Value Judgments: None E

Intentional Vagueness: Length of time for follow up described as a range (1-2 weeks) due to variability in the documented literature.

Role of Patient Preferences: Patients often prefer to stop taking medications, especially if the medications present with side effects or are costly. As a result of stopping medications earlier than prescribed, patients may not continue to improve and may be at greater risk of recurrence. In addition, medication may not be appropriate for certain patients and may fail to reduce the original clot.

Exclusions: None known

Quality Improvement: Service delivery will improve and referral back for medical evaluation will be increased in patients not improving.

Implementation and Audit: Guides for re-evaluation can be developed to improve patient care.

Supporting Evidence and Clinical Interpretation:

An individual with successful treatment post VTE will typically demonstrate improvement in mobility and exercise tolerance with less symptoms of pain, swelling and elevated limb temperature if the clot is in the upper or lower extremity, and less shortness of breath, particularly with exertion if the clot is a PE.[18, 33] While medical interventions are typically successful in treating a VTE, there are situations where the thrombus remains or grows in size. As described in **Action Statement 14**, there also times when no medical intervention is prescribed. While this is the best course of action in some cases, for a portion of individuals, the thrombus will not resolve on its own.

Then there are other times that an individual may not follow through on the prescribed intervention. If patients are not compliant with their medical treatment for VTE and/or the treatment is shorter than the recommended prophylaxis, patients may demonstrate a lack of improvement of signs and symptoms of

VTE. These patients have an increased risk for developing a new VTE and/or the continued presence of the original VTE. Physical therapists need to monitor individuals post VTE diagnosis and be aware of indicators of lack of improvement or worsening symptoms. In these cases, a referral back to the medical team for further assessment would be necessary.

Even when receiving medical intervention, there is a slight risk of further thrombus remaining. As described in the background information of this document, the coagulation cascade may remain active after orthopedic surgery for 5 to 6 weeks.[8-10] The length of time of risk for VTE in the postoperative time period may be related to the type of surgical procedure. In a prospective study of 4,840 joint surgery patients, VTE symptoms appeared a mean of 27 days after total hip arthroplasty (THA) and a mean of 17 days after total knee arthroplasty (TKA).[10] In hip fracture cases, there is often a delay between injury and surgery. Therefore, the patient is already in a prothrombotic state at time of surgery, and the surgery increases the risk for VTE further. In addition, VTE risk remained increased for the greatest time after hip fracture surgery (mean time to symptomatic DVT, 36 days) than after all other orthopedic surgeries.[10]

Declining mobility for any reason appears to increase risk for VTE and should be monitored in ALL settings. A study of nursing home residents and community patients showed a decline in ambulatory status in both groups immediately after hip fracture surgery.[147] A more recent study of VTE in nursing home residents demonstrated that immobility leads to increased risk for VTE.[148] Thus, a decline in ambulatory status might increase the risk for VTE.

Recurrent VTE can occur early post event, yet risk of recurrence may continue to be a problem many years after the event. Recurrent VTE can occur in individuals who have discontinued anticoagulation; as well as, in those individuals continuing to take anticoagulant therapy. Recurrence after DVT occurs more frequently as a DVT, whereas recurrence after a PE recurs as a PE.[149] However, the incidence of recurrent VTE in patients who have a PE is double that of the incidence of recurrence of LE DVT.[150, 151] The risk of recurrence of VTE following discontinuation of treatment was found to be approximately 2.5% to 8%/year after initial PE in the majority of patients low to moderate risk (see **Table 15**).[92] However, the risk of PE recurrence is high (> 8% /year) for those who have active cancer, one or more previous VTE or an antiphospholipid antibody syndrome).[92] Recurrence in UE DVT has been reported to be approximately 9% yet if an individual has documented cancer the risk is double and a higher rate of recurrence if patients have catheter associated UE DVT.[5]

There are no randomized trials or prospective cohort studies that have evaluated management of patients with recurrent VTE on anticoagulant therapy. Risk factors for recurrent VTE while on anticoagulant therapy can be divided into two broad categories: (1) treatment factors (individuals may require a different anticoagulant or may not be adherent to treatment) and (2) the patient's intrinsic risk of recurrence. Following treatment for VTE, patients should be encouraged to be mobile, as continued risk for VTE decreases with mobility.[4, 114, 115] However, compliance with medication for VTE often decreases over time following the VTE as individuals may not understand the need to take the medication for the full duration.[152] Alternatively, pharmacologic treatment is often prescribed for limited time or may even be progressively decreased over time with the patient's increased mobility by physicians who may not be

aware of current antithrombotic guidelines.[153] Evidence has shown that many apparent "treatment failure" presentations are in fact residual venous disease masquerading as recurrent VTE.[152] In the REVERSE study, imaging was performed on 646 patients with VTE and 60% of the study group had abnormal scans 5-7 months after an unprovoked VTE.[152] In another meta-analysis of 2,527 patients with DVT, 55% of the study population had residual venous obstruction 6 months after their index scans.[154] A systematic review on patients with PE demonstrated residual abnormalities on V/Q scans or CTPA in 50% of the study population six months post initial event.[155]

Physical therapists treating patients post VTE should feel confident in working with individuals medically managed, but be aware of the risk of recurrent VTE in both patients currently taking anticoagulation and those that have discontinued treatment. Medical interventions do not guarantee a complete resolution of the issues and adjustments in treatment plan may be needed within the first few weeks post diagnosis. Additionally, the risk of recurrent VTE can be as much as 8% risk in those identified as intermediate risk for up to a year, which is discussed in **Action Statement 18**. Assessing risk for recurrent VTE can be as simple as reviewing **Table 15**, assessment of risk using a risk assessment tool as outlined in **Action Statement 5** and watching for signs/symptoms of VTE during the time the patient is under physical therapy care. Physical therapists should consider referring patients back to the physician for VTE follow-up if they suspect the patient is demonstrating signs/symptoms of continued VTE.

Action Statement 18: Refer Patients for Medical Management of the Long-term Consequences of VTE

When a patient presents with long term consequences of VTE (post-thrombotic syndrome, chronic thromboembolic pulmonary hypertension or history of VTE), consider referring patients for management strategies to minimize secondary long term complications of VTE to improve function or quality of life and to prevent recurrent VTE.
(Evidence Quality: V; Recommendation Strength: P – Best Practice)

Action Statement Profile

Level of Evidence (I-V): V Expert Opinion
Recommended Grades (A-R): P: Best Practice
Status Definition: Revised and Updated
Aggregate Evidence Quality: Level V expert opinion for best practice to minimize long term complications despite the lack of existence of high-quality evidence proving these management strategies are effective in prevention.
Benefits: Long term management will decrease the risk of another VTE, decrease complications, and help to improve their function and quality of life.
Risk, Harm Cost: No risk or harm with a medical consult, increased cost of diagnostic testing and/or physician consult
Benefit-Harm Assessment: Preponderance of benefit
Value Judgments: None
Intentional Vagueness: Length and frequency of long-term management is not provided.

Role of Person/Patient Preferences: Patients who experience VTE do not know or realize there may be complications with VTE or that recurrence is possible. Patients would prefer recommendations from the provider or other healthcare providers to reduce complications and prevent recurrence of VTE.
Exclusions: None known
Quality Improvement: Service delivery will be improved and streamlined possibly resulting in improved quality of life and function
Implementation and Audit: By developing this action statement, health care professionals will be more aware of complications and strategies to treat these complications, and these complications and strategies will be documented. Awareness of risk of recurrence will be increased which should result in improved education of patients to continue taking their medications for the length of the prescribed treatment.

Supporting Evidence and Clinical Interpretation:
Patients who experience a VTE (UE DVT, LE DVT and PE) may suffer from long term consequences of the VTE which can affect quality of life as well as optimal physical function. Complications after a VTE can continue for years and include PTS and chronic thromboembolic pulmonary hypertension (up to 3.8% incidence after 2 years).[156, 157] Physical therapists can help reduce symptoms of PTS with mechanical compression, provide exercise recommendations for prevention of recurrent VTE, and provide education of the consequences and risks of CTEPH; as well as, a referral to a pulmonologist or pulmonary hypertension clinic for those presenting with shortness of breath/dyspnea on exertion post pulmonary embolism. Therefore, physical therapists should consider the long-term consequences as well as the risk of recurrence of VTE and manage or refer for management to optimize movement function.

Post-Thrombotic Syndrome
Physical therapists should be able to recognize the signs and symptoms of post-thrombotic syndrome which include edema and swelling, chronic arm or leg pain, skin changes and heaviness of the limb affected by DVT.[156, 158] Physical therapists should assess patients for and residual impairments in the affected extremities as well as mobility impairments following a DVT, and those presenting with PTS should be given recommendations for maintaining adequate hydration, use of mechanical compression, importance of mobility, and education to improve knowledge of PTS and VTE.[158] Approximately 20% to 50% of patients post LE DVT and 8-28% post UE DVT[5] develop PTS as a long term complication which can occur up to and beyond 2 years post DVT.[5, 158] The risk factors for developing PTS after LE DVT include increased age, increased body mass index, thrombophilia, recurrent DVT events and effectiveness of initial oral anticoagulation regimen.[159-162] Risk factors for developing PTS after UE DVT have not been identified as PTS post UE DVT is not as common and most patients only present with mild symptoms.

PTS is a significant clinical diagnosis in LE DVT as it is associated with high morbidity and lower quality of life for patients experiencing these symptoms.[158] The decreased quality of life and effect on work and recreation financially impacts the healthcare system and has an impact on quality of life similar to chronic diseases such as chronic lung disease, diabetes and arthritis.[163] Therefore identifying signs and symptoms of PTS and the impact of these symptoms on patient function is a key role for physical therapists; as well as, assisting in providing management strategies or referral for these long-term consequences of VTE.

Persistent symptoms post PE and CTEPH

Following a pulmonary embolism, the patency of the pulmonary arterial bed will be restored within the first few months after the acute event.[164] However 20% to 75% of individuals who are diagnosed with a PE report decreased quality of life and health status 6 months after diagnosis.[165-167] Klok identified predictors of exertional dyspnea at long-term follow up post PE which include advanced age, cardiac or pulmonary comorbidities, higher BMI and a history of smoking.[165] Other predictors of exertional dyspnea include elevated systolic pulmonary arterial pressure and right ventricular dysfunction at the time of PE diagnosis; as well as, residual pulmonary vascular obstruction upon discharge from hospital.[166, 168, 169] Due to the long-term symptoms identified in the post PE population, the ESC guidelines recommend further evaluation in asymptomatic PE survivors who present with an increased risk for CTEPH.[92]

In a prospective study that followed a cohort of individuals for one year following discharge from the hospital for an acute PE, approximately 47% of the patients demonstrated a decreased maximal aerobic capacity (< 80% if predicted value) on a cardiopulmonary exercise test.[170] These individuals presented with decreased quality of life and significantly reduced 6 minute walk distances in addition to their decreased aerobic capacity.[170] Predictors of reduced functional capacity included female sex, higher body mass index, presence of history of lung disease, higher pulmonary artery systolic pressures on echo and higher main pulmonary artery diameter on the CTPA baseline study. Yet, large residual thrombi were not identified in these individuals who demonstrated poor physical performance following acute PE. Other factors may have contributed to the poor exercise tolerance including muscle deconditioning in the presence of cardiopulmonary morbidity and/or excess body weight.[170]

Persistent obstruction of the pulmonary arteries by thrombi often leads to the development of CTEPH, resulting in redistribution of blood flow and remodeling of the pulmonary vascular bed. Individuals with CTEPH report increasing dyspnea on exertion, decreased exercise tolerance, and decreased oxygen saturation with activity.[92] The ESC 2019 guidelines report the incidence of CTEPH is in the range of 1% to 9% within the first two years after a symptomatic PE event. However, the incidence of CTEPH may be lower due to low referral for diagnosis and/or treatment when symptoms of PH present themselves post PE.[92] As a result, the 2019 ESC guidelines recommend that symptomatic patients with mismatched perfusion defects identified from a V/Q scan performed > 3 months after an acute PE event be referred to a pulmonary hypertension or CTEPH expert.[92]

In addition, the ACCP guidelines for antithrombotic treatment recommends patients with CTEPH should be assessed by a team with expertise in evaluation and management of pulmonary hypertension.[11, 171, 172 173, 174] In addition, the ACCP guidelines support pulmonary thromboendarterectomy by an experienced thromboendarterectomy team in the presence of large PEs or the development of CTEPH post PE.[33] This is a change from previous guidelines due to improvements in surgical technique that now make it possible to remove thrombi from peripheral pulmonary arteries.[11, 175, 176] In addition, those individuals with CTEPH who are not candidates for thromboendarterectomy may be potential candidates for other mechanical and pharmacological interventions including pulmonary vasodilator therapy to attempt to lower pulmonary arterial pressures.[177]

Exercise training for muscle and aerobic reconditioning may be indicated for individuals with inoperable CTEPH. Individuals with CTEPH who performed exercise training resulted in improved walk distance of 61 meters following three weeks of training as well as, improved performance on peak VO_2 testing, maximal workload and improved scores on quality of life questionnaire.[178] Therefore, referral for assessment and management of dyspnea is recommended in individuals with persistent symptoms following PE and may include referral to specialists who treat CTEPH.

Recurrent VTE

Recurrent VTE, although not a long-term consequence of VTE but possibly a consequence of treatment or adherence to treatment failure may be a likelihood post VTE. The purpose of medical treatment (anticoagulation, IVC filter, catheter lysis, or surgical intervention) for a documented VTE is to dissolve the clot and improve the blood flow; as well as, decrease the signs and symptoms of the VTE.[18, 44, 65] IVC filters prevent embolization of clots from the lower extremities to the lungs and are typically used for short term prevention when individuals are at continued risk of VTE and are not able to be treated with anticoagulation due to risk of bleeding. Typically, catheter lysis and surgical intervention are aggressive treatments for large clots and often remove most, if not all the clot.[134, 179] Patients will be on anticoagulation following the lysis or surgical intervention unless contraindications for these medications exist.[18, 116]

The purpose of anticoagulation after a VTE is to treat the acute coagulopathic state as well as prevent recurrence of VTE in the future. Recurrent VTE can occur early post event yet risk of recurrence may continue to be a problem many years post event. Recurrent VTE can occur in individuals who have discontinued anticoagulation as well as in those individuals continuing to take anticoagulant therapy. Recurrence after DVT occurs more frequently as DVT, whereas recurrence after a PE recurs as a PE.[149] However, the incidence of recurrent VTE in patients who have a PE is double that of the incidence of recurrence of LE DVT.[150, 151] The risk of recurrence of VTE following discontinuation of treatment was found to be approximately 2.5 - 8%/year after initial PE in the majority of patients low to moderate risk (see **Table 15**).[92] However, the risk of PE recurrence is high (> 8% /year) for those who have active cancer, one or more previous VTE or an antiphospholipid antibody syndrome.[92] Recurrence in UE DVT has been reported to be approximately 9% yet if an individual has documented cancer the risk is double and a higher rate of recurrence if patients have catheter associated UE DVT.[5] There is no evidence evaluating patient with recurrent VTE while currently taking anticoagulant therapy. Risk factors for recurrent VTE while on anticoagulant therapy can be divided into two broad categories: (1) treatment factors (individual may require a different anticoagulant) and (2) the patient' s intrinsic risk.

In summary, patients who have experienced VTE whether it is UE or LE DVT or PE and continue to have consequences of the VTE such as PTS, CTEPH or recurrent VTE should be referred for medical management of the long-term consequences of VTE. Physical therapists should continue to provide recommendations around mobility (Key Action Statement 1) and preventive steps (Key Action Statement 4) being aware of complications, and compression in certain situations.

Action Statement 19: Recommend Mechanical Compression When Signs and Symptoms of PTS are Present.

When a patient presents with signs and symptoms consistent with post-thrombotic syndrome (PTS), recommend mechanical compression (e.g. intermittent pneumatic compression &/or graduated compression stockings). (Evidence Quality: I; Recommendation Strength: B - Moderate)

Level of Evidence (I-V): Level I - High quality studies (> 50% of criteria)
Recommended Grades (A-R): B, Moderate - Level II studies, at least one level II study directly on topic supports rec
Status Definition: Downgraded with new evidence
Aggregate Evidence Quality: Systematic reviews and other CPG have reviewed this topic. They note the low quality of the studies and heterogeneity between studies making this a difficult issue to give a high recommendation on.
Benefits: Compression may lead to faster resolution of symptoms and decreasing PTS severity.
Risk, Harm Cost: Improper fit can lead to skin irritation, ulceration, or interruption of blood flow. Added cost and inconvenience of wearing compression stockings.
Benefit-Harm Assessment: Equilibrium
Value Judgments: None
Intentional Vagueness: The specific type(s) of mechanical compression was/were not recommended. Physical therapists should work within their healthcare system to develop institution-specific protocols.
Role of Person/Patient Preferences: Individual may or may not want to use compression based on ease of use, comfort-level, and/or ability to don and doff compression garments or mechanical compression equipment properly.
Exclusions: Patients who have severe peripheral neuropathy, arterial insufficiency, dermatologic diseases, or lesions may have contraindications to selective mechanical compression modes.
Quality Improvement: Better prescription of mechanical compression to those individuals who will benefit the most.
Implementation and Audit: Given that this recommendation is downgraded, education on this change needs to be implemented. While not recommended for most patients, some may benefit from compression.

Supporting Evidence and Clinical Interpretation:
Post-thrombotic syndrome is a serious condition that can lead to limb edema, varicose veins, eczema, hyperpigmentation, fibrosis, pain and venous ulceration. Of those diagnosed with a DVT, approximately one in three patients will experience PTS within five years.[180-182] In the 2016 VTE CPG, compression was recommended for those with symptoms of PTS with Level I evidence and Grade A recommendation. Since that time, other clinical practice guidelines and systematic reviews have lowered their support for compression and PTS.

As stated in **Action Statement 12**, compression is not supported to be used with every person diagnosed with a DVT to prevent PTS or another VTE. However, when a person demonstrates the early onset of PTS, compression may play role in lessening the symptoms and complications. A 2019 Cochrane systematic review[183] on compression for treatment of post-thrombotic syndrome found very-low certainty of evidence regarding the effectiveness of graduated elastic compression stockings for treatment of PTS and low certainty evidence favoring use of intermittent pneumatic compression devices for the treatment of severity. They also found a lack of high certainty of evidence to support compression to prevent PTS. A 2018 Evidence-Based Consensus Statement on medical compression stockings in venous and lymphatic disorders recommended the use of MCS for the treatment of symptomatic PTS at a Grade 1B level.[184]

The findings of the studies are mixed with heterogeneity between the studies making it difficult to write a strong recommendation. While the findings are mixed if compression should be used in all individuals diagnosed with PTS, there is agreement that for the individual with symptoms, compression can provide some minor relief and benefit. Physical therapists may consider compression for their patients with PTS, especially if they have symptoms such as pain and swelling that could respond well to compression.

Summary

After a review of the original CPG, identifying places where more guidance on VTE management is needed and a thorough review of new literature since the original CPG publication, the GDG wrote 19 key action statements. Based on these statements, the following conclusions can be made.

- Physical therapists should play a significant role in identifying patients who are at high risk for a VTE. Once these individuals are identified, preventive measures such as referral for medication, initiation of activity or mobilization, and education should be implemented to decrease the risk of a first or reoccurring VTE.
- Physical therapists should be aware of the signs and symptoms of an VTE. When signs and symptoms are present, the likelihood of a VTE should be determined through the standardized tools, and the results shared with the interprofessional team to consider treatment options.
- In patients with a diagnosed UE or LE DVT, once a medication's therapeutic levels or an acceptable time period has been reached after administration, mobilization should begin. Although there are risks associated with mobilization, the risk of inactivity is greater.
- In patients with a diagnosed PE, once they are medically stable and a medication's therapeutic levels or an acceptable time period has been reached after administration, mobilization should begin.
- Complications following VTE can continue for years or even a lifetime. Physical therapists can help decrease these complications through education, mechanical compression, and exercise.

Implementation

In order to implement and disseminate the recommendations of this CPG, the GDG has taken or is in the process of taking the following steps:

- Preliminary sharing of CPG recommendations at a Town Hall meeting for the Academy of Cardiovascular and Pulmonary Physical Therapy during APTA's Virtual Combined Sections Meeting February 2021.
- Open access to the CPG and all reference materials.
    - Creation of a pocket guide/brochure about VTE for physical therapists. Creation of patient brochures and information flyers about the role of physical therapists in preventing VTE and managing patients with UE and LE DVT and PE.
- Creation of an App on VTE that includes the key action statements, the algorithms and the risk factor assessments for physical therapists
- Production of podcasts about the CPG aimed at physical therapists.
- Presentations on the CPG by the GDG at local, state, regional, and national seminars.
- Creation of checklist and sample evaluation forms incorporating the recommendations of the CPG.

In order to implement these recommendations, physical therapists and the entire health care team should take the following steps:

- Integrate key action statements into clinical practice. Making resources easily accessible in the clinic, such as lists of signs and symptoms of UE and LE DVT as well as PE, and copies of the risk assessment criteria for the VTE tools, and the algorithms in this CPG, are some examples.
- Form interprofessional teams that address VTE and ensure all providers know about and then implement the recommendations in this CPG. This recommendation may be done through embedding risk assessment into standardized examination forms or working with referral sources to encourage early mobilization after diagnoses of VTE.
- Physical therapists need to seek out membership in these interprofessional committees and serve as clinical champions in the areas of VTE prevention and management. As movement specialists, physical therapists understand the importance of mobilization and activity and have the ability to modify interventions based on medical history and patient problems. Physical therapists can add greatly to the scope and depth of these teams.

Research Needs

Although researchers have addressed multiple aspects of VTE management, there are still many unanswered questions. A few future research questions that are specific to the physical therapy management are listed below:

- Does aggressive screening for UE or LE DVT lead to a decline in the incidence of PE?
- Does the implementation of guidelines for mobilization of patients with UE or LE DVT lead to earlier mobilization and improved patient outcomes?
- Should mobility recommendations for UE DVT be more specific or limiting given the thrombus location in relationship to the heart and lungs?
- What is the appropriate degree of graded compression (e.g., elastic, inelastic stockings, IPC) and timing of treatment intervention for PTS and LE DVT prevention?

- Patient/person concerns/perspectives about having a VTE

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Table 1. Key Action Statements

Number		Key Phrase
1	Advocate for a culture of mobility and physical activity in all practice settings unless medical contraindications for mobility exist. (Evidence Quality: I, Recommendation Strength: A - Strong)	Advocate for a Culture of Mobility and Physical Activity
2	During initial interview and physical examination assess risk of VTE in patients with reduced mobility (Evidence Quality: I, Recommendation Strength: A - Strong)	Assess for Risk of VTE with reduced mobility
3	When a patient presents with conditions (i.e. cancer or inherited clotting disorder) that independently increase VTE risk, therapists should have a high index of suspicion for VTE and assess for additional risk factors. (Evidence quality: I; Recommendation strength: B - Moderate)	Assess for Additional Risk Factors of VTE in all High-Risk Patients
4	When a patient is identified as high risk for VTE, provide preventive measures including education on the signs and symptoms of VTE, activity, hydration, mechanical compression and referral for medical treatment. (Evidence Quality: I; Recommendation Strength: A - Strong)	Provide Preventive Measures for Those Who are High Risk for VTE.
5	Establish the likelihood of a LE DVT if the patient presents with pain, tenderness, swelling, warmth and/or discoloration in the lower extremity and take appropriate action based on results. (Evidence Quality: I, Recommendation Strength: A - Strong)	Establish Likelihood of LE DVT When a Patient Presents with Symptoms
6	Establish the likelihood of UE DVT if patients present with clinical symptoms including swelling, pain, edema, cyanosis and/or dilation of superficial veins and take appropriate action based on results. (Evidence Quality: I, Recommendation Strength: B - Moderate)	Establish the Likelihood of UE DVT When Patient Presents with Symptoms
7	When a patient presents with dyspnea, chest pain, presyncope or syncope, and/or hemoptysis, evaluate the likelihood of PE and take appropriate action based on results. (Evidence Quality: I Recommendation Strength: A - Strong)	Establish the Likelihood of PE When a Patient Presents with Symptoms
8	When a patient presents with a recently diagnosed provoked or unprovoked VTE, assess medical intervention. (Evidence Quality: V; Recommendation Strength: P – Best Practice)	Assess Medical Intervention
9	With a recently diagnosed VTE treated pharmacologically, confirm medication class and date/time initiated prior to mobilizing patient. (Evidence Quality: I Recommendation Strength: Strong)	Confirm Pharmacological Intervention and time initiated
10	When a patient with a recently diagnosed lower extremity DVT reaches therapeutic threshold of anticoagulant medication, mobilize the patient. (Evidence Quality: I, Recommendation Strength: Strong)	Mobilize Patients with LE DVT when Therapeutic Level of Anticoagulation is Achieved

11	When a patient with a recently diagnosed upper extremity DVT reaches therapeutic threshold of anticoagulant medication, mobilize the patient. (Evidence quality: V; Recommendation Strength: R – Absence of research on topic)	Mobilize Patients with UE DVT when Therapeutic Level of Anticoagulation is Achieved.
12	When a patient has a newly diagnosed LE DVT, do not routinely recommend mechanical compression (e.g. intermittent pneumatic compression &/or graduate compression stockings) (Evidence quality: II; Recommendation Strength: B - Moderate)	Do Not Routinely Recommend Mechanical Compression for those with a New DVT
13	When a patient has an inferior vena cava (IVC) filter implanted, mobilize the patient once they are hemodynamically stable and there is no bleeding at the puncture site. (Evidence Quality: V; Recommendation Strength: P-Best Practice)	Mobilize Individuals with an Inferior Vena Cava Filter
14	Consult with the medical team when a patient presents with a documented LE DVT below the knee, is not anticoagulated, does not have an IVC filter and patient is prescribed out of bed mobility by the physician. (Evidence Quality: V; Recommendation Strength: P - Best Practice)	Consult the Medical Team to Safely Mobilize a Patient with LE DVT Not Treated with IVC Filter or Anticoagulant
15	When a patient with a non-massive, low risk PE achieves the therapeutic threshold of anticoagulant medication, physical therapists may mobilize the patient. (Evidence Quality: I; Recommendation Strength: A - Strong)	Mobilize Patient with Non-massive (low risk) PE when Therapeutic Level of Anticoagulation is Achieved
16	When a patient presents with a massive or submassive PE categorized as high or intermediate risk, do not mobilize patient until criteria are met for low risk PE and the patient is hemodynamically stable. (Evidence Quality: V; Recommendation Strength: P - Best practice)	Do Not Mobilize Massive PE or Submassive/Intermediate High-Risk PE until Low Risk and Hemodynamically Stable
17	When a patient with a documented VTE does not show improvement in signs/symptoms of VTE after one to two weeks of medical treatment (anticoagulation, IVC filter, catheter or surgical intervention), refer the patient for medical re-evaluation. (Evidence Quality: V; Recommendation Strength: P - Best Practice)	Refer Patient for Medical Re-Evaluation if No Improvement in Signs and Symptoms of VTE after One to Two Weeks
18	When a patient presents with long term consequences of VTE (post-thrombotic syndrome, chronic thromboembolic pulmonary hypertension or history of VTE), consider referring patients for management strategies to minimize secondary long	Refer Patients for Medical Management of the Long-term Consequences of VTE

	term complications of VTE to improve function or quality of life and to prevent recurrent VTE. (Evidence Quality: V; Recommendation Strength: P - Best Practice)	
19	When a patient presents with signs and symptoms consistent with post-thrombotic syndrome (PTS), recommend mechanical compression (e.g. intermittent pneumatic compression &/or graduated compression stockings). (Evidence Quality: I; Recommendation Strength: B - Moderate)	Recommend Mechanical Compression When Signs and Symptoms of PTS are Present.

Table 2. Search Strategy by Key Words and MeSH terms

Key Words		MeSH Terms
DVT	Rivaroxaban	“Venous Thrombosis”
“Venous Thrombosis”	Apixaban	“Pulmonary Embolism”
“Deep Vein Thrombosis”	“DOAC”	“Walking”
VTE	“Direct Oral Anticoagulant”	“Movement”
“Venous Thromboembolism“	“NOAC”	“Immobilization”
“Pulmonary Embolism”	“non-Vitamin K antagonist	“Mobility Limitation”
“Pulmonary	oral anticoagulants”	“Motor Activity”
Thromboemoblism”	“novel oral anticoagulants”	“Early Ambulation”
Walking	Betrixaban	“Activities of Daily Living”
Walk	“YM150”	“Anticoagulants”
Ambulation	Razaxaban	“Coumarins”
Ambulate	“Factor Xa Inhibitor”	“Fibrin Modulating Agents”
Ambulated	“Direct Thrombin Inhibitors”	“Factor Xa/antagonists and inhibitors”
Movement	“Direct Thrombin Inhibitor”	“Thrombosis/prevention and control”
Mobility	Warfarin	“Antithrombins”
Immobilization	“VKA therapy”	“NOAC therapy”
Immobilisation	“Coumadin”	“DOAC therapy”
“Mobility Limitation”	Heparin	“Citric Acid”
“Motor Activity”	“low molecular weight	“Heparinoids”
“Early Ambulation”	heparin”	“Heparin, low-molecular-weight”
“Early Activization”	Fondaparinux	“Vitamin K/antagonists and inhibitors”
“Early Activisation”	Idraparinux	“Antithrombin Proteins”
“Early Mobilization”	Enoxaparin	“Fibrinolytic Agents”
“Early Mobilisation”	International Normalized	“Antithrombotic therapy”
Anticoagulants	Ratio	“International Normalized Ratio”
Anticoagulant	“INR”	“Prothrombin Time”
Anticoagulation	“Prothrombin Time”	“Vena Cava Filters”
Antithrombotic therapy	Vena Cava Filter	“Intermittent Pneumatic Compression
Dabigatran	“Umbrella filter”	Devices”
Desirudin	Intermittent Pneumatic	“Stockings, Compression”
Ximelagatran	Compression Devices	"Embolic Protection Devices"
Edoxaban	“Compression Stockings”	
	“Compression Socks”	
	“Compression Hose”	
	“Compression Hosiery”	

**Databases searched: PubMed, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Physiotherapy Evidence Database (PEDro).*

Table 3. Levels of Evidence[22]

Level	Level Criteria
I	Evidence obtained from high-quality diagnostic studies, prognostic or prospective studies, cohort studies or randomized controlled trials, meta-analyses or systematic reviews (critical appraisal score 50% of criteria)
II	Evidence obtained from lesser-quality diagnostic studies, prognostic or prospective studies, cohort studies or randomized controlled trials, meta-analyses or systematic reviews (eg, weaker diagnostic criteria and reference standards, improper randomization, no blinding, 80% follow-up) (critical appraisal score 50% of criteria)
III	Case-controlled studies or retrospective studies
IV	Case studies and case series
V	Expert opinion

Table 4. Grades of Recommendation for Action Statements[22]

Grade Recommendation	Quality of Evidence
A – Strong	A preponderance of level I studies but at least 1 level I study directly on the topic support the recommendation.
B - Moderate	A preponderance of level II studies but at least 1 level II study directly on the topic support the recommendation.
C - Weak	A single level II study at 25% critical appraisal score or a preponderance of level III and IV studies, including statements of consensus by content experts support the recommendation.
D- Theoretical/ Foundational	A preponderance of evidence from animal or cadaver studies, from conceptual/theoretical models/principles, or from basic science/bench research, or published expert opinion in peer reviewed journals supports the recommendation.
P – Best Practice	Recommended practice based on current clinical practice norms, exceptional situations where validating studies have not or cannot be performed and there is a clear benefit, harm, or cost, and/or the clinical experience of the guideline development group.
R - Research	There is an absence of research on the topic, or higher-quality studies conducted on the topic disagree with respect to their conclusions. The recommendation is based on these conflicting conclusions or absent studies.

Table 5. Status Definitions[22]

New; not in prior version
Upgraded with new evidence
Downgraded with new evidence
Revised and updated
Revised; no new evidence
Reaffirmed and updated
New; not in prior version
Reaffirmed; no new evidence

Table 6. Padua Prediction Score[40]

Baseline Features	*Score*
Active cancer[1]	3
Previous VTE (excluding superficial vein thrombosis)	3
Reduced mobility[2]	3
Already known thrombophilic condition[3]	3
Recent (≤1 mo) trauma and/or surgery	2
Elderly age (≥70 y)	1
Heart and/or respiratory failure	1
Acute MI or Ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI ≥ 30)	1
Ongoing hormonal treatment	1
High Risk of VTE	*≥ 4*

[1]Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 mo.
[2]Anticipated bed rest with bathroom privileges (either because of patient's limitations or on physician's order) for at least 3 d.
[3]Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome.

Table 7. Khorana risk score[52, 53]

Patient Characteristics	Risk Score
Site of Cancer	
Very high risk (stomach, pancreas)	2
High risk (lung, lymphoma, gynecological, bladder, or testicular)	1
Pre-chemotherapy platelet count ≥ 350 x 10^9 /L	1
Pre-chemotherapy hemoglobin level < 100 g/dL or use of red cell growth factors	1
Pre-chemotherapy leukocyte count ≥ 11 x 10^9 /L	1
Body Mass Index ≥35 kg/m^2	1

Table 8. Wells DVT Likely Scale[70, 71]

Clinical Feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	−2
Clinical probability simplified score	
DVT 'likely'	2 points or more
DVT 'unlikely'	Less than 2 points

Table 9. The Revised Geneva Clinical Prediction Rule for Pulmonary Embolism[185]

Variable	Original Version	Simplified Version
Age > 65 yrs	1	1
Previous DVT or PE	3	1
Surgery (under general anesthesia) or Fracture (of lower limb) within 1 month	2	1
Active malignant condition (solid or hematologic, currently active or considered cured < 1 year)	2	1
Unilateral lower-limb pain	3	1
Hemoptysis	2	1
Heart rate 75 – 94 ≥ 95 bpm	 3 2	 1 1
Pain on lower-limb deep venous palpation and unilateral edema	4	1

Original Version: Low probability 0-3, Intermediate 4-10, and High ≥ 11.
Simplified Version: Low probability 0-1, Intermediate 2-4, and High ≥ 5.

Table 10. Current Anticoagulation Options for VTE Treatment and Prevention[95-99, 102-105, 135]

Classifications and Mechanism of Action	Medication Names	Dosage and Method of Delivery	Peak Therapeutic Levels and Monitoring	PT Considerations
Unfractionated Heparin (UFH):[102] binds and activates antithrombin (through a high-affinity pentasaccharide) causing inactivation of thrombin and factor Xa and IXA	Heparin	Delivery: IV Dose: Bolus 80 units/kg followed by infusion of 18 units/kg/hr	>24 hours Monitor: aPTT (needs to be 1.5-2.5 times the control value (seconds) and/or check with medical team	Patients are given heparin due to renal dysfunction or presence of mechanical valve. Occasionally heparin is used in low risk PE or proximal DVT. Assess chart to determine reason for use of Heparin
Low Molecular Weight Heparins (LMWH):[97-99, 102] binds and activates antithrombin (via unique pentasaccharide sequence) causing inactivation of thrombin and factor Xa and IXA	Lovenox (*enoxaparin*) Innohep (*tinzaparin sodium*) Fragmin (*dalteparin*)	Delivery: Subcutaneous injections Prophylactic dose: 30-40 mg q 12-24 hr Therapeutic dose: 1-1.5 mg/kg q 12-24 hr	3-5 hours Monitor: anti-factor Xa (peak level between 0.6 – 1.0 IU/mL if receiving 2x/day; 1.0-2.0 IU/mL if reeiving 2x/day) or aPTT (see above)	Primary drug of choice for patient with active CA or undergoing CA treatment, genetic blood factor history, pregnancy, or low risk PE. Patient or caregiver must be able to give shots.
Fondaparinux (synthetic drug):[102, 135] selectively binds to antithrombin III resulting in Factor Xa inhibition	Arixtra	Delivery: subcutaneous injections Prophylactic Dose: 2.5 mg/day Therapeutic Dose: 5-10 mg/day (based on weight)	2-3 hours Monitor: not indicated but anti-factor Xa could be used	Similar to LMWH, often used for those with history of HIT or undergoing surgical procedure and requires prophylaxis. Patient and/or caregiver must be able to give shots.
Vitamin K antagonists:[95, 96, 99, 102, 135] inhibits the synthesis of vitamin K-dependent clotting factors, especially the C1	Coumadin (*warfarin*)	Delivery: oral Dose: individualized based upon individual's INR	No timeline Monitor: INR to achieve 2-3	Not a first line drug for VTE so not important with early mobility Crosses the blood brain barrier increasing risk for

subunit of vitamin K epoxide reductase (VKORC1) enzyme complex		response to drug		intracranial or subdural hemorrhages Frequent blood monitoring required for INR levels (every 4-6 weeks)
Direct Oral Thrombin Inhibitor (Direct Oral Anti-coagulant; DOAC):[104, 105] directly inhibits thrombin	Pradaxa (*dabigatran*)	Delivery: oral Dose: 150 mg bid	2 hours Monitor: none necessary	No blood monitoring < risk of brain bleed than oral vit K antagonists Drug interactions not yet tested in newer medications
Direct Oral Xa Inhibitors (Direct Oral Anti-coagulant; DOAC):[104, 105] direct inhibition of factor Xa.	Xarelto (*rivaroxaban*) Eliquis (*apixaban*) Savaysa (*edoxaban*)	Delivery: oral Xarelto Dose: 15 mg bid for first 21 days, 20 mg qd after day 21 Eliquis dose:10 mg bid for 7 days then 5 mg bid; 60 mg daily (30 mg for renal impairment)	2-3 hours Monitor: none necessary	No blood monitoring < risk of brain bleed than oral vit K antagonists Increased usage of these drugs in orthopedic population Drug interactions not yet tested in newer medications

Table 11. Long Term Medical Management of Venous Thromboembolism

Intervention	Factors
Low Molecular Weight Heparin	Utilized as primary long term medication for VTE in patients with cancer
Direct Acting Oral Anticoagulant	Easier to use for long term treatment than LMWH in non-cancer patients due to oral versus injection
Coumadin	The INR levels should be between 2-3 for mobilization. If outside of this range, consult with medical team about mobilization
Inferior Vena Cava Filter	Once filter is in place and the person is stable, can mobilize. Person may also be on anticoagulant with filter

Table 12. Risk Factors of Increased Bleeding[100, 101]

Active bleeding
Acute stroke
Acquired bleeding disorders (such as acute liver failure)
Concurrent use of anticoagulants known to increase the risk of bleeding (i.e. warfarin with an INR >2)
Lumbar puncture/epidural/spinal anesthesia expected to be given within next 12 hours
Thrombocytopenia (platelets less than 7,500)
Uncontrolled systolic hypertension (defined as BP of 230/120 mm Hg or higher)
Untreated inherited bleeding disorders such as hemophilia or von Willebrand's disease

Table 13. Classification of PE and Risk of Early (in-hospital or 30 day) Death[18]

Early Mortality Risk		Indicators of Risk			
		Hemodynamic Instability[1]	Clinical Parameters of PE Severity and/or Comorbidity: PESI class III-IV OR sPESI >/= 1	RV dysfunction on TTE or CTPA[2]	Elevated Cardiac Troponin Levels[3]
High		+	+[4]	+	+
Intermediate	Intermed -High	-	+[5]	+	+
	Intermed - Low	-	+[5]	One (or none) positive	
Low		-	-	-	Assessment optional: if assessed, negative

BP = blood pressure; CTPA = computed tomography pulmonary angiography; H-FABP = heart-type fatty acid-binding protein; NT-proBNP = N-terminal pro B-type natriuretic peptide; PE = pulmonary embolism; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; sPESI = simplified Pulmonary Embolism Severity Index; TTE = transthoracic echocardiogram.

1 - One of the following clinical presentations : cardiac arrest, obstructive shock (systolic BP <90 mmHg or vasopressors required to achieve a BP >_90 mmHg despite an adequate filling status, in combination with end-organ hypoperfusion), or persistent hypotension (systolic BP <90 mmHg or a systolic BP drop >_40 mmHg for >15 min, notcaused by new-onset arrhythmia, hypovolaemia, or sepsis).

2 - Prognostically relevant imaging (TTE or CTPA) findings in patients with acute PE, and the corresponding cut-off levels

3 - Elevation of further laboratory biomarkers, such as NT-proBNP >_600 ng/L, H-FABP >_6 ng/mL, or copeptin >_24 pmol/L, may provide additional prognostic information. These markers have been validated in cohort studies but they have not yet been used to guide treatment decisions in randomized controlled trials.

4 - Haemodynamic instability, combined with PE confirmation on CTPA and/or evidence of RV dysfunction on TTE, is sufficient to classify a patient into the high-risk PE category. In these cases, neither calculation of the PESI nor measurement of troponins or other cardiac biomarkers is necessary.

5 S- igns of RV dysfunction on TTE (or CTPA) or elevated cardiac biomarker levels may be present, despite a calculated PESI of III or an sPESI of 0.234 Until the implications of such discrepancies for the management of PE are fully understood, these patients should be classified into the intermediate-risk category

TABLE 14. Definition of Hemodynamic Instability[18]

Cardiac Arrest	**Obstructive Shock**	**Persistent hypotension**
Need for cardiopulmonary resuscitation	Systolic BP < 90 mm Hg or vasopressors required to achieve a BP ≥ 90 mm Hg despite adequate filling status	Systolic BP < 90 mm HG or systolic drop ≥ 40 mm Hg, lasting longer than 15 minutes and not caused by new onset arrhythmia, hypovolemia, or sepsis
	and	
	End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate	

Table 15. Risk of Recurrent VTE[18]

Estimated Risk for Long Term VTE recurrence ≥ 3 Months Post Medication Discontinuation	Risk factor category for Index PE
Low (<3%/year)	Major transient or reversible factors associated with > 10 fold increased risk for the index VTE event (compared to patients without the risk factor). Examples: • Surgery w/anesthesia for > 30 minutes • Confined to bed in hospital for ≥ 3 days due to an acute illness or acute exacerbation of a chronic illness • Trauma with fractures
Moderate/intermediate (3-8%/year)	Transient or reversible factors associated with ≤ 10 fold increased risk for first index VTE • Minor surgery • Admission to hospital for < 3 days with acute illness • Estrogen Therapy • Leg Injury w/o fracture associated with reduced mobility for > 3 days • Long air flight Non-malignant persistent risk factors * Inflammatory bowel disease * Active autoimmune disease No **identifiable** risk factor
High > 8%/year	*Active cancer *One or more episodes of VTE previously in absence of major transient or reversible factor *Antiphospholipid antibody syndrome

FIGURES

Figure 1. Actions for a Suspected Upper or Lower Extremity Deep Vein Thrombosis[68, 70, 75]

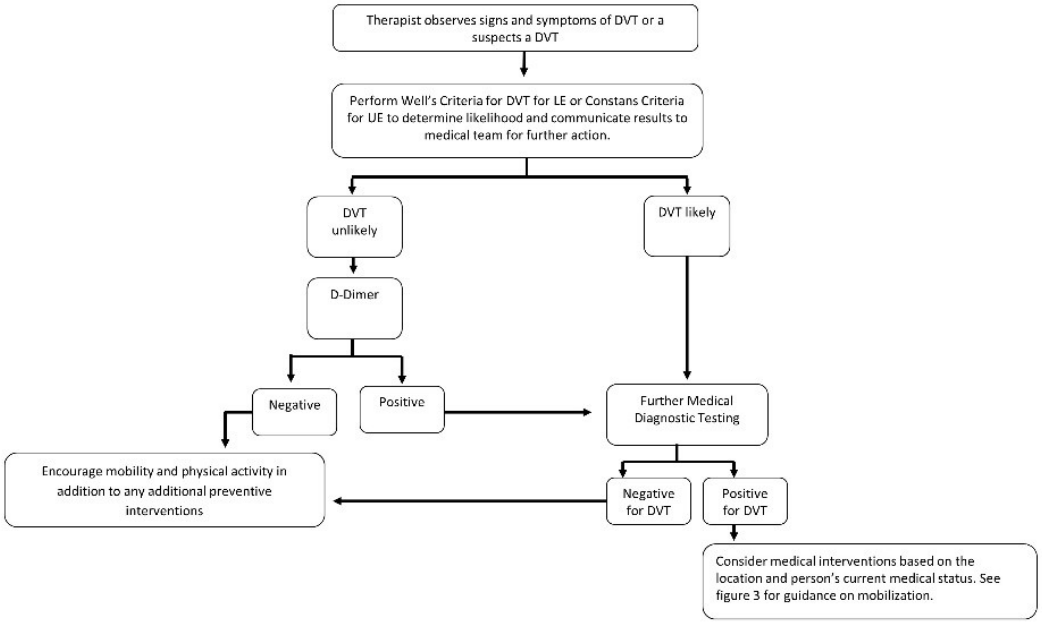
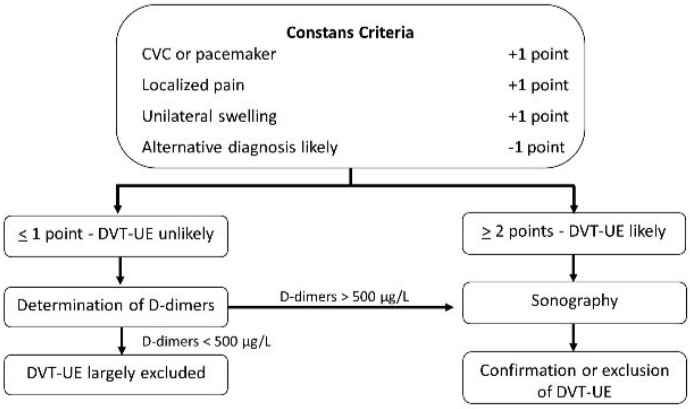
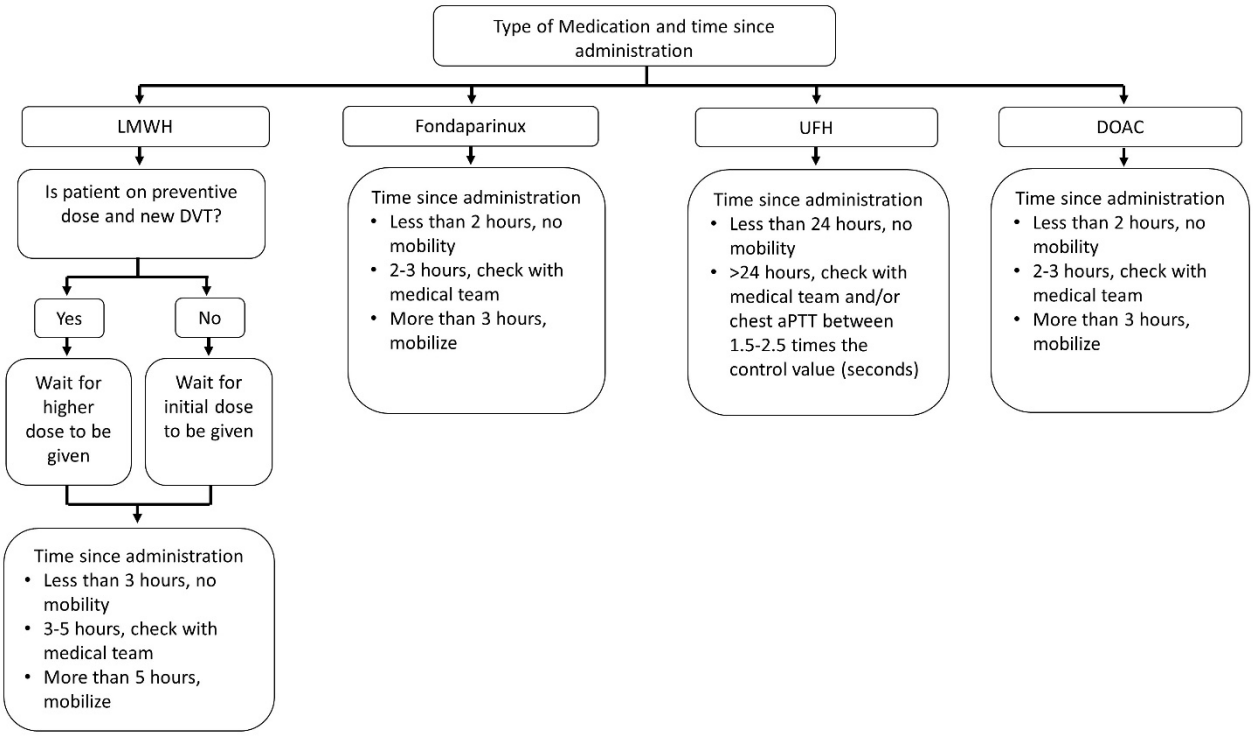


Figure 2. Constans Criteria[91]



Diagnostic algorithm based on the Constans criteria. CVC, central venous catheter; DVT-UE, deep vein thrombosis of the upper extremity D-dimers >500 µg/L D-dimers

Figure 3. Mobilization with an Acute UE or LE DVT Based on Anticoagulant and Time Since Administration[95-99, 102-105, 135]



Algorithm for mobilizing patients with acute upper or lower extremity deep vein thrombosis based on anticoagulant and time since administration. DVT = deep vein thrombosis, LMWH = low-molecular weight heparin, UFH = unfractionated heparin, DOAC = direct acting oral anticoagulants. aPTT = activated partial thromboplastin time. See **Table 11** for long term medical management interventions

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