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| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

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| For a 60 yo female with a lower extremity deep vein thrombosis diagnosed in the last 24 hours (P), is early ambulation (I) or bed rest (C) more appropriate to reduce incidence of pulmonary embolism, recurrence of DVT, post-thrombotic syndrome and mortality (O) in the acute care setting? |

**AUTHOR**

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**CLINICAL SCENARIO**

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| A 60 yo female patient is admitted to the hospital with a primary diagnosis of failure to thrive. Patient has comorbidities of BMI >35, CHF, Type II DM, peripheral neuropathy. Since admission the patient has been immobile and begins complaining of pain in her right calf. With imaging, a DVT was discovered in her posterior tibial vein. Her medical team has proceeded to treat with anticoagulants and an order remains from yesterday for “PT eval and treat” and “progressive mobility”. Due to the risk for developing a fatal PE, it is critical that physical therapists proceed with caution when patients are at risk for or have a confirmed LE DVT. Evidence also supports early mobility for hospitalized patients to reduce risk of readmission, debility and falls. Clinical research is needed to identify the most recent mobility recommendations and considerations for patients with recent diagnoses of LE DVT. |

**SUMMARY OF SEARCH**

[Best evidence appraised and key findings]

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| Eight studies met the inclusion and exclusion criteria including 5 systematic reviews, 1 prospective RCT, 1 retrospective quasi-experimental study and 1 clinical practice guideline.* Early ambulation as an intervention in patients with a diagnosed acute lower extremity deep vein thrombosis (DVT) does not put patients at increased risk for developing a pulmonary embolism, progression of the DVT or mortality when compared to bed rest.[1](https://sciwheel.com/work/citation?ids=11706841&pre=&suf=&sa=0)
* Early ambulation is favored over bed rest when comparing proportions of individuals in each group who experienced a DVT-related adverse event.[1](https://sciwheel.com/work/citation?ids=11706841&pre=&suf=&sa=0)
* Early ambulation should be initiated immediately after peak therapeutic levels of the prescribed anticoagulant have been achieved.[2](https://sciwheel.com/work/citation?ids=4300067&pre=&suf=&sa=0)
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**CLINICAL BOTTOM LINE**

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| Patients who have been diagnosed with an acute lower extremity DVT should participate in early ambulation after therapeutic levels of anticoagulant have been achieved. Early ambulation does not increase the clinically meaningful outcomes of pulmonary embolism, progression of the DVT or mortality compared to individuals prescribed bed rest. |

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| ***This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor*** |

*The above information should fit onto the first page of your CAT*

**SEARCH STRATEGY**

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| **Terms used to guide the search strategy** |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| Deep vein thrombosisVenous thrombosisVenous thromboembolismLower extremity DVT | Ambulat\*Gait trainingGaitWalk\*Early mobilityEarly ambulationMobilityRange of motion, articular | Bed mobilityTherapeutic exerciseExercise therapyExercise Functional transfers | MortalityLength of stayHospital readmissionPatient readmissionPulmonary embolism |

**Final search strategy (history):**

*Show your final search strategy (full history) from PubMed. Indicate which “line” you chose as the final search strategy.*

1 ((Deep vein thrombosis) OR (venous thrombosis) OR (venous thromboembolism) OR (lower extremity DVT))

2 ((Ambulat\*) OR (gait training) OR (gait) OR (walk\*) OR (early mobility) OR (early ambulation) OR (mobility) OR (range of motion, articular))

3 ((Bed mobility) OR (therapeutic exercise) OR (exercise therapy) OR (exercise) OR (functional transfers))

4 ((Mortality) OR (length of stay) OR (hospital readmission) OR (patient readmission) OR (pulmonary embolism))

5 ((#1) AND (#2) AND (#3) AND (#4))

6 ((#1) AND (#2) AND (#3))

7 (((Deep vein thrombosis) OR (venous thrombosis) OR (venous thromboembolism) OR (lower extremity)) NOT ((prevention) OR (prophylaxis)))

8 ((Therapeutic exercise) OR (exercise therapy) OR (exercise) OR (functional transfers))

9 ((#7) AND (#2) AND (#8))

10 ((bed rest) AND (bed mobility))

**11 ((#7) AND (#2) AND (#10))**

*In the table below, show how many results you got from your search from each database you searched.*

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| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| **PubMed****CINAHL****Pedro** | **59****47****16** | **Human, English, past 10 years**  |

## INCLUSION and EXCLUSION CRITERIA

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| **Inclusion Criteria** |
| * English,
* Acute care setting,
* Published in last 10 years,
* Randomized controlled trials
* Systematic reviews
 |
| **Exclusion Criteria** |
| * Case reports
* Pediatrics
* Geriatrics
* Outpatient setting
 |

**RESULTS OF SEARCH**

**Summary of articles retrieved that met inclusion and exclusion criteria**

*For each article being considered for inclusion in the CAT, score for methodological quality on an appropriate scale, categorize the level of evidence, indicate whether the relevance of the study PICO to your PICO is high/mod/low, and note the study design (e.g., RCT, systematic review, case study).*

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| --- | --- | --- | --- | --- |
| **Author (Year)** | **Risk of bias (quality score)\*** | **Level of Evidence\*\*** | **Relevance** | **Study design** |
| **Aissaoui et al. (2009)**[3](https://sciwheel.com/work/citation?ids=11706566&pre=&suf=&sa=0) | **AMSTAR 2 (moderate)** | **Level 1** | **High** | **Meta-analysis of RCTs** |
| **Aldrich and Hunt (2004)**[4](https://sciwheel.com/work/citation?ids=11706572&pre=&suf=&sa=0) | **AMSTAR 2 (critically low)** | **Level 1** | **Low** | **Systematic Review, RCTs, prospective and retrospective cohort studies** |
| **Anderson et al. (2009)**[5](https://sciwheel.com/work/citation?ids=11706579&pre=&suf=&sa=0) | **AMSTAR 2 (low)** | **Level 1** | **High** | **Systematic review of RCTs** |
| **Gay et al. (2009)**[6](https://sciwheel.com/work/citation?ids=11706592&pre=&suf=&sa=0) | **AMSTAR 2 (critically low)** | **Level 1** | **Low** | **Systematic review, mix of RCTs and other quantitative studies** |
| **Hillegass et al. (2016)**[2](https://sciwheel.com/work/citation?ids=4300067&pre=&suf=&sa=0) | **AGREE II (high)** | **Unable to assign due to collection of variety of study designs** | **High** | **Clinical Prediction Guideline** |
| **Liu et al. (2015)**[1](https://sciwheel.com/work/citation?ids=11706841&pre=&suf=&sa=0) | **AMSTAR 2 (high)** | **Level 1** | **High** | **Meta-analysis of RCTs, prospective and retrospective cohort studies** |
| **Manganaro et al. (2008)**[7](https://sciwheel.com/work/citation?ids=7941054&pre=&suf=&sa=0) | **Downs and Black Checklist (18/27, fair)** | **Level 3** | **High** | **Retrospective quasi-experimental study** |
| **Romeras-Villegas et al. (2008)**[8](https://sciwheel.com/work/citation?ids=11707039&pre=&suf=&sa=0) | **PEDro (6/10, good)** | **Level 2** | **Moderate** | **Prospective RCT** |

\*Indicate tool name and score

\*\*Use Portney Table 36-1: Summary of Levels of Evidence (2020). If downgraded, indicate reason why.

**BEST EVIDENCE**

The following 2 studies were identified as the ‘best’ evidence and selected for critical appraisal. Rationale for selecting these studies were:

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| * **Liu et al.**[1](https://sciwheel.com/work/citation?ids=11706841&pre=&suf=&sa=0)

**This article is the highest quality systematic review I appraised with articles included from all over the world. There were no major flaws in methodology as assessed by the AMSTAR 2. The authors made every effort to maximize the internal and external validity and performed extensive statistical analysis to answer their research questions that were directly relevant to my PICO.*** **Hillegas et al.**[2](https://sciwheel.com/work/citation?ids=4300067&pre=&suf=&sa=0)

**The supporting evidence for recommendations directly related to my PICO were of high quality in this CPG. The overall guideline is also well designed and has good validity based on the AGREE II tool. I found it especially relevant to my clinical scenario because the review included an algorithm that not only detailed who should participate in early ambulation over bed rest, but what specific factors we as PTs should consider before initiating mobility. The direct recommendations for physical therapy practice cannot be overlooked.** |

**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of (Bed Rest versus Early Ambulation with Standard Anticoagulation in the Management of Deep Vein Thrombosis: A Meta-Analysis) by (Liu et al., 2015)**[1](https://sciwheel.com/work/citation?ids=11706841&pre=&suf=&sa=0)

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| **Aim/Objective of the Study/Systematic Review:** |
| The systematic review by Liu et al. aims to determine the effect of early ambulation vs. bed rest on several outcomes of interest in patients with a diagnosed DVT, including development of a pulmonary embolism, progression of the DVT and improvement of pain and edema. |
| **Study Design**[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| The study by Liu et al. is a systematic review and meta-analysis that included 13 RCTs, prospective and retrospective cohort studies. **Search Strategy:** Several databases were included in the search: Embase, Medline, PubMed, Cochrane Library, Sinomed, WanFangData and Chinese National Knowledge Infrastructure. Authors used terms such as deep vein thrombosis, ambulation, bed rest and pulmonary embolism as well as related Mesh terms and synonyms for the Chinese databases. **Selection Criteria:** Criteria included: RCTs or cohort studies with good design and low risk of bias, study participants that have acutely diagnosed DVT, interventions compared early ambulation and bed rest in addition to evidence based medical management such as anticoagulation therapy, study outcomes investigating at least one of the following- development of a pulmonary embolism, progression of diagnosed DVT, pain and edema. **Methods:** An online search was conducted in the databases listed in the Search Strategy, to include articles published up to 2014, whose titles and abstracts appeared to adhere with selection criteria. Authors screened 1,727 titles and abstracts and narrowed the literature to 50 full text articles for further analysis. After careful consideration by 2 reviewers, 13 studies were selected and included RCTs, prospective and retrospective designs. A publication bias assessment was conducted using a funnel plot created by the Review Manager version 5.3 software (RevMan 5.3) and additional Beggs and Eggers tests to determine there was no publication bias in the group of studies selected. A thorough risk of bias assessment was conducted using the RevMan 5.3 Risk of bias table for RCTs and the Newcastle-Ottawa Scale for non-randomized cohort studies. Data relevant to the authors research question was extracted including details about the participants, anticoagulation therapy, interventions, outcome measures and results. These results were compiled in a meta-analysis with subgroup and sensitivity analyses where appropriate. Sources of heterogeneity were investigated and discussed. |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| Studies were conducted in several different countries including Germany, Switzerland, Austria, Spain, Sweden, Italy, Turkey and China. The majority of studies took place in the hospital setting as participants were being treated for acute DVT. There was a minority of studies that investigated the possibility of home management of acute DVT in the early ambulation group. |
| **Participants**[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| The 13 studies included based on the selection criteria had designs as follows: 10 randomized control trials, 1 non-randomized control trial, 1 prospective cohort study and 1 retrospective case-control study. 10 of these articles were published in English while 3 were published in Chinese. Studies were determined to have low or moderate risk of bias. A total of 3,269 participants with median ages in the 50s and 60s who had been recently diagnosed with a lower extremity DVT were represented in the 13 studies. |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| Participants in the control group were placed on bed rest in addition to appropriate anticoagulation therapy. There was some heterogeneity in the studies about the duration of bed rest, but overall the participants remained in bed for at least 3 days (with most studies using at least 7 days) after diagnosis of LE DVT. |
| *Experimental* |
| Participants in the experimental group also received appropriate anticoagulation therapy and counsel to begin early ambulation with nursing or therapy staff. The initiation of early ambulation also varied between studies, but overall participants began ambulating no later than 3 days after diagnosis of DVT. There was some heterogeneity about the prescription of ambulation, as some researchers instructed this group to walk as much as possible while others had more specific guidelines. |
| **Outcome Measures**[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| The authors of this paper divided outcome measures into primary and secondary endpoints as they were searching for articles. Three main outcomes were considered primary endpoints for statistical analysis and included: 1) Confirmation of new PE with CT scan or scintigraphy, differed between studies as to how often this was assessed and some only assessed in symptomatic participants. 2) Progression of DVT assessed by ultrasound or plebography. For some studies this included an analysis of whether vein health had improved by measuring recanalization of the occluded vein and venous outflow. 3) Mortality. Data were collected by trained professionals blinded to the patients experimental group assignment. Several different time points were used for follow-up from 10 days to 6 months after DVT treatment began for each of these primary endpoints.The authors included analysis of two secondary endpoints including VAS pain score, and edema measured by limb circumference that will be omitted from this appraisal due to low relevance to the clinical question at hand. |
| **Main Findings**[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. You may summarize results in a table but you must explain the results with some narrative.] |
| Table 1. Study Characteristics and Main Findings

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| --- | --- | --- | --- | --- |
| **Author(year)** | **Study design** | **Bed rest duration/ambulation date** | **Primary endpoint assessed** | **P** |
| Schellong (1999) | RCT | 8 days/ day 0 | PE in 8-10 days | 0.25 |
| Ashwanden(2001) | RCT | 4 days/ day 0 | PE in 3 months | 0.44 |
| Blattler(2003) | RCT | 9 days/ day 0 | Progression of DVT | 0.01 (favoring ambulation) |
| Trujillo-Santos (2005) | Prospective | ≥3 days/ no details | Symptomatic PE in 15 days | Not significant |
| Junger (2006) | RCT | ≥5 days/ day 0 | PE, progression of DVT and mortality | 0.088 |
| Romera (2006) | RCT | 5 days/ day 0  | Symptomatic PE in 10 days | 0.33 |
| Isma (2007) | RCT | No details/ immediately | Recanalization of vein in 6 months | Not significant |
| Romera (2008) | RCT | 5 days/ day 0  | Symptomatic PE in 10 days | 0.54 |
| Manganaro (2008) | Retrospective case-control | 7± 2 days or permanently/ day 0 | PE, progression of DVT and mortality in 30 days | 0.001 (favoring ambulation) |
| Rahman (2009) | RCT | 7 days/ day 0 | Venous outflow at day 7 | Not significant |
| Huang (2010) | RCT | 7-10 days/ day 1-2 | Symptomatic PE in 3months | Not significant |
| Feng (2011) | nRCT | 7 days/day 0 | PE in 7 days | >0.05 |
| Liu (2013) | RCT | 7-14 days/day 1-2 | Symptomatic PE in 3 months | Not significant |

 Table 2. Meta-analysis of primary endpoints

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| Study or Subgroup | Risk difference (95% confidence interval) |
| Schellong (1999) | 0.05 (-0.09, 0.19) |
| Ashwanden(2001) | 0.04 (-0.07, 0.16) |
| Blattler(2003) | -0.18 (-0.52, 0.16) |
| Trujillo-Santos (2005) | -0.00 (-0.01, 0.00) |
| Junger (2006) | -0.15 (-0.30, 0.01) |
| Romera (2006) | -0.00 (-0.06, 0.05) |
| Isma (2007) | 0.00 (-0.06, 0.06) |
| Romera (2008) | 0.01 (-0.03, 0.05) |
| Manganaro (2008) | -0.43 (-0.55, -0.31) |
| Rahman (2009) | 0.00 (-0.15, 0.015) |
| Huang (2010) | 0.00 (-0.09, 0.09) |
| Feng (2011) | 0.01 (-0.16, 0.18) |
| Liu (2013) | 0.00 (-0.06, 0.06) |
| **Total** | -0.03 (-0.05, -0.02) |

The main findings of this study are summarized above Table 1. and include the article, its design, a brief description of intervention, the primary endpoint assessed and statistical significance in the form of a p-value when given. All patients were treated with anti-coagulants unless contraindicated. One limitation is the omission of confidence intervals for these values as they were not included by the authors. It is clear there is some heterogeneity with regards to the duration of bed rest and initiation of ambulation, but this heterogeneity was investigated using a random effect model and was found not to affect the overall findings. Every article included in this review found either no statistical significance when comparing primary endpoint events between groups, or differences that statistically favored the ambulation group rather than the bed rest control group. The meta-analysis results of primary endpoints are presented in Table 2. This data is best visualized by referring to the forest plot in the Liu et al. article. When comparing the difference between proportions of participants in the bed rest vs. ambulation groups that had primary endpoints, the meta-analysis determined a risk difference of -0.03(95% CI -0.05 to -0.02) with a p-value of 0.22. |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| Meta-analysis of primary endpoints indicates patients who were treated with early ambulation vs. bed rest were no more likely to develop a new PE, experience progression of the current DVT or die from the condition. The authors highlight the importance of standard anti-coagulation therapy that precedes mobility interventions but assert that early ambulation is appropriate after pharmaceutical management is achieved.  |
| **Critical Appraisal** |
| **Validity**[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.] |
| This systematic review and meta-analysis by Liu et al. is a high quality study with a low risk of bias as determined by the AMSTAR II instrument and assessment instructions by Shea et al.[9](https://sciwheel.com/work/citation?ids=4704447&pre=&suf=&sa=0) Based on the instrument, the results presented by Liu et al. can be interpreted with high confidence because of the excellent internal and external validity of the study. One of the biggest strengths of this article was the extensive investigation of heterogeneity and risk of bias in individual articles through multiple tests, and transparency of these results with regards to the influence this may have on study findings. The authors also thoroughly investigated the possibility of publication bias first through a funnel plot and then with Begg's and Egger's tests to make sure the included studies were representative of the available literature on the topic at hand. A comprehensive literature search was conducted including articles published in academic journals around the world. Multiple authors were used to select studies and extract data to reduce the possibility of introducing bias. The only weakness found in the AMSTAR II appraisal was not including sources of funding for individual articles included in the review, but authors did include a statement of no competing interests for the current review. The quality of this study could have been improved by including only RCTs and excluding non-randomized designs, but authors assessed risk of bias and accounted for this in their discussion. |
| **Interpretation of Results**[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| Due to the high quality of evidence, the findings presented by Liu et al. can be interpreted with confidence. It seems that this collection of randomized and high quality non-randomized studies all tell similar stories about the appropriateness of early ambulation when patients have an acute DVT. While some individual studies and the risk difference forest plot indicate a potential significant reduction in primary endpoints in the early ambulation groups, this conclusion may be premature due to insufficient research and confidence interval so close to zero. This article did not include specifics on when to initiate ambulation and what frequency, duration, intensity to use due to the heterogeneity of study designs. It is clear that early ambulation does not increase adverse DVT related events when patients have been treated with standard anti-coagulation therapy, including the formation of a PE, progression of DVT or DVT related mortality. This does not mean that there is no risk of these events occurring, and physical therapists should be careful to monitor for signs of rapidly worsening conditions during or after mobility. To specifically address the clinical question at hand, early ambulation does not increase risk of these primary endpoints, but we cannot say for certain that this intervention reduces them when compared to bed rest. Future research should strive to outline indicators of when to initiate activity safely and parameters to use for exercise prescription. |
| **Applicability of Study Results**[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.] |
| This study is highly relevant to the clinical scenario, as the participants were on average in their 5th or 6th decade of life with an acute DVT. Participants were not excluded based on comorbidities so it can be assumed these results are generalizable to patients with common comorbidities such as those outlined in the clinical scenario: obesity, chronic heart failure, type II diabetes mellitus and associated peripheral neuropathy. The patient in this scenario has been treated with anti-coagulants in a standard manner like the current study’s participants and with further information about indicators of successful anti-coagulation, I would be confident in applying early ambulation recommendations to this patient. These results support the general idea that mobility training early and often in the hospital setting is best for promoting positive outcomes for patients and watching for rapid changes in patient condition is well within the expertise of acute care physical therapists. PTs conduct chart reviews every day to assess the appropriateness of individual patients for mobility, so when given clear evidence-based recommendations they will be able to make informed clinical decisions about mobilization in this medically complex population. |

**(2) Description and appraisal of (Role of Physical Therapists in the Management of Individuals at Risk for or Diagnosed With Venous Thromboembolism: Evidence-Based Clinical Practice Guideline) by (Hillegass et al., 2016)**[2](https://sciwheel.com/work/citation?ids=4300067&pre=&suf=&sa=0)

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| **Aim/Objective of the Study/Systematic Review:** |
| The clinical practice guideline (CPG) by Hillegass et al. aimed to present recommendations in the form of key action statements based on the current evidence to guide treatment of patients at risk for venous thromboembolism (VTE) or after diagnosis of a lower extremity DVT. This guideline covers prevention, screening and treatment recommendations for patients at risk of or with a diagnosed VTE which includes DVT and PE. |
| **Study Design**[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| The American Physical Therapy Association (APTA) formed a VTE Guideline Development Group from select members of the Cardiovascular & Pulmonary and Acute Care sections to create this CPG. This group collaborated with the APTA to develop a list of topics to be included in the scope of this review, guide the literature search and synthesize results into key action statements.**Search Strategy:** The following databases were included in the search: PubMed, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), and Physiotherapy Evidence Database (PEDro). Existing published CPGs were also searched in the National Guideline Clearinghouse database and Trip database. Key words, MeSH terms and CINAHL headings were used to narrow down the search and included but were not limited to: venous thrombosis, pulmonary embolism, movement, immobilization, early ambulation, anticoagulants and compression stockings.**Selection Criteria:** Articles that investigated key topics within an appropriate population were included in the CPG. Case reports and articles with pediatric subjects were excluded. Only articles written in English were included.**Methods:** After determining the topic areas to be included in the CPG, a search was performed by a librarian to identify articles published between May 1, 2003 and May 2014 that included mobilization and anticoagulation therapy as they relate to prevention and treatment of VTE. The authors reviewed 350 abstracts and 43 relevant CPGs from the databases to be considered for inclusion in the current CPG. Each article that was included was appraised with a validated tool by 3 individuals based on the study design, including the Assessment of Multiple Systematic Reviews (AMSTAR) tool for systematic reviews. This information was used to assist in determining the level of evidence presented by each article. External stakeholders including the American College of Chest Physicians, Society for Vascular Nursing, physical therapy clinicians and patient representatives were invited to review drafts of the CPG as it was developed. The results of the literature search and appraisal were used to develop 14 key action statements with associated recommendation grades to guide clinical practice related to prevention and treatment of VTE.**Levels of Evidence and Grades of Recommendations:** In order to determine the strength of recommendation for each key action statement, the level of evidence of each article discussed in a topic was determined. Level I evidence was defined as studies of high-quality and low risk of bias according to a critical appraisal score of 50% or more on the respective tool. Level II evidence was defined as lower quality studies, potentially with sources of bias such as improper randomization or no blinding of subjects/investigators. Level III evidence came from case-control studies or retrospective studies. Level IV evidence comes from case studies or case series (excluded from this CPG) and expert opinion is considered Level V evidence.Recommendations were given grades to quickly describe the quality of evidence backing a statement. Grade A are strong recommendations which are developed from mostly Level I evidence, Grade B recommendations are developed from mostly Level II evidence, Grade C recommendations are weak and derived from low quality Level II studies or a majority of Level III and IV evidence, Grade D recommendations are theoretical and come from evidence in animal or cadaver studies or expert opinion, Grade P signifies best practice and this recommendation is based on current accepted practice and expertise of authors, Grade R recommendations indicate that the literature is conflicted, and the recommendation is a synthesis of these conflicting conclusions. Each author reviewed the literature related to each key action statement and voted to assign level of evidence and grade of recommendations. |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| Focusing on the studies included for key action statements 7 and 8 that directly address my PICO, studies occurred in a hospital setting as individuals had been diagnosed with DVT within the last 24 hours. |
| **Participants**[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| Each key action statement includes information about the population of included articles/participants related to that topic in the “summary of evidence” subheading. The majority of included articles studied hospitalized participants and middle aged to older adults. Participants were either at risk for developing VTE or diagnosed with a lower extremity DVT or PE via gold standard tools that include the presence of clinical signs as well as diagnostic imaging. Participants in studies that provided evidence for key action statements 7 and 8 all had diagnosed acute lower extremity DVTs. |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| Very little specific information is included about the definition/duration of bed rest in the current CPG, however investigation into included evidence suggests bed rest of at least 3 days was the treatment provided. |
| *Experimental* |
| Ambulation was initiated when patients reached therapeutic levels of prescribed anti-coagulants. Specifics about exercise prescription like duration, intensity and frequency were not included in this CPG. |
| **Outcome Measures**[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Included articles measured mainly new pulmonary embolisms and progression or extension of deep vein thrombosis via scinctigraphy or CT scan (this occurred on average 7 days after initiation of intervention); but some investigated pain with VAS scale, leg circumference as a measure of edema, both of which were measured at baseline and after a set time frame at intervals of around 7 days and 3 months after initiation of treatment. Some articles investigated the development of long-term post-thrombotic syndrome symptoms after 6 or 12 months. |
| **Main Findings**[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. Use a table to summarize results if possible.] |
| Due to the nature of the CPG, tables of specific statistical analysis were not included. The key action statements 7 and 8 are directly relevant to my clinical question. While American College of Chest Physician guidelines include strong evidence that anticoagulation therapy be initiated immediately after diagnosis of DVT, the current CPG was only able to issue a Grade D recommendation that physical therapists verify the type of anti-coagulant the patient was prescribed and when it was initiated. This recommendation is based on expert opinion of the authors and experience from other practicing clinicians. There is however strong evidence to support that mobilization is contraindicated before proper anticoagulation levels have been reached (or medical management of another kind for those with bleeding disorders such as IVC filter placement). This CPG has compiled a list of common anticoagulants and the time it takes after administration to reach peak therapeutic levels. As a general rule, physical therapists should double check with the physician if attempting to mobilize a patient before the high end of the range of time to peak therapeutic level. For patients prescribed Coumadin, International Normalized Ratio (INR) values are used to determine appropriateness for ambulation rather than time since administration. If patients have had an IVC filter placed, they are also appropriate for mobilization. This information is summarized in the following table.

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| Drug Class (Common Names) | Time to Peak Therapeutic Level | When to Check with Physician before mobilization |
| Low molecular weight heparin (Lovenox, Fragmin, Enoxaparin, Innohep) | 3-5 hours | <5 hours since administration |
| Unfractionated heparin (Heparin) | 24-48 hours | <48 hours since administration |
| Fondaparinux (Arixtra) | 2-3 hours | <3 hours since administration |
| Novel Oral Anticoagulants (Pradaxa, Eliquis, Xarelto) | 2-3 hours | <3 hours since administration |
| Vitamin K antagonists (Coumadin, Warfarin) | INR 2-5 | INR >5 |

The CPG puts forward a Grade A recommendation that mobilization should be initiated as soon as possible after peak therapeutic levels of anticoagulant have been reached. This is due to a collection of Level I studies that have found no increase in development of new PE or progression of DVT when early ambulation is utilized rather than bed rest. |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| The risk of PE or progression of DVT should be reduced as much as possible with standard anticoagulation therapy at peak therapeutic levels before mobilization should be initiated. When patients reach this level and are appropriate for mobilization, they should do so immediately to reduce harmful effects of bed rest due to the high-quality evidence suggesting ambulation will not increase their risk of having a DVT related event. |
| **Critical Appraisal** |
| **Validity**[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.] |
| This CPG by Hillegass et al. is a high-quality guideline based on the Appraisal of Guidelines for Research and Evaluation tool (AGREE II). Scoring of this guideline across six domains was guided by the instructions put forth by Brouwers et al., specifically using a cut off score of 70% for each domain to signify a quality guideline.[10](https://sciwheel.com/work/citation?ids=11847277&pre=&suf=&sa=0) The 6 domains evaluated were Scope and Purpose, Stakeholder Involvement, Rigour of Development, Clarity of Presentation, Applicability and Editorial Independence. Some strengths of this guideline include the clarity with which the scope and key topics were defined and the applicability of results to the patient population discussed and physical therapy practice. The authors are also of great expertise in their fields, with the Cardiovascular & Pulmonary and Acute Care sections of the APTA combining to draw upon their experience. It is clear the authors made every effort to include stakeholders at every level including providers in the ACCP, nurses and physical therapists as well as patients for whom this CPG will directly affect. Authors conducted a thorough literature search with the help of a librarian to identify all relevant evidence and the methods used to assign levels of evidence and recommendation grades were clearly outlined. Key action statements presented are clear and explained when there is an intentional ambiguity, and benefits and costs of implementation are discussed. One limitation of interpreting the evidence in this guideline is the lack of specific information about all studies included as one would expect in a systematic review. This is in accordance with the general practice of writing CPGs but limits readers from interpreting statistical analyses themselves. |
| **Interpretation of Results**[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| Due to the high-quality synthesis and development of this CPG, I feel confident the recommendations presented can be safely and effectively implemented in clinical practice. The clear discussion of assigning grades to recommendations made it easy to determine which statements had the highest levels of evidence supporting them. A Grade A recommendation to mobilize after peak therapeutic levels of anticoagulants have been reached provides clear direction for physical therapists in practice based on level I studies. While the recommendations state physical therapists can begin mobilization after the requisite time has passed since administration of anticoagulant, individual physical therapists should likely become familiar with the culture in their hospital and respect physicians wishes while also sharing current literature when necessary to best serve the patient. Physical therapists should therefore be familiar with the time to peak therapeutic levels as presented and use this information to operate in an interdisciplinary team. |
| **Applicability of Study Results**[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.] |
| This guideline gives the most concrete recommendations about when to initiate mobilization in the articles appraised for this CAT. This information is highly relevant to physical therapist practice and the treatment of the patient described in the clinical scenario. Participants in included studies had similar demographics to the patient in the scenario and treatment occurred in the hospital setting. This guideline was developed to help physical therapists treat patients in the same population as the scenario and presents evidence compiled and appraised by clinicians who are experts in the field. Recommendations to begin mobilization after appropriate anticoagulation are based on studies that support the finding that early ambulation does not cause an increase in adverse DVT-related events. The algorithm and flow map of when to mobilize patients with acute DVT provides direct recommendations of when to begin early ambulation to minimize the adverse effects of bed rest in our patients without unduly increasing their risk of DVT related events.  |

**SYNTHESIS AND CLINICAL IMPLICATIONS**

[Synthesize the results, quality/validity, and applicability of the two studies reviewed for the CAT. Future implications for research should be addressed briefly. Limit: 1 page.]

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| Overall, through appraisal of the best evidence available on the topic of mobilization in patients with acute DVT, it appears patients can begin ambulating early after therapeutic levels of anticoagulant have been achieved, without increased risk of developing a pulmonary embolism or progression of the current deep vein thrombosis. The first article appraised by Liu et al. was a well-designed systematic review and meta-analysis that was directly relevant to the clinical question as it investigated the incidence of several adverse DVT-related events in patients assigned to a bed rest or early ambulation treatment group. This review contained articles from a plethora of databases and did not discriminate to research published only in English. This along with their extensive investigation of publication bias leaves readers confident that the articles reviewed are representative of all the current literature on the topic. This review also did an excellent job of searching individual articles for bias and heterogeneity and their causes, to discuss the impact of these factors on the strength of the main findings. Subgroup and sensitivity analyses indicate that the heterogeneity present in the review articles did not influence the outcome of the meta-analysis and therefore results can be confidently interpreted and applied to the current clinical scenario and others. While results were unclear on whether early ambulation could reduce the likelihood of patients developing a PE or VTE-related mortality, the meta-analysis indicates there is no increase in adverse events in patients who begin ambulation before the third day after DVT diagnosis when compared to patients who are placed on bed rest for at least three days. The results of this meta-analysis leave a couple questions including the best exercise prescription for the early ambulation/mobilization group, whether the experimental intervention can actually reduce adverse events and how this intervention impacts other meaningful measures such as quality of life and long-term disability. Future research should venture into these realms to further develop the support behind implementation of early ambulation in patients who have been diagnosed with an acute DVT.The second article by Hillegass et al. is a high-quality clinical practice guideline with clear key action statements that directly effect physical therapist practice. Due to this aspect of applicability and the excellent design and development of the guideline, algorithms and recommendations related to mobilization of patients with an acute DVT should be considered and implemented in cases such as the current clinical scenario. One of the strengths of this article is the development of an evidence-based decision tree to help physical therapists determine when it is appropriate to mobilize patients based on the type of anticoagulant prescribed and time since administration to assure peak therapeutic levels have been reached. A Grade A recommendation was provided stating physical therapists should use the algorithm to mobilize patients as soon as possible after therapeutic levels of anticoagulant were in systemic circulation. This recommendation is based on the synthesis of Level I evidence and therefore should be interpreted with confidence. Despite this CPG being published in 2016 with included articles published up to 2014, it is the best and most contemporary research available at this time. It would be advised that evidence guiding clinical practice be updated regularly to reflect novel research roughly every 5 years.Through a synthesis of evidence including the finding that patients who ambulate early are not at increased risk of adverse events and the evidence to support early ambulation after appropriate anticoagulation, current best practice should be to assist patients with acute DVT in mobilization after proper medical management has taken place. To directly address the clinical question at hand, this 60 yo woman with comorbidities should engage in early mobility after the physical therapist and interdisciplinary team are certain she has reached appropriate levels of anticoagulation. The patient can be informed with confidence that ambulation is just as safe as remaining in bed, and has potential benefits for their condition in the short and long term.  |

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[List all references cited in the CAT]

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