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## **[H1]Abstract**

No matter the practice setting, physical therapists work with patients who are at risk for or who have a history of venous thromboembolism (VTE). In 2016, the first clinical practice guideline (CPG) addressing the physical therapist management of VTE was published with support by the American Physical Therapy Association's (APTA) Academy of Cardiovascular and Pulmonary Physical Therapy and Academy of Acute Care, with a primary focus on lower extremity deep vein thrombosis (DVT). This CPG is an update of the 2016 CPG and contains the most current evidence

available for the management of patients with lower extremity DVT (LE DVT) and new key action statements (KAS) including guidance on upper extremity DVT (UE DVT), pulmonary embolism (PE), and special populations. This document will guide physical therapist practice in the prevention of and screening for VTE and in the management of patients who are at risk for or who have been diagnosed with VTE. Through a systematic review of published studies and a structured appraisal process, KAS were written to guide the physical therapist. The evidence supporting each action was rated, and the strength of statement was determined. Clinical practice algorithms based upon the KAS were developed that can assist with clinical decision making. Physical therapists, along with other members of the health care team, should implement these KAS to decrease the incidence of VTE, improve the diagnosis and acute management of VTE, and reduce the long-term complications of VTE.

## **[H1]Introduction**

### **[H2]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), typically 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,<sup>1</sup> and those with a diagnosis of PE have a mortality rate of 4.9% over the first 30 days after diagnosis.<sup>2</sup>

In addition to the acute risk of death, one-third to one-half will have long-term complications such as postthrombotic syndrome (PTS) or chronic thromboembolic pulmonary hypertension (CTEPH).<sup>1</sup> 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, and 36% will have a repeat VTE within the following 10 years.<sup>3</sup>

In 2016, the first clinical practice guideline (CPG) addressing the physical therapist management of VTE was published with support from APTA's Academy of Cardiovascular and Pulmonary Physical Therapy and the Academy of Acute Care, which focused primarily on LE DVT.<sup>4</sup> Beginning in 2019, the VTE 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 to add new key action statements (KAS) 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 CPGs on prevention, risk factors, and screening for VTE and its secondary clinical consequences. The updated CPG contains 19 KAS (Tab. 1), with 3 additional figures and 15 tables. This CPG is intended to be used as a reference document to guide physical therapist practice in the prevention of, screening for, and treatment of adult patients in all practice settings at risk for 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 initiation 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 are present.
- Assist clinicians in making appropriate referrals for medical management of long-term 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 or diagnosed with VTE.

## **[H1]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 extremities. Upper extremity DVT (UE DVT) is included in the current update due to the rise in incidence, which is likely related to the increased use of central venous catheters, peripherally inserted central catheters and cardiac pacemakers.<sup>5</sup> The risk factors for thrombosis formation are best described through Virchow's Triad of vascular stasis, endothelial injury, and/or hypercoagulability.<sup>6</sup> These factors can trigger the coagulation cascade and the formation of a blood clot.<sup>7</sup>

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.<sup>8-10</sup> It has been shown that 45% to 80% of symptomatic VTE events occur after hospital discharge. Length of prophylactic medication can vary based on the medical diagnosis. For example, according to the recommendations in the British National Institute for Health and Care and Excellence (NICE) Guidelines on reducing risk of hospital acquired VTE, prescription length should be during periods of inactivity for nonsurgical patients, 7 days for acutely ill medical patients, and 28 days for elective hip replacement surgery. Yet even if individuals are on anticoagulant medications, a clot can still progress, and the process of breaking down a 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 pulmonary embolism (PE). This complication occurs when the clot dislodges, travels through the venous system, through the right side of the heart, and causes a blockage in the pulmonary circulatory system. Severity of PE is classified by the American Heart Association based on clinical symptoms and degree of right ventricular involvement as massive, submassive, and non-massive<sup>11</sup>; whereas the European Society of Cardiology (ESC) classifies PE as high, intermediate (low and high intermediate) and low risk.<sup>12</sup> 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 and its sequelae, LE DVT may lead to long-term complications of PTS. Postthrombotic syndrome (PTS) develops in 20% to 50% of patients presenting with a LE DVT even when an appropriate anticoagulant is used.<sup>13, 14</sup> 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.<sup>15</sup> These symptoms include chronic aching pain, intractable edema, limb heaviness, and leg ulcers.<sup>16</sup> 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.<sup>16</sup>

In those who survive PE, significant cardiopulmonary morbidity can occur, most notably CTEPH, but the incidence of CTEPH is relatively low (approximately 1%–2%).<sup>17</sup> 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.<sup>18</sup> 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.<sup>19-21</sup> Chronically, the vascular tissue becomes fibrotic which causes a fixed mechanical obstruction and results in reduced vascularization and concomitant pulmonary hypertension.<sup>18</sup> Over time, the workload imposed on the right heart increases and contributes to right heart dysfunction and then failure.<sup>12, 16, 17</sup> Chronic thromboembolic pulmonary hypertension involves symptoms of dyspnea/shortness of breath (especially with exertion), fatigue, swelling of legs, dizziness, fainting, chest tightness with exertion and sometimes palpitations.<sup>12, 16, 19-21</sup>

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) prevent VTE, (2) assess for UE and LE DVT and PE, (3) contribute to the health care team in decision making regarding initiation of safe mobility for these patients, (4) educate patients and share decision making, and (5) prevent 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.

## [H2]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 LE 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 did guide clinicians' practice (74.2% agreed and 21% said somewhat guided their practice), and that more information was needed on: management of pulmonary embolism and upper extremity DVT, decision making based on the location of VTE, exercise prescription and progression for those with VTE, efficacy and prescription of compression, and management of persons with VTE who are not anticoagulated.

Based on this feedback, the GDG's own analysis of new findings in the literature (including updated CPGs on VTE by other organizations), and contemporary physical therapist practice, the GDG determined that the revised CPG should focus on the following areas: (1) update the previous KAS in the 2016 VTE CPG by combining some of the statements as appropriate, (2) address screening and management of those with PE, (3) address screening and management of those with UE DVT, (4) provide more guidance on management of those who are not prescribed anticoagulation and (5) include adult special populations (age >17 years) but not the pediatric population (age <18 years). Literature from January 2015 to February 2021 was reviewed with an emphasis on other CPGs, systematic reviews, meta-analyses, and randomized controlled trials (RCTs).

This CPG led to 19 KAS with mixed updates from the 2016 KAS and the new KAS. Ten of the KAS were carried over from the 2016 CPG with 2 of them being reaffirmed with no new literature, 4 reaffirmed with new literature, 3 revised and updated with new literature and 1 downgraded with new literature. There are 9 KAS that were not included in the 2016 KAS.

## [H2] 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 KAS 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.

## [H1]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, 2 of whom were involved in the original guideline. This revision of the 2016 CPG includes an updated literature review of LE DVT since the original publication date of 2015, as well as a literature review of PE, UE DVT, and special populations with coagulopathies.

### [H2]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.<sup>4</sup> 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 1559 articles and determined which articles represent new or updated information on the key topics. There were a number of systematic reviews, meta-analyses, and CPGs that covered the main focus of our action statements and, thus, dramatically reduced the number of articles that needed to be sent out for external review. In the end, 24 publications were sent out for external review and used to determine the level of evidence of our action statements.

### [H2]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.<sup>4</sup> 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 quality 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: (1) Assessment of Multiple Systematic Review (AMSTAR) tool for systematic reviews, (2) Appraisal of Guidelines for Research and Evaluation (AGREE II) for CPGs, and/or (3) APTA Critical Appraisal Tool for Experimental Intervention Studies (CAT-EI) for intervention studies.

## [H2]Levels of Evidence and Grades of Recommendations

The GDG followed a previously published process on developing physical therapy CPGs.<sup>22</sup> 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 KAS 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: (1) new; not in prior version, (2) upgraded with new evidence, (3) downgraded with new evidence, (4) revised and updated, (5) revised; no new evidence, (6) reaffirmed and updated, (7) new; not in prior version, (8) reaffirmed; no new evidence. Under each statement is a summary which provides 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.

## [H2]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 (Suppl. Appendix 2).

## [H2]External Review Process by Stakeholders

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

## [H2]Role of the Funding Source

The funders had no influence on the content or the key action statements of this CPG.

## [H1]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/>).<sup>23</sup> 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 KAS.

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## [H1]Key Action Statements With Supporting Evidence

### [H1]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)**

#### [H2]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 1 level I on topic supports recommendation.

**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.

#### [H2]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.<sup>24</sup> 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.<sup>24</sup> A 2020 systematic review found that ambulation decreased the rate of VTE in patients who are

hospitalized, but acknowledged difference in how ambulation and mobility are defined and mixed results on the effectiveness of ambulation in higher quality studies.<sup>25</sup> 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.<sup>26</sup> 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 as a way to decrease the risk of VTE.

While mobility has benefits, medication for prophylaxis still has an important role in preventing VTE. In a systematic review of 9 studies and 20,000 patients who were hospitalized, prophylaxis reduced the rate of symptomatic VTE in at-risk hospitalized medical patients without increasing major bleeding.<sup>27</sup> Best results are found when medication is combined with mobility. In a combined medication and ambulation study, ambulation was indicated for VTE prevention, the incidence of VTE was significantly lower when patients received enoxaparin in comparison to a placebo medication.<sup>28</sup> The importance of combining medication with activity for patients who are hospitalized is also stressed in a 2020 systematic review.<sup>25</sup>

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 bed rest 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<sup>29</sup> and that the exact amount of mobility needed to decrease the risk of VTE remains unknown.

## [H1]Action Statement 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)**

### [H2]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 1 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 risk assessment models (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 physical therapist 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:** Health care systems can implement RAMs across their system.

### [H2] Supporting evidence and clinical interpretation

As stated in the original VTE CPG, the physical therapist examination includes comprehensive screening and specific testing leading to diagnostic classification or, as appropriate, a referral to another practitioner.<sup>30</sup> 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 having 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.<sup>31</sup> 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.<sup>24, 32-36</sup>

The NICE guidelines on VTE states all patients should be assessed for risk of VTE using a standardized tool.<sup>24</sup> Risk assessment models 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, the Department of Health VTE risk assessment tool,<sup>24</sup> IMPROVE VTE RAM,<sup>37</sup> the Autar DVT Risk Assessment Scale,<sup>38</sup> and the Geneva Risk Score,<sup>39</sup> but did not recommend a specific tool. In the current update, the CPG committee has agreed on recommendations for preferred RAM usage.

The Padua Prediction Score ([PPS], Tab. 5) is favored for VTE risk assessment of all patients who are hospitalized based on recommendation in the ACCP guidelines.<sup>33</sup> The PPS is recommended because it requires minimal time to implement while still providing the best available risk assessment of those who are hospitalized.<sup>36</sup> In this RAM, points are assigned to baseline features increasing the patient's risk of VTE categorizing a patient as either high ( $\geq 4$  points) or low ( $< 4$  points) risk of VTE.<sup>40</sup> The PPS has been validated in patients who are non-ambulatory and is appropriate for use with patients who are hospitalized. 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.<sup>41</sup> 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  $\geq 10$  points identifies a patient as high risk and  $\leq 9$  is considered low risk.<sup>42</sup> 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.<sup>42, 43</sup> 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.

### **[H1]Action Statement 3: Assess for additional risk factors of VTE in all high-risk patients**

**When a patient presents with conditions (ie, 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)**

#### **[H2]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.



this group.<sup>52</sup> The Khorana score, shown in Table 6, allocates points based on 5 clinical and pre-chemotherapy laboratory values: (1) primary tumor site, (2) platelet count, (3) hemoglobin concentration or the use of erythropoiesis-stimulating agents, (4) leukocyte count, and (5) body mass index (BMI).<sup>52,53</sup> Based on points accumulated, patients are put into a low-risk, intermediate-risk, or high-risk category. The Khorana score has been validated to identify high risk ambulatory patients with cancer 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.<sup>53</sup> This shows that while this score helps to identify those at the highest risk, individuals in the intermediate and low-risk categories 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 (ie, antithrombin, factor V Leiden, and others) and acquired thrombophilia (ie, antiphospholipid syndrome).<sup>31,36</sup> Factor V Leiden mutation, for example, is present in 5% of the population and carries a 3- to 8-fold increased risk of VTE.<sup>50</sup> While these groups are also represented in the PPS, 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 RAMS 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)<sup>54</sup> likely due to the cytokine storm from a hyperactive immune response and profound systemic inflammation.<sup>55-57</sup> Even with the use of prophylactic anticoagulation, VTE has been reported in 27% of patients hospitalized with severe COVID-19.<sup>58</sup> In addition, the risk of PE in patients who are hospitalized with COVID-19 has been reported to be more than double compared to patients in the ICU with influenza.<sup>59</sup> 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 experiencing and recovering from COVID-19.<sup>54</sup>

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.<sup>60,61</sup> 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.<sup>62</sup> Hispanic and African American children under the age of 21 years are at highest risk, with most cases falling between the ages of 3 to 12 years old.<sup>63</sup> 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 (fever, rash, swelling of the hands and feet, irritation, and redness of the whites of the eyes, swollen lymph glands in the neck, and irritation and inflammation of the mouth, lips, and throat). This condition can progress to myocarditis, cardiogenic shock, toxic shock syndrome, and macrophage activation syndrome.<sup>64</sup> 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.

### **[H1]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, exercise, hydration, mechanical compression, and referral for medical treatment. (Evidence Quality: I; Recommendation Strength: B - Moderate)**

#### **[H2]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 1 level I on topic supports recommendation.

**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.

#### **[H2] Supporting evidence and clinical interpretation**

This KAS maintains the same level of evidence and strength with additional support from other updated CPGs. In the updated ACCP Guidelines<sup>33</sup> there were no changes from their 2012<sup>65</sup> recommendation on prevention. The 2018 NICE Guideline<sup>66</sup> established guidance on reducing the risk of hospital-acquired VTE that was then updated again in 2019.<sup>24</sup> 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 KAS 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.<sup>24</sup>

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.

## [H1]Action Statement 5: Establish likelihood of LE DVT when a patient presents with symptoms

**When a patient presents with pain, tenderness, swelling, warmth and/or discoloration in the lower extremity, establish the likelihood of a LE DVT and take appropriate action based on results. (Evidence Quality I; Recommendation Strength: A – Strong)**

### [H2]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 1 level I on topic supports recommendation.

**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:** Health care systems can implement likelihood assessment tools across their system. The screening tool is published in this document (Tab. 7) and available in online calculator formats (ie, <https://www.mdcalc.com/wells-criteria-dvt>).

### [H2]Supporting evidence and clinical interpretation

The recommendation for screening of LE DVT has not changed from the original VTE CPG published in 2016.<sup>4</sup> There have 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.<sup>67-69</sup> The ACCP Guidelines<sup>68</sup> recommend the use of a standardized tool to take the clinical features indicative of LE DVT and determine the likelihood of the VTE; the Wells criteria continues to be the most well-studied prediction tool.<sup>68, 70-72</sup> For these reasons, the GDG recommends the use of the Wells criteria (Tab. 7) 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 categories.<sup>68</sup> 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.<sup>72,73</sup> The “I-DVT” clinical decision rule was 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.<sup>74</sup>

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.

### **[H1]Action Statement 6: Establish the likelihood of UE DVT when patient presents with symptoms**

**When a patient present with clinical symptoms including swelling, pain, edema, cyanosis and/or dilation of superficial veins, establish the likelihood of UE DVT and take appropriate action based on results. (Evidence Quality II; Recommendation Strength: B – Moderate)**

#### **[H2]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 1 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:** Health care systems can implement likelihood assessment tools across their system. The screening tool is published in this document (Fig. 2).

## [H2]Supporting evidence and clinical interpretation

Deep vein thrombosis of the UE can develop in any of the deep veins of the UE including both proximal (ie, subclavian, axillary) and distal (ie, brachial, ulnar and radial) veins.<sup>5</sup> Historically, UE DVTs are less common than LE DVTs, but the prevalence is increasing related to the frequent use of indwelling central venous catheters.<sup>5</sup> 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.<sup>75</sup> Similar to LE DVT, a DVT in the UE carries the risk of traveling to the lungs. Constans et al<sup>75</sup> reported approximately 20% of patients diagnosed with UE DVT are complicated by pulmonary embolism. In addition to the acute risk of PE, approximately 25% of patients with UE DVT will develop PTS.<sup>75</sup> The major signs and symptoms of UE DVT are due to venous congestion and include swelling, pain, edema, cyanosis, and dilation of superficial veins.<sup>5</sup> These clinical signs are not always present and many cases of UE DVT (33% to 60%) are asymptomatic and can go undetected.<sup>5</sup>

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 4 points of evidence: (1) presence of central venous catheter, (2) pacemaker or internal cardiac defibrillator, (3) localized pain, unilateral edema, and (4) whether another diagnosis is plausible (Fig. 2).<sup>76</sup> Kleinjan et al<sup>77</sup> added determination of D-dimers to increase the negative predictive accuracy of an “unlikely” categorization by Constans criteria. In a multicenter 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.<sup>77</sup> 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 diagnostic 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.<sup>5</sup>

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  $< 500 \mu\text{g/L}$ , physical therapists should feel confident that a UE DVT is largely excluded. However, if the D-dimer is  $>500 \mu\text{g/L}$  then sonography should be performed. If the Constans criteria indicates that a UE DVT is likely, the D-dimer should be skipped, and sonography should be performed prior to initiating mobility.

**[H1]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)**

## [H2] 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 1 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:** Assists the physical therapist in a more accurate screening tool for appropriate referral.

**Implementation and Audit:** Health care systems can implement likelihood assessment tools across their system. The screening tool is published in this document (Tab. 8) and available in online calculator formats (<https://www.mdcalc.com/geneva-score-revised-pulmonary-embolism>).

## [H2] Supporting evidence and clinical interpretation

The clinical presentation of PE can be evasive because the symptoms can be variable and non-specific, but accurate diagnosis is critical given the risk of death.<sup>12</sup> Long et al<sup>78</sup> reported mortality rates of missed, untreated PE as high as 26%. The most common symptoms of acute PE include dyspnea, chest pain, pre-syncope or syncope, or hemoptysis.<sup>12,79,80</sup> 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.<sup>79</sup>

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.<sup>12,81</sup> Despite reports of the accuracy of implicit clinician opinion, this process lacks standardization leading to the development of clinical prediction rules for PE.<sup>81,82</sup> Clinical prediction rules allow clinicians to determine pretest probability of PE, but these scores alone do not diagnose or rule in the condition. A high probability of PE determined by a clinician requires imaging (ie, computed tomographic pulmonary angiography) to confirm PE.<sup>83</sup>

There are several clinical prediction rules that have been utilized and validated to determine the probability of PE including Wells score, Geneva score, YEARS rule, Miniati score, and Charlotte rule.<sup>84,85</sup> The 2019 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 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.<sup>12</sup>

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 (Tab. 8). 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 to 1 point, intermediate probability as 2 to 4 points, and high probability as  $\geq 5$  points. In 2 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.<sup>86,87</sup> 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.<sup>88</sup> The PERC utilizes 8 clinical features highly associated with the absence of PE including age < 50 years, pulse < 100 bpm, SaO<sub>2</sub> > 94%, no unilateral leg swelling, no hemoptysis, no recent trauma or surgery, no history of VTE, and no oral hormone use.<sup>12,89</sup> When all 8 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.<sup>89</sup> 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.<sup>12,87</sup> 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.

### **[H1] 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)**

## [H2] Action statement profile

**Level of Evidence (I-V):** Level 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 therapist interventions.

**Implementation and Audit:** A review of medical interventions should be a standard part of physical therapy management.

## [H2] Supporting evidence and clinical interpretation

After diagnosis of 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 supporting 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.<sup>33</sup> They are also commonly prescribed for UE DVT and PE.<sup>18,33,90,91</sup> 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 as when hypotension is present during a massive pulmonary embolism.<sup>33</sup>

If an individual is already on an anticoagulant, often at a lower dose (prophylactic dosage which is often half the normal strength dosage) and develops a VTE, then oftentimes the medical team will prescribe the full strength dosage of the medication (or another) and the physical therapist should wait the appropriate time frame for the new medication before initiating mobilization.

There may be a concern with the prescription of anticoagulants, especially Warfarin (Coumadin), for individuals with poor balance given their risk for a fall and then experiencing a major bleed

event. The issue of falls and major bleeds should be considered, especially in populations at high risk for falls, such as aging adults. When looking at individuals who have atrial fibrillation and are commonly prescribed anticoagulants, the benefits of being on an anticoagulant and preventing a stroke outweigh the risk of a fall and major bleed.<sup>92-94</sup> A 2020 review on oral anticoagulation for atrial fibrillation and VTE in the elderly stated that while anticoagulants have risks, the benefits outweigh those risks.<sup>95</sup> This review also recommended DOACs due to the lower risk of intracranial bleeding. Based on this evidence, there should be very few reasons that an individual, even if they are at a fall risk, are not placed on anticoagulants following a VTE diagnosis. If a physical therapist finds anticoagulants are being withheld, further discussion with the medical team should take place.

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.<sup>33</sup> It can also be used with an UE DVT or PE when severe symptoms are present.<sup>18, 91</sup> 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.<sup>18, 33</sup> If the person shows signs of right ventricular failure, mechanical ventilation, extracorporeal membrane oxygenation (ECMO), volume optimization, vasopressors, and inotropes may be needed.

If a person with LE DVT cannot be on anticoagulants, 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 can break it down. IVC filters are not typically recommended, but might be used in unique situations.<sup>18</sup> More details on IVC filters and mobilization are in Action Statement 13.

There may be a situation in which a person who already has an IVC filter in place develops a LE DVT. In those situations, the filter will prevent that clot from traveling to the lungs or brain. These individuals would be safe to immediately mobilize. However, it is important to note that an IVC filter would not protect against a UE DVT traveling to the lungs or brain. In that situation, therapists would follow the guidance in Action Statement 11.

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

### **[H1]Action Statement 9: Confirm pharmacological management**

**When a patient presents 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)**

#### **[H2]Action statement profile**

**Level of Evidence (I-V):** Level IV – Case studies and case series.

**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 Fig.1 and Fig. 3).

## [H2] 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 and 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.<sup>33</sup> Anticoagulation should be initiated as soon as possible.<sup>24, 33, 96-99</sup>

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.<sup>100-102</sup> Anticoagulants do not actively degrade the clot, but rather allow the body's natural clot lysis mechanisms to break down the thrombus. For example, low molecular weight heparin (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.<sup>100-102</sup>

Therefore, prior to initiating mobility out of bed, a physical therapist should review all medications each patient is prescribed. The physical therapist 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 physical therapists do not play a role in recommending the anticoagulant of choice, physical therapists should initiate mobility when the anticoagulant that is prescribed has achieved therapeutic level based on the time since initiation.<sup>42</sup>

The current options for anticoagulation include unfractionated heparin (UFH), LMWH, direct oral Xa inhibitors (DOACs), Fondaparinux (Arixtra; an indirect inhibitor of factor Xa or Argatroban), and warfarin (Coumadin, which is a vitamin K antagonist) (see Tab. 9).<sup>100</sup> Individuals should continue with their anticoagulant for 3 to 6 months following the first episode of diagnosed thrombosis.<sup>18, 24, 33</sup> 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.<sup>97,98,103</sup> 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.

Physical therapists should 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 (see Tab. 10).<sup>104</sup> Risk of bleeding complications decreases after 6 months of taking an anticoagulant. The 2018 NICE VTE guideline<sup>66</sup> 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 (see Tab. 10). These risk factors include, among others: thrombocytopenia or concomitant use of antiplatelet agents, anemia, concomitant treatment with nonsteroidal anti-inflammatory drugs, hypertension, poor adherence to the prescribed anticoagulant regimen, or poor control of international normalized ratio (INR) if on vitamin K antagonist treatment.<sup>105</sup>

Unfractionated heparin is indicated for individuals with high bleeding risk (see Tab. 9) and/or renal disease who are hospitalized, as it is a slower anticoagulant with a shorter half-life.<sup>106</sup> The initial dose of heparin is particularly critical when heparin is administered by subcutaneous injection, because an adequate anticoagulant response is not achieved in the first 24 hours unless a high starting dose is used.<sup>106</sup> Therapeutic heparin levels and activated partial thromboplastin time (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.<sup>106</sup> 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.<sup>106</sup> Heparin is considered to be in the therapeutic range when the aPTT is equivalent to 1.5 to 2.5 times the control value (in seconds).<sup>106</sup> Therefore, the GDG recommends waiting at least 24 hours to mobilize a patient started on intravenous UFH. Physical therapists can assess the 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% to 3% of patients treated with UFH and approximately 1% of patients treated with LMWH.<sup>97,107</sup> 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) and Argatroban are similar to LMWH and are often used when individuals need treatment or prophylaxis for VTE but have a history of

heparin-induced thrombocytopenia (HIT).<sup>97,107</sup> 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 for subsequent VTE.<sup>97,107</sup> DOACs, Argatroban 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.<sup>108</sup> Current direct oral anticoagulation drugs include rivaroxaban (Xarelto), dabigatran (Pradaxa), apixaban (Eliquis) and edoxaban (Savaysa) and are discussed in Table 9. 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 for their use.<sup>109</sup> 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.<sup>110,111</sup>

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 1 during administration of another loading anticoagulant (usually with LMWH or UFH).<sup>98</sup> 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 and first episodes of VTE should be treated with a target INR range of 2.5.<sup>24,33,96</sup> UFH or LMWH are often discontinued when the INR is greater than 2.0. Currently, warfarin has been used less often due to the popularity of the DOACs, and because warfarin crosses the blood brain barrier and can be responsible for brain bleeds, particularly in individuals who fall.<sup>112-115</sup>

Early mobility decisions in the acute setting for an individual who will be going home on warfarin should be made on the initial loading anticoagulant (which is usually UFH or LMWH) based upon the time to therapeutic level of the initial loading anticoagulant, since the INR associated with warfarin will not achieve therapeutic values for at least a few days. For patients on warfarin, treatment decision will be based on INR once the INR has reached a therapeutic level and the initial anticoagulant has been discontinued. Elevated INR (ie, >4) should raise concern regarding exercise and out of bed activity when patients are taking warfarin.<sup>116</sup> According to expert opinion, if INR is between 4.0 and 5.0, resistive exercises should be held and participation in light exercise (Rating of Perceived Exertion [RPE] ≤ 11) should be performed.<sup>116</sup> If gait is unsteady, ambulation should be restricted when the INR is 4.0 or greater, due to risk of bleeding if a fall or injury occurs.<sup>116</sup> The likelihood of bleeding is reported to rise steeply as INR increases above 5.0.<sup>112-116</sup> 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.<sup>108,116</sup> International normalized ratios can usually be corrected within 2 days.<sup>116</sup> When reversal of anticoagulation is needed for a patient on warfarin requiring surgery, fresh frozen plasma is used to replace vitamin K dependent coagulation

factors.<sup>112</sup> 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; 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 to 6 months following diagnosis of DVT or PE.<sup>24, 33, 96</sup> Those at greatest need for extended treatment include those with cancer and genetic clotting disorders.<sup>18, 65, 66</sup>

Physical therapists should confirm the medication class and the date/time medication was initiated prior to mobilizing the patient. In addition, physical therapists 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.<sup>24, 96</sup>

### **[H1]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)**

#### **[H2]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 bed rest, 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 bed rest 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.

## [H2] 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 to prevent venous stasis. In doing so, deconditioning is minimized, length of hospital stay may be shortened,<sup>117</sup> and other adverse effects of prolonged bed rest, such as pressure ulcers, can be avoided. A common concern for mobilizing a patient with a LE DVT is that the clot will dislodge and travel 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.<sup>118,119</sup>

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.<sup>118,119</sup> 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.<sup>33,118,119</sup> In addition, patients who experienced moderate or severe pain from the DVT had better outcomes in the affected limb if early mobility was implemented.<sup>119</sup> Similar conclusions were reported in 2 earlier systematic reviews, 1 which had 3 studies totaling 300 patients<sup>120</sup> and the other with 9 studies.<sup>121</sup>

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.<sup>122,123</sup> 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<sup>124</sup> and improve quality of life.<sup>120</sup> In summary, early mobilization of patients with a 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 has been initiated and therapeutic levels achieved.

Based on the evidence that exists on time to peak therapeutic levels of the anticoagulants discussed in 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.

**[H1] Action Statement 11: Allow upper extremity activities in 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, upper extremity activities can begin. (Evidence Quality: V; Recommendation Strength: R – Absence of research on topic)**

## **[H2] Action statement profile**

**Level of Evidence (I-V):** Level 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 a UE DVT. This action statement is applying information from the studies examining mobilization of those with a LE DVT.

**Benefits: Mobility will limit the negative effects of bed rest, 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 bed rest 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 UE DVT, clinicians should contribute to data collection surrounding this topic.

## **[H2] Supporting evidence and clinical interpretation**

A thorough review of CPGs, systematic reviews, meta-analyses and research studies found no studies or even guidance on mobilizing individuals with a UE DVT. All of the studies surrounding management of those with a UE DVT address medications or interventional procedures. Because of the lack of information on mobilization after a 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,<sup>91,125</sup> it would seem that a person with an UE DVT could be treated similarly after medical intervention. According to the results from 2 meta-analyses and a separate systematic review, mobilization for those with a LE DVT is safe once therapeutic levels of anticoagulants are met.<sup>118, 119, 122</sup> Based on this

information, the GDG felt that as long as therapeutic levels of anticoagulants are met, mobilization and movement of the UE DVT should be safe.

There is the question of what kind of mobilization is safe for those with a 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 treated clot in their LE, movement and intensity are not limited, but the leg typically stays below the level of the heart and lungs. For individuals with a 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 UE 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 UE activity post UE DVT diagnosis.

### **[H1]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 (eg, intermittent pneumatic compression and/or graduate compression stockings). (Evidence Quality: II; Recommendation Strength: B - Moderate)**

#### **[H2]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 1 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.

## [H2] 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.<sup>65</sup> 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.<sup>126,127</sup> Smaller studies have also questioned the value of compression after a diagnosis of DVT to prevent PTS.<sup>128</sup> 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.<sup>66</sup> The Guidelines on VTE Management<sup>33</sup> 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,<sup>129</sup> compression therapy after DVT led to a reduction in PTS (relative risk [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<sup>130</sup> 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<sup>131</sup> 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.

### [H1]Action Statement 13: Mobilize individuals with an inferior vena cava filter for LE DVT

**When a patient has an inferior vena cava (IVC) filter implanted for LE DVT, 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)**

## [H2]Action statement profile

**Level of Evidence (I-V):** Level 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:** Potential for discomfort after 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.

## [H2] Supporting evidence and clinical interpretation

Inferior vena cava filter placement is a type of percutaneous endovascular intervention for LE VTE 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 LE and pelvic VTE is just inferior to the renal artery access veins.<sup>132</sup>

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 LE DVT with an absolute contraindication to anticoagulation treatment or who are at a decidedly high risk of PE and not anticoagulated.<sup>33, 96</sup> 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.<sup>96</sup> There are risks associated with IVC filter placement including penetration of the venous wall (up to 19% in 1 study)<sup>133</sup> and adjacent organ involvement with symptoms in 8% of the population provided an IVC filter.<sup>133</sup> Up to 5% of the patients with IVC filters require surgical removal of the permanent filter.<sup>133</sup> 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.<sup>134, 135</sup>

Two RCTs<sup>136, 137</sup> and a systematic review combined with a meta-analysis<sup>138</sup> 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 2 groups had no difference in all-cause mortality or PE related mortality.

Following placement of an IVC filter, initiate mobilization once the patients are hemodynamically stable and there is no bleeding at the puncture site; initiating mobility carries the same risk of dislodging an existing clot, but the presence of the filter would prevent a catastrophic PE.<sup>132</sup> 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.<sup>132</sup> In patients who have an IVC filter not recently inserted, assessment should be made of the LE vascular system for pain and/or swelling indicating blockage of the filter (ie, clots trapped blocking flow). One should also identify the time frame since IVC filter placement. The longer the IVC remains in place, the higher the risk of complications from filters.<sup>96</sup>

### **[H1]Action Statement 14: Consult the medical team to initiate mobility with a patient with distal LE DVT not treated with IVC filter or anticoagulant**

**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, consult with the medical team. (Evidence Quality: V; Recommendation Strength: P-Best Practice)**

#### **[H2]Action statement profile**

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

**Recommended Grades (A-R):** P, Best Practice.

**Status Definition:** Reaffirmed and updated.

**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 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 dislodge 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 with distal LE DVT will not have anticoagulants prescribed or an IVC filter unless severe symptoms or risk factors exist for extension of clot exist<sup>180</sup>(Chest 2020 guidelines). 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 not treated with anticoagulants might help health care providers understand the importance of mobility and increase awareness of the impact of location on DVT prognosis and risk.

## [H2] 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 (ie, post-acute subdural hematoma) or they do not meet the criteria for an IVC filter (ie, 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 into or 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 (repeat ultrasound imaging once weekly for 2 weeks if not given medications for anticoagulation).<sup>33</sup> 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.<sup>139</sup>

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 2 weeks rather than treatment with anticoagulation.<sup>33</sup> 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.<sup>4,118,119</sup> 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 these factors with the interprofessional team and the patient when making a clinical judgment about mobilization. Although a physician may consult physical therapists 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.

### [H1] 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)**

## [H2] 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 1 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 non-massive 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 this 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.

## [H2] Supporting evidence and clinical interpretation

Acute PE has an annual incidence of 100,000 cases in the United States and can result in severe dyspnea, CTEPH and even death. Pulmonary embolism is classified based on the severity and risk for early (< 30 day) mortality (see Tab. 13).<sup>18, 96</sup> 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.<sup>140</sup> There are 2 classification systems: one from the ESC which uses high, intermediate (subdivided into intermediate-high and intermediate-low) and low risk.<sup>18</sup> The ESC system is equivalent to the classification system used by the ACCP who uses massive (high risk), submassive (includes intermediate-high and intermediate-low risk) and non-massive (low risk).<sup>11,</sup>

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Non-massive PE, 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.<sup>96</sup> 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,<sup>141</sup> as well as determination of right ventricular function post-PE. In a meta-analysis of 21 cohort studies and over 3000 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 right ventricle by imaging methods or laboratory biomarkers should be performed, even in the presence of a low PESI or a negative sPESI.<sup>142</sup> 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.<sup>33, 96</sup>

If the PE is classified as low risk, the ESC guidelines recommend early discharge from the hospital in addition to continuation of anticoagulation treatment.<sup>96</sup> The British Medical Society further recommends that individuals diagnosed with a low risk PE be treated in the outpatient setting with continuous follow-up.<sup>143</sup> 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 bed rest in individuals treated with anticoagulants.<sup>118, 119</sup> 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.<sup>118</sup>

Therefore, the recommendation is for individuals with a non-massive PE to be active once anticoagulation is initiated and therapeutic levels have been achieved.<sup>144</sup> 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 heart rate response, decrease in SpO<sub>2</sub>, hypotension, as well as any sign of abnormal dyspnea, or chest pain. Physical therapists should promote mobility and provide therapeutic interventions as needed to encourage activity.

### **[H1]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)**

#### **[H2]Action statement profile**

**Level of Evidence (I-V):** Level 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.

**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 therapist services.

**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 PE, 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.

## [H2]: Supporting evidence and clinical interpretation

Pulmonary embolism is classified based on the severity and risk for early (< 30 days) mortality (see Tab. 13).<sup>96</sup> 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 ECMO.<sup>96,145</sup> Hemodynamic instability in the presence of PE often indicates a central or extensive PE.<sup>146</sup> Syncope may also occur and has been associated with higher prevalence of instability including right ventricular dysfunction.<sup>146</sup> 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 and the early clinical outcomes of PE.<sup>11,96,147,148</sup> Individuals defined as intermediate-high-risk for adverse outcomes may also benefit from more advanced treatments including reperfusion therapy (ie, pharmacologic agents such as thrombolytics and fibrinolytics or endovascular procedures).<sup>96,145</sup> 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 after PE include ruling out right ventricular dysfunction and right heart thrombi (within the first 24 to 48 hours).<sup>142</sup>

Patients in the PEITHO trial identified as intermediate-high risk PE required 2 to 3 days of anticoagulation to ensure they were stable due to the mean time identified before hemodynamic decompensation or death (mean = 1.79 [SD = 1.6] days).<sup>149</sup> 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.<sup>142</sup> A prospective trial found that ruling out right ventricular dysfunction and/or thrombi early after hospital admission decreases risk for recurrent VTE within 3 months following the initial event.<sup>142</sup> Hemodynamic stability and lack of right ventricular dysfunction defines low risk PE and therefore, candidacy for mobility.

Physical therapists, when working with patients after PE, should review patients' admitting and subsequent medical information to identify hemodynamic status, presence of an adequate blood pressure, and evaluate for right ventricular involvement by reviewing echocardiogram results. Physical therapists should not mobilize patients after acute PE in the presence of signs of instability such as persistent hypotension, right ventricular involvement, or labile hemodynamics (see Tab. 14).<sup>96,144,150</sup> Once hemodynamic stability is attained, blood pressure improved, and treatment initiated; mobility may be indicated according to the time to therapeutic threshold of the anticoagulation medication prescribed for the PE. For those patients with high-risk PE treated with reperfusion treatment (ie, thrombolysis), the ESC guidelines state mobility can be initiated once the patient is hemodynamically stable and anticoagulation therapy has reached therapeutic levels.<sup>12</sup> 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 physical therapists working with these patients should continue monitoring due to the potential stresses on the right ventricle.<sup>12</sup>

## [H1]Action Statement 17: Refer patient for medical re-evaluation if no improvement in signs and symptoms of VTE after 1 to 2 weeks

When a patient with a documented VTE does not show improvement in signs/symptoms of VTE after 1 to 2 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)

### [H2]Action statement profile

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

**Recommended Grades (A-R):** 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.

**Intentional Vagueness:** Length of time for follow up described as a range (1 to 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.

**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.

### [H2]: Supporting evidence and clinical interpretation

An individual with successful treatment after 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.<sup>18, 33</sup> 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 are also times when no medical intervention is prescribed. While in some cases is the best course of action, for a small portion of individuals the thrombus will not resolve on its own.

There are other times when an individual may not follow through on the prescribed intervention. If patients are not adherent with their medical treatment for VTE and/or the treatment is shorter

than recommended, 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 and adhering to 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.<sup>8-10</sup> The length of time of risk for VTE in the postoperative period may be related to the type of surgical procedure. In a prospective study of 4840 joint surgery patients, VTE symptoms appeared a mean of 27 days after total hip arthroplasty and a mean of 17 days after total knee arthroplasty.<sup>10</sup> In hip fracture cases, there is often a delay between injury and surgery. Therefore, the patient is already in a prothrombotic state at the time of surgery, and the surgery further increases the risk for VTE. In addition, VTE risk remains increased for the greatest time after hip fracture surgery (mean time to symptomatic DVT, 36 days) compared to all other orthopedic surgeries.<sup>10</sup>

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.<sup>151</sup> A more recent study of VTE in nursing home residents demonstrated that immobility leads to increased risk for VTE.<sup>152</sup> Thus, a decline in ambulatory status might increase the risk for VTE.

There are no RCTs 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 2 broad categories: (1) treatment factors (individuals may require a different anticoagulant or may not be adherent to treatment) and (2) patient-specific intrinsic risk of recurrence. Following treatment for VTE, patients should be encouraged to be mobile, as continued risk for VTE decreases with mobility.<sup>4, 118, 119</sup> However, adherence with medication for VTE often decreases over time as individuals may not understand the need to take the medication for the full duration.<sup>153</sup> Alternatively, pharmacologic treatment is often prescribed for a 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.<sup>154</sup> Evidence has shown that many apparent "treatment failure" presentations are in fact residual venous disease masquerading as recurrent VTE.<sup>153</sup> In the REVERSE study, imaging was performed on 646 patients with VTE and 60% of the study group had abnormal scans 5 to 7 months after an unprovoked VTE.<sup>153</sup> In another meta-analysis of 2527 patients with DVT, 55% of the study population had residual venous obstruction 6 months after their index scans.<sup>155</sup> A systematic review on patients with PE demonstrated residual abnormalities on V/Q scans or CTPA in 50% of the study population 6 months post initial event.<sup>156</sup>

Physical therapists treating patients after 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 who have discontinued treatment. Medical interventions do not guarantee a complete resolution of symptoms, 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, assessing 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 a physical therapist's 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.

### **[H1]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 (postthrombotic syndrome, chronic thromboembolic pulmonary hypertension [CTEPH] 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)**

#### **[H2]Action statement profile**

**Level of Evidence (I-V):** Level 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 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 may not understand that there may be complications with VTE or that recurrence is possible. Patients would prefer recommendations from the provider or other health care providers to reduce complications and prevent recurrence of VTE.

**Exclusions:** None.

**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. Improved health care professional awareness

should result in improved education to patients to continue taking their medications for the length of the prescribed treatment.

## **[H2] 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 CTEPH (up to 3.8% incidence after 2 years).<sup>157,158</sup> Physical therapists can help reduce symptoms of PTS with mechanical compression, provide exercise recommendations for prevention of recurrent VTE, provide education about the consequences and risks of CTEPH, and refer to a pulmonologist or pulmonary hypertension clinic for those presenting with shortness of breath/dyspnea on exertion after 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.

## **[H2] Postthrombotic syndrome (PTS)**

Physical therapists should be able to recognize the signs and symptoms of PTS which include edema and swelling, chronic arm or leg pain, skin changes and heaviness of the limb affected by DVT.<sup>157,159</sup> Physical therapists should assess patients for residual impairments in the affected extremities as well as mobility impairments following a DVT. Once PTS is suspected, a specific and sensitive rating instrument referred to as the Villalta scale can be used to grade the severity of PTS and guide interventions (Kahn, 2009, Measurement properties of the Villalta scale to define and classify the severity of the postthrombotic syndrome). 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.<sup>159</sup> Approximately 20% to 50% of patients post LE DVT and 8% to 28% post UE DVT<sup>5</sup> develop PTS as a long-term complication which can occur up to and beyond 2 years post DVT.<sup>5,159</sup> The risk factors for developing PTS after LE DVT include increased age, increased BMI, thrombophilia, recurrent DVT events and effectiveness of initial oral anticoagulation regimen.<sup>160-163</sup> 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.<sup>159</sup> The decreased quality of life and effect on work and recreation financially impacts the health care system and has an impact on quality of life similar to chronic diseases such as chronic lung disease, diabetes and arthritis.<sup>164</sup> Therefore identifying signs and symptoms of PTS, and the impact of these symptoms on patient function, is a key role for physical therapists; as is providing management strategies or referral for these long-term consequences of VTE.

## **[H2] Persistent symptoms after pulmonary embolism (PE) and chronic thromboembolic pulmonary hypertension (CTEPH)**

Following a PE, the patency of the pulmonary arterial bed will be restored within the first few months after the acute event.<sup>165</sup> However, 20% to 75% of individuals who are diagnosed with a PE report decreased quality of life and health status 6 months after diagnosis.<sup>166-168</sup> 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.<sup>166</sup> Other predictors of exertional dyspnea include elevated systolic pulmonary arterial pressure and right ventricular dysfunction at the time of PE diagnosis, and residual pulmonary vascular obstruction upon discharge from hospital.<sup>167,169,170</sup> 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.<sup>96</sup>

In a prospective study that followed a cohort of individuals for 1 year following discharge from the hospital for an acute PE, approximately 47% of the patients demonstrated a decreased maximal aerobic capacity (<80% of predicted value) on a cardiopulmonary exercise test.<sup>171</sup> These individuals presented with decreased quality of life and significantly reduced 6 minute walk distances in addition to their decreased aerobic capacity.<sup>171</sup> Predictors of reduced functional capacity included female sex, higher BMI, history of lung disease, higher pulmonary artery systolic pressures on echo and higher main pulmonary artery diameter on the computed tomography pulmonary artery (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.<sup>171</sup>

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 increased dyspnea on exertion, decreased exercise tolerance, and decreased oxygen saturation with activity.<sup>96</sup> The ESC 2019 guidelines report the incidence of CTEPH is in the range of 1% to 9% within the first 2 years after a symptomatic PE event. However, the incidence of CTEPH may be higher due to low referral for diagnosis and/or treatment when symptoms of pulmonary hypertension are present post PE.<sup>96</sup> 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.<sup>96</sup>

In addition, the ACCP guidelines for antithrombotic treatment recommend that patients with CTEPH should be assessed by a team with expertise in evaluation and management of pulmonary hypertension.<sup>11,172,173,174,175</sup> The ACCP guidelines support pulmonary thromboendarterectomy by an experienced thromboendarterectomy team in the presence of large PEs or the development of CTEPH post PE.<sup>33</sup> 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.<sup>11,176,177</sup> 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.<sup>178</sup>

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 3 weeks of training, as well as improved performance on peak VO<sub>2</sub> testing, and improved scores on quality of life questionnaire.<sup>179</sup> 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.

## [H2] Recurrent venous thromboembolism (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 after VTE. The purpose of medical treatment (anticoagulation, IVC filter, catheter lysis, or surgical intervention) for a documented VTE is to dissolve the clot, improve blood flow, and decrease signs and symptoms of VTE.<sup>18, 44, 65</sup> IVC filters prevent embolization of clots from the LEs 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.<sup>138,180</sup> Patients will be on anticoagulation following the lysis or surgical intervention unless contraindications for these medications exist.<sup>18, 120</sup>

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 occurs as a PE.<sup>181</sup> However, the incidence of recurrent VTE in patients who have a PE is double that of the incidence of recurrence of LE DVT.<sup>182, 183</sup> 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 Tab.16).<sup>96</sup> However, the risk of PE recurrence is high (>8% per year) for those who have active cancer, 1 or more previous VTE or an antiphospholipid antibody syndrome.<sup>96</sup> Recurrence in UE DVT has been reported to be approximately 9%, yet if an individual has documented cancer the risk is double, and if a patient has catheter-associated UE DVT, the risk is even higher.<sup>5</sup> There is no evidence evaluating patients with recurrent VTE while currently taking anticoagulant therapy. Risk factors for recurrent VTE while on anticoagulant therapy can be divided into 2 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 (Action Statement 1) and preventive steps (Action Statement 4) including compression in certain situations (Action Statement 19).

**[H1] Action Statement 19: Recommend mechanical compression when signs and symptoms of postthrombotic syndrome (PTS) are present**

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

## **[H2] Action statement profile**

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

**Recommended Grades (A-R):** B, Moderate – Level II studies, at least 1 level II study directly on topic supports recommendation.

**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 decreased PTS severity.**

**Risk, Harm Cost:** Improper fit can lead to skin irritation, ulceration, or interruption of blood flow. Potential for 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 health care 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.

## **[H2] Supporting evidence and clinical interpretation**

Postthrombotic 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 1 in 3 patients will experience PTS within 5 years.<sup>184-186</sup> 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 CPGs 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<sup>187</sup> on compression for treatment of PTS found very-low-

certainty 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 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 medical compression stockings for the treatment of symptomatic PTS at a Grade 1B level.<sup>188</sup>

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 regarding compression use 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.

## [H1]Summary

After a review of the original CPG, identification of 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 (KAS). Based on these statements, the following conclusions can be made:

- Physical therapists should play a significant role in identification of 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 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 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.

Compression is mentioned in 3 different KAS (4, 12 and 19) and the recommendations on its use are different based on the situation. Additionally, the recommendations have changed from our 2016 recommendations based on new research. Because of these factors, below is a summary of all our recommendations on compression in a single location to help with implementation.

- Compression should be recommended when the individual is classified as a high risk for VTE (KAS 4). Compression can counter inactivity and decrease pooling of blood in the

venous system. The research is unclear if 1 form of compression (stockings or pneumatic compression) is better than another.

- Compression should not be routinely used when an individual is diagnosed with a new DVT (KAS 12). While earlier research showed benefits, these were lower level studies and stronger more recent studies have shown no benefits for prevention of long term negative effects, reducing pain or preventing PTS. Thus, compression should not be recommended for as a default for every person. If an individual wants to use compression or they have unresolved pain or swelling, it is acceptable to try compression as it has low risk. Therapists should ensure proper fit to reduce risk of skin breakdown
- Compression can be recommended when symptoms of PTS are present, especially pain and swelling (KAS 19). It should be noted these findings are mixed, but support is strong enough to recommend and try when symptoms are present.

## [H1]Implementation

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

- Presentation 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.
- Development of an app on VTE that includes the KAS, 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 KAS into clinical practice. Make resources easily accessible in the clinic, such as: lists of signs and symptoms of UE and LE DVT and PE, copies of the risk assessment criteria for the VTE tools, and the algorithms in this CPG.
- Form interprofessional teams that address VTE; ensure all providers are familiar with and 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.
- 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 can

modify interventions based on medical history and patient problems. Physical therapists can add greatly to the scope and depth of these teams.

This CPG represents a view of current treatment and may become outdated as new evidence becomes available. It will be reviewed in 5 years and will be updated in accordance with new evidence, changing practice, rapidly emerging treatment options, and new technology, reaffirmed, or withdrawn.

## **[H1]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 (eg, 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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## **Disclosure and Presentations**

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## Figure Captions

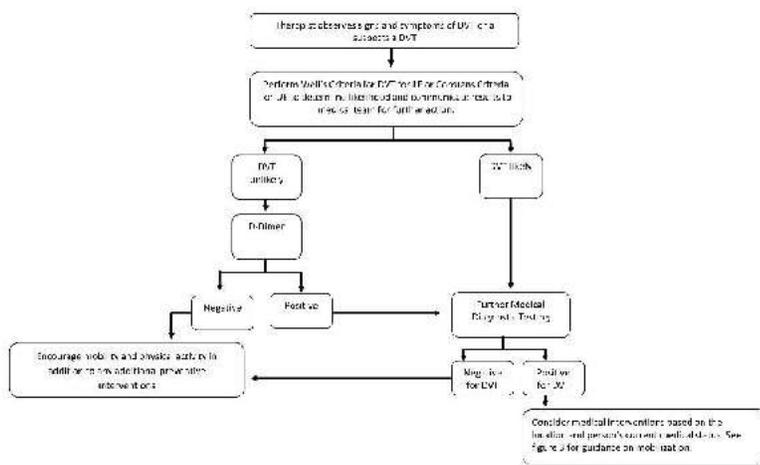
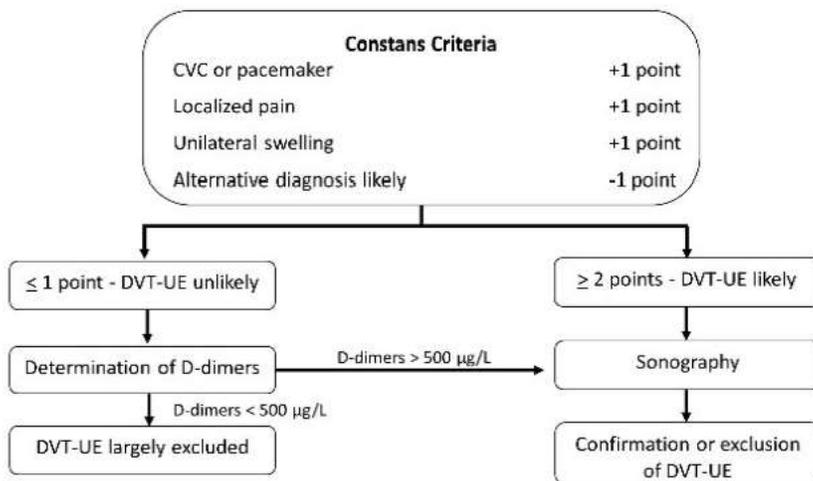


Figure 1. Actions for a suspected upper or lower extremity deep vein thrombosis.<sup>68, 70, 75</sup>



CRIPPT

Figure 2. Constans Criteria.<sup>91</sup> 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

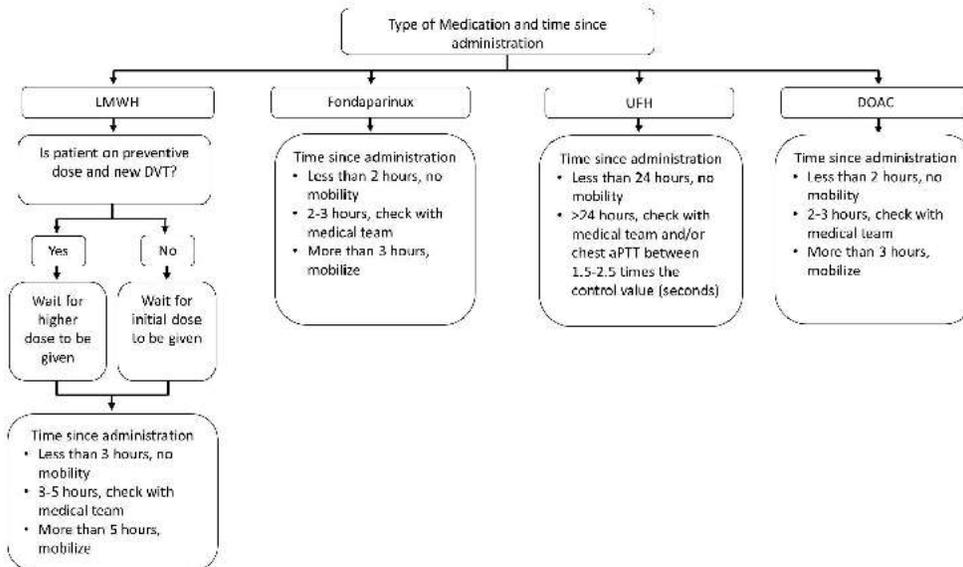


Figure 3. Mobilization with an acute UE or LE DVT based on anticoagulant and time since administration.<sup>99-103, 106-109, 139</sup> Algorithm for mobilizing patients with acute upper or lower extremity deep vein thrombosis based on anticoagulant and time since administration. See Table 11 for long term medical management interventions. aPTT = activated partial thromboplastin time; DOAC = direct acting oral anticoagulants; DVT = deep vein thrombosis; LMWH = low-molecular weight heparin, UFH = unfractionated heparin.

## Tables

**Table 1.** Key Action Statements<sup>a</sup>

Number		Key Phrase
1	Advocate for a culture of mobility and physical activity in all practice settings unless medical contraindications for mobility	Advocate for a culture of mobility and physical activity

	exist. (Evidence Quality: I; Recommendation Strength: A–Strong)	
2	During initial interview and physical therapist 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 (ie, cancer or inherited clotting disorder) that independently increase VTE risk, physical 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	When a patient presents with pain, tenderness, swelling, warmth and/or discoloration in the lower extremity, establish the likelihood of a LE DVT 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	When a patient presents with clinical symptoms including swelling, pain, edema, cyanosis and/or dilation of superficial veins, establish the likelihood of UE DVT 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: V; Recommendation Strength: P–Best Practice)	Confirm pharmacological intervention and time initiated
10	When a patient with a recently diagnosed LE DVT reaches therapeutic threshold of anticoagulant medication, mobilize the patient. (Evidence Quality: I; Recommendation Strength: A–Strong)	Mobilize patients with LE DVT when therapeutic level of anticoagulation is achieved
11	When a patient with a recently diagnosed UE DVT reaches the therapeutic threshold of anticoagulant medication, upper extremity activities can begin.	Mobilize patients with UE DVT when therapeutic level of

	(Evidence quality: V; Recommendation Strength: R–Absence of Research on Topic)	anticoagulation is achieved
12	When a patient has a newly diagnosed LE DVT, do not routinely recommend mechanical compression (eg, intermittent pneumatic compression and/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 IVC filter for LE DVT 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 IVC filter
14	When a patient presents with a documented LE DVT below the knee, is not anticoagulated, does not have an IVC filter and the patient is prescribed out of bed mobility by the physician, consult with the medical team. (Evidence Quality: V; Recommendation Strength: P–Best Practice)	Consult the medical team to initiate mobility with a patient with distal 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 1 to 2 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 1 to 2 weeks
18	When a patient presents with long-term consequences of VTE (PTS, CTEPH, or history of VTE), consider referring patient 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)	Refer patients for medical management of the long-term consequences of VTE
19	When a patient presents with signs and symptoms consistent with PTS, recommend mechanical compression (eg, intermittent pneumatic compression and/or graduated compression stockings).	Recommend mechanical compression when signs and symptoms of PTS are present

(Evidence Quality: I; Recommendation Strength: B–Moderate)

<sup>a</sup> CTEPH = chronic thromboembolic pulmonary hypertension; DVT = deep vein thrombosis; IVC = inferior vena cava; LE DVT = lower extremity deep vein thrombosis; PE = pulmonary embolism; PTS = postthrombotic syndrome; UE DVT= upper extremity deep vein thrombosis; VTE = venous thromboembolism.

**Table 2.** Search Strategy by Key Words and MeSH Terms<sup>a</sup>

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

<sup>a</sup> Databases searched included: PubMed, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), and the Physiotherapy Evidence Database (PEDro).

**Table 3.** Levels of Evidence<sup>22</sup>

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<sup>22</sup>

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.** Padua Prediction Score<sup>40,a</sup>

Baseline Features	Score
Active cancer <sup>b</sup>	3

Previous VTE (excluding superficial vein thrombosis)	3
Reduced mobility <sup>c</sup>	3
Already known thrombophilia condition <sup>d</sup>	3
Recent ( $\leq 1$ mo) trauma and/or surgery	2
Elderly age ( $\geq 70$ y)	1
Heart and/or respiratory failure	1
Acute MI or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI $\geq 30$ )	1
Ongoing hormonal treatment	1
<i>High risk of VTE</i>	$\geq 4$

<sup>a</sup> BMI = body mass index; MI = myocardial infarction; VTE = venous thromboembolism.

<sup>b</sup> Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 months.

<sup>c</sup> Anticipated bed rest with bathroom privileges (either because of patient's limitations or on physician's order) for at least 3 days.

<sup>d</sup> Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome.

**Table 6.** Khorana Risk Score<sup>52,53</sup>

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 $\geq 350 \times 10^9$ /L	1
Pre-chemotherapy hemoglobin level $< 100$ g/dL or use of red cell growth factors	1
Pre-chemotherapy leukocyte count $\geq 11 \times 10^9$ /L	1
Body Mass Index $\geq 35$ kg/m <sup>2</sup>	1

**Table 7.** Wells Criteria for the Prediction of Deep Vein Thrombus<sup>70,71,a</sup>

Clinical Feature	Points
Active cancer (treatment ongoing, within 6 mo, or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for 3 d or more, or major surgery within 12 wk requiring general or regional anesthesia	1
Localized 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
<b>Clinical probability simplified score</b>	
DVT "likely"	2 points or more
DVT "unlikely"	Less than 2 points

<sup>a</sup> DVT = deep vein thrombus.

**Table 8.** Revised Geneva Clinical Prediction Rule for Pulmonary Embolism<sup>189,a</sup>

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

<sup>a</sup> bpm = beats per minute; DVT = deep vein thrombus; mo = month(s); PE = pulmonary embolism; y = year(s).

<sup>b</sup> Original version: low probability 0–3, intermediate 4–10, and high ≥ 11.

<sup>c</sup> Simplified version: low probability 0–1, intermediate 2–4, and high ≥ 5.

**Table 9.** Current Anticoagulation Options for Venous Thromboembolism (VTE) Treatment and Prevention<sup>99-103,106-109,139,a</sup>

Classification	Mechanism of Action	Medication Names	Dosage and Method of Delivery	Peak Therapeutic Levels and Monitoring	Physical Therapist Considerations
Unfractionated heparin <sup>106</sup>	Binds and activates antithrombin (through a high-affinity pentasaccharide) causing	Heparin	Delivery: IV  Dose: bolus 80 units/kg followed by infusion of 18 units/kg/h	>24 h  Monitor: aPTT (needs to be 1.5–2.5 times the control value)	Patients are given heparin due to renal dysfunction or presence of mechanical valve. Occasionally heparin is used in

	inactivation of thrombin and factor Xa and IXA			(sec) and/or check with medical team	low risk PE or proximal DVT.  Assess chart to determine reason for use of heparin.
Low molecular weight heparins (LMWH) <sup>101-103, 106</sup>	Binds and activates antithrombin (via unique pentasaccharide sequence) causing inactivation of thrombin and factor Xa and IXA	Lovenox ( <i>enoxaparin</i> )  Innohep ( <i>tinzaparin sodium</i> )  Fragmin ( <i>dalteparin</i> )	Delivery: subcutaneous injections  Prophylactic dose: 30–40 mg q 12–24 h  Therapeutic dose: 1–1.5 mg/kg q 12–24 h	3–5 h  Monitor: anti-factor Xa (peak level between 0.6–1.0 IU/mL if receiving 2x/d; 1.0–2.0 IU/mL if receiving 2x/d)	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) <sup>106, 139</sup>	Selectively binds to antithrombin III resulting in Factor Xa inhibition	Arixtra	Delivery: subcutaneous injections  Prophylactic Dose: 2.5 mg/d  Therapeutic dose: 5–10 mg/d (based on weight)	2–3 h  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 <sup>99, 100, 103, 106, 139</sup>	Inhibits the synthesis of vitamin K-dependent clotting factors, especially the C1 subunit of vitamin K epoxide reductase (VKORC1) enzyme complex	Coumadin ( <i>warfarin</i> )	Delivery: oral  Dose: individualized based upon individual's INR response to drug	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 intracranial or subdural hemorrhages.  Frequent blood monitoring required for INR levels (every 4-6 wk).

Direct oral thrombin inhibitor (DOAC) <sup>108, 109</sup>	Directly inhibits thrombin	Pradaxa ( <i>dabigatran</i> )	Delivery: oral Dose: 150 mg bid	2 h Monitor: none necessary	No blood monitoring. Less risk of brain bleed than oral vitamin K antagonists. Drug interactions not yet tested in newer medications.
Direct oral Xa inhibitors (DOAC) <sup>108,109</sup>	Direct inhibition of factor Xa	Xarelto ( <i>rivaroxaban</i> ) Eliquis ( <i>apixaban</i> ) Savaysa ( <i>edoxaban</i> )	Delivery: oral Xarelto dose: 15 mg bid for first 21 d, 20 mg qd after day 21 Eliquis dose: 10 mg bid for 7 d then 5 mg bid; 60 mg daily (30 mg for renal impairment)	2-3 h Monitor: none necessary	No blood monitoring. Less risk of brain bleed than oral vitamin K antagonists. Increased usage of these drugs in orthopedic population. Drug interactions not yet tested in newer medications.

<sup>a</sup> aPTT = activated partial thromboplastin time; bid = twice a day; CA = cardiac arrest; d = day(s); DOAC = direct oral anti-coagulant; DVT = deep vein thrombosis; h = hour(s); HIT = heparin-induced thrombocytopenia; INR = international normalized ratio; LMHW = low molecular weight heparins; PE = pulmonary embolism; q = every; sec = second(s); VTE = venous thromboembolism; wk = week(s).

**Table 10.** HAS-BLED Score<sup>a</sup>

	Condition	Points
<b>H</b>	<b>H</b> ypertension: uncontrolled, >160 mmHg systolic	1
<b>A</b>	<b>A</b> bnormal renal function: dialysis, transplant, Cr >2.26 mg/dL or >200 μmol/L	1
	<b>A</b> bnormal liver function: cirrhosis or bilirubin >2x normal or AST/ALT/AP >3x normal	1
<b>S</b>	<b>S</b> troke: prior history of stroke	1
<b>B</b>	<b>B</b> leeding: prior major bleeding or predisposition to bleeding	1
<b>L</b>	<b>L</b> abile INR: (unstable/high INR), time in therapeutic range < 60%	1
<b>E</b>	<b>E</b> lderly: age > 65 y	1
<b>D</b>	<b>D</b> rug or alcohol usage history (≥ 8 drinks/wk)	1
	medication usage predisposing to bleeding: (antiplatelet agents, NSAIDs)	1

<sup>a</sup> INR = international normalized ratio; NSAID = non-steroidal anti-inflammatory drug; wk = week(s); y = year(s).

**Table 11.** Long-Term Medical Management of Venous Thromboembolism<sup>a</sup>

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 those without cancer 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.

<sup>a</sup> INR = international normalized ratio; LMWH = low molecular weight heparin; VTE = venous thromboembolism.

**Table 12.** Risk Factors of Increased Bleeding<sup>104,105,a</sup>

Active bleeding
Acute stroke
Acquired bleeding disorders (such as acute liver failure)
Concurrent use of anticoagulants known to increase the risk of bleeding (ie, warfarin with an INR >2)
Lumbar puncture/epidural/spinal anesthesia expected to be given within next 12 h
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

<sup>a</sup> BP = blood pressure ; h = hour(s); INR = international normalized ratio

**Table 13.** Classification of Pulmonary Embolism and Risk of Early (In-Hospital or 30 Day) Death<sup>18,a</sup>

Early Mortality Risk		Indicators of Risk			
		Hemodynamic Instability <sup>b</sup>	Clinical Parameters of PE Severity and/or Comorbidity: PESI class III-IV OR sPESI >= 1	RV dysfunction on TTE or CTPA <sup>c</sup>	Elevated Cardiac Troponin Levels <sup>d</sup>
High		+	+ <sup>e</sup>	+	+
Intermediate	Intermed -High	-	+ <sup>f</sup>	+	+
	Intermed - Low	-	+ <sup>f</sup>	1 (or none) positive	

Low	-	-	-	Assessment optional: if assessed, negative
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<sup>a</sup> 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.

<sup>b</sup> 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, not caused by new-onset arrhythmia, hypovolemia, or sepsis).

<sup>c</sup> Prognostically relevant imaging (TTE or CTPA) findings in patients with acute PE, and the corresponding cut-off levels.

<sup>d</sup> 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.

<sup>e</sup> Hemodynamic 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.

<sup>f</sup> Signs 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<sup>18,a</sup>

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
	<i>and</i>	
	End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)	

<sup>a</sup> BP = blood pressure.

Table 15. Risk of Recurrent Venous Thromboembolism (VTE)<sup>18,a</sup>

Estimated Risk for Long-Term VTE Recurrence ≥ 3 mo Post Medication Discontinuation	Risk Factor Category for Index PE
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<p>Low (&lt;3% per y)</p>	<p>Major transient or reversible factors associated with &gt; 10-fold increased risk for the index VTE event (compared to patients without the risk factor). Examples:</p> <ul style="list-style-type: none"> <li>• Surgery w/anesthesia for &gt; 30 min</li> <li>• Confined to bed in hospital for ≥ 3 d due to an acute illness or acute exacerbation of a chronic illness</li> <li>• Trauma with fractures</li> </ul>
<p>Moderate/intermediate (3%–8% per y)</p>	<p>Transient or reversible factors associated with ≤ 10-fold increased risk for first index VTE</p> <ul style="list-style-type: none"> <li>• Minor surgery</li> <li>• Admission to hospital for &lt; 3 d with acute illness</li> <li>• Estrogen therapy</li> <li>• Leg injury without fracture associated with reduced mobility for &gt; 3 d</li> <li>• Long air flight</li> </ul> <p>Non-malignant persistent risk factors</p> <ul style="list-style-type: none"> <li>• Inflammatory bowel disease</li> <li>• Active autoimmune disease</li> </ul> <p>No identifiable risk factor</p>
<p>High &gt; 8% per y</p>	<ul style="list-style-type: none"> <li>• Active cancer</li> <li>• One or more episodes of VTE previously in absence of major transient or reversible factor</li> <li>• Antiphospholipid antibody syndrome</li> </ul>

<sup>a</sup> d = day(s); min = minute(s); mo = month(s); PE = pulmonary embolism; VTE = venous thromboembolism; y = year(s).