Appendix A. Core Technical Experts and Peer Reviewers

Core Technical Experts		
Expert Area and Organization	**Name**	**Location**
Partner Organization		
American Academy of Family Physicians	Lee Green MD	University of Michigan, Ann Arbor, MI
Cochrane Collaboration		
Dutch Cochrane Center	Jeroen van der Heijden MD	Academic Medical Centre, Amsterdam, the Netherlands
Diagnostic Testing Expert		
	Steven W. Heim MD	University of Virginia, Charlottesville, VA
Payor		
Center for Medicare and Medicaid Services	Steve Phurrough MD, MPA	Baltimore, MD
Primary Care Organizations		
American College of Physicians–American Society of Internal Medicine	Rodney E. Hornbake MD	Gentiva Health Services, Melville, NY
	Patricia Barry MD	Merck Institute of Aging and Health, Washington, DC
Society of General Internal Medicine	Richard White MD	University of California at Davis, CA
Professional Organizations		
American College of Chest Physicians	Gordan Guyatt MD	McMaster University, Hamilton, Ontario
	Jack Hirsch MD	Hamilton Civic Hospitals Research Centre, Hamilton, Ontario
	Agnes YY Lee MD	McMaster University, Hamilton, Ontario
	Phillip Wells MD	Ottawa Hospital, Ottawa, Ontario
American Association of Health Plans		Washington DC
American College of Radiology	Michael A. Bettmann MD	Dartmouth University, Hanover, NH
Funding Organization		
Agency for Healthcare Research and Quality (AHRQ)	David Atkins MD	Rockville, MD

Appendix B. Priority Journals for Hand Searching*

Priority Journal Titles
American Journal of Respiratory and Clinical Care Medicine
American Journal of Roentgenology (AJR)
Annals of Internal Medicine
Arteriosclerosis, Thrombosis, and Vascular Biology
Blood
British Journal of Haematology
British Medical Journal
Chest
Circulation
Circulation Research
JAMA
Journal of Computer Assisted Tomography
Journal of Nuclear Medicine
Lancet
Magnetic Resonance Medicine
New England Journal of Medicine
Radiology
Seminars in Nuclear Medicine
Thorax
Thrombosis and Haemostasis

* Tables of Contents reviewed from 1 October 2001 to 31 March 2002.

Appendix C. Literature Search Strategies

Question 1 and Question 2 — Low molecular weight heparin for deep venous thrombosis and pulmonary embolism (systematic reviews)

Medline

(quantitative* OR methodolog* OR systematic* OR meta-analysis OR "metaanalysis" OR " meta analysis" OR "meta-analyses" OR " metaanalyses" OR "meta analyses" OR (MEDLINE AND review[pt]) OR "clinical conference"[pt] OR "consensus development conference"[pt] OR "guideline"[pt] OR "meta analysis"[pt] OR "practice guideline"[pt] OR (review [pt] AND systematic*)) AND (deep venous thrombosis OR venous thromboembolism OR pulmonary embolism) AND (low molecular weight heparin OR lmwh OR enoxoparin OR Lovenox OR logiparin OR Innohep OR nadroparin OR fraxoparine OR dalteparin OR Fragmin OR reviparin OR clivarin OR CY222 OR tinzaparin OR innohep OR logiparin OR certoparin OR sandoparin OR embolex OR parnaparin OR fluxum OR clexane OR tedelparin OR Tedral)

Cochrane

((LOW and (MOLECULAR and (WEIGHT and HEPARIN))) AND ((DVT or PE) OR (VENOUS AND THROMBOSIS)))

Question 3a. Inpatient versus outpatient (primary literature)

(inpatients OR hospital) AND (ambulatory care OR ambulatory care facility OR outpatient) AND (deep venous thrombosis OR venous thromboembolism OR pulmonary embolism) AND (low molecular weight heparin OR lmwh OR enoxoparin OR Lovenox OR logiparin OR Innohep OR nadroparin OR fraxoparine OR dalteparin OR Fragmin OR reviparin OR clivarin OR CY222 OR tinzaparin OR innohep OR logiparin OR certoparin OR sandoparin OR embolex OR parnaparin OR fluxum OR clexane OR tedelparin OR Tedral)

Question 3b. Low molecular weight heparin costs (primary literature)

(cost OR charge) AND (low molecular weight heparin OR lmwh OR enoxoparin OR Lovenox OR logiparin OR Innohep OR nadroparin OR fraxoparine OR dalteparin OR Fragmin OR reviparin OR clivarin OR CY222 OR tinzaparin OR innohep OR logiparin OR certoparin OR sandoparin OR embolex OR parnaparin OR fluxum OR clexane OR tedelparin OR Tedral) AND (deep venous thrombosis OR pulmonary embolism OR venous thromboembolism)

Question 4. Duration of treatment (primary literature)

duration of treatment OR ("time factors/adverse effects" [MESH] OR "time factors/standards"[MESH]) AND (deep vein thrombosis OR pulmonary embolism or venous thromboembolism) AND (warfarin OR coumadin OR low molecular weight heparin)

Question 5. Clinical prediction rules
(sensitivity AND specificity) AND (deep venous thrombosis or pulmonary embolism and venous thromboembolism) AND clinical

Question 6. Ultrasound (systematic reviews)
(quantitative* OR methodolog* OR systematic* OR meta-analysis OR "metaanalysis" OR " meta analysis" OR "meta-analyses" OR " metaanalyses" OR "meta analyses" OR (MEDLINE AND review[pt]) OR "clinical conference"[pt] OR "consensus development conference"[pt] OR "guideline"[pt] OR "meta analysis"[pt] OR "practice guideline"[pt] OR (review [pt] AND systematic*)) AND (deep vein thrombosis OR venous thromboembolism) AND (ultrasonography OR ultrasound OR Doppler)

Question 7. Computerized tomography or magnetic resonance imaging (systematic reviews)
(quantitative* OR methodolog* OR systematic* OR meta-analysis OR "metaanalysis" OR " meta analysis" OR "meta-analyses" OR " metaanalyses" OR "meta analyses" OR (MEDLINE AND review[pt]) OR "clinical conference"[pt] OR "consensus development conference"[pt] OR "guideline"[pt] OR "meta analysis"[pt] OR "practice guideline"[pt] OR (review [pt] AND systematic*)) AND (pulmonary embolism) AND (computed tomography OR magnetic resonance imaging)

(Primary literature)
evaluation AND pulmonary embolism AND (computed tomography OR magnetic resonance imaging)

Question 8. D-dimer (systematic reviews)
(quantitative* OR methodolog* OR systematic* OR meta-analysis OR "metaanalysis" OR " meta analysis" OR "meta-analyses" OR " metaanalyses" OR "meta analyses" OR (MEDLINE AND review[pt]) OR "clinical conference"[pt] OR "consensus development conference"[pt] OR "guideline"[pt] OR "meta analysis"[pt] OR "practice guideline"[pt] OR (review [pt] AND systematic*)) AND d-dimer AND (deep venous thrombosis OR pulmonary embolism OR venous thromboembolism)

Appendix D. Abstract Review Form for Primary Literature

Record Number: **EPC Venous Thromboembolism Project** **Reviewer: __< >____**

Abstract review Form **Data Entry: _____**

Title:

☐ **Article for reference only**

Article relates to Key Questions (check **all** that apply**):** ☐ LMWH for DVT (**Q1**) ☐ LMWH for PE (**Q2**) ☐ efficacy and cost-effectiveness of outpatient treatment with LMWH or UFH for DVT **(Q3**) ☐ duration of therapy (**Q4)**	☐ use of clinical prediction rules (**Q5**) ☐ ultrasonography for DVT diagnosis (**Q6**) ☐ helical CT or MRI/MRA scan for PE diagnosis (**Q7**) ☐ d-dimer for thromboembolism diagnosis (**Q8**) ☐ does not apply to any question
Do not review article, because article … (check 1 or more**):** ☐ is not in English ☐ does not include human data ☐ is a meeting abstract (no full article for review) ☐ involves *only* prevention	☐ has no original data ☐ is a case report (single patient) ☐ other _____
If Question 3: **Do not review article, because …** ☐ does not involve a comparison group (in an RCT or observational study) **or** is not a cost-effectiveness analysis	**If Question 4:** **Do not review article, because…** ☐ does not involve a comparison group (in an RCT or observational study
If Question 5: **Do not review article, because …** (check 1 or more) ☐ does *not* include 2 of 3 (history, physical exam, laboratory testing) ☐ does not specify a reference standard (gold standard)	**If Question 7:** **Do not review article, because …** (check 1 or more) ☐ does not report test characteristics of CT **or** MRI for diagnosis of PE ☐ does not use angiography **or** VQ scan as reference

Appendix E. Abstract Review Form for Systematic Reviews

Record Number: **EPC Venous Thromboembolism Project** **Reviewer: __< >____**

First Abstract Review: **Abstract review Form** **Data Entry: _____**

Title:

Do not review article, because article … (check 1 or more):	**Article relates to Key Questions (check all that apply)**
☐ is not in English ☐ does not include human data ☐ is a meeting abstract (no full article for review) ☐ does *not* include a systematic review, meta-analysis, or cost-effectiveness analysis ☐ reports primary data, not a review article ☐ focuses on *prevention* of venous thromboembolism ☐ does not apply to a key question ☐ other: (specify)_____ ☐ Uncertain; retrieve article to decide **Do not continue if any item above is checked. Otherwise, continue to next column and check *at least one box***	☐ LMWH for DVT (Q1a) ☐ LMWH for PE (Q1b) ☐ outpatient treatment of DVT (Q2a) ☐ cost-effectiveness of LMWH/ outpatient treatment (Q2b) ☐ duration of therapy (Q3) ☐ use of clinical prediction rules (Q4) ☐ ultrasonography for DVT diagnosis (Q5) ☐ helical CT scan for PE diagnosis (Q6a) ☐ MRI/MRA for PE diagnosis (Q6b) ☐ d-dimer for thromboembolism diagnosis (Q7) ☐ does not apply to any question

☐ **Article for reference only**

Appendix F. Quality Review Form for Key Questions 3 and 4

Johns Hopkins Evidence-based Practice Center

DVT Project - Quality Review Form, Primary Literature

Q3 and 4 (Treatment Studies)

Article ID _____ First Author _____ 1st reviewer (initials) _____ 2nd reviewer (initials) _____

Primary reasons for exclusion: (Check all that apply)	
☐ Not in English	☐ Does not involve a comparison group in a(n) RCT or observational study
☐ Does not include human data	☐ Involves 5 or fewer patients
☐ Does not apply to out key question	☐ All data reported in a subsequent publication
☐ Focuses only on prevention of VTE	☐ Other: (specify)_____

If ANY of the above items is CHECKED - STOP: Do Not Continue: return article and form to Mollie

REPRESENTATIVENESS OF STUDY POPULATION

1. Did the study team describe the setting and population from which the study sample was drawn, and the dates of the study?			
	a. Adequate	(Setting AND population described AND start and end date specified)	2
	b. Fair	(One or more of these NOT reported OR poor description)	1
	c. Inadequate	(Not Specified)	0

2. Were detailed inclusion/exclusion criteria provided?			
	a. Adequate	(Detailed description of specific inclusion and exclusion criteria OR statement that all eligible patients enrolled)	2
	b. Fair	(Some description, but would be difficult to replicate based on information provided)	1
	c. Inadequate	(Minimal description or none at all)	0

3. Was information provided on excluded or not participating patients?			
	a. Adequate	(All reasons for exclusion AND number excluded OR no exclusions)	2
	b. Fair	(Only one of above criteria specified or information not sufficient to allow replication)	1
	c. Inadequate	(Non of the above criteria specified)	0

4. Does the study describe key patient characteristics at enrollment?

Demographics: age, gender

VTE Features: **Type:** DVT, PE **Event Number:** first VTE, recurrent VTE **Cause:** idiopathic VTE, malignancy-associated temporary risk factor

	a. Adequate	(Demographic AND VTE features well described)	2
	b. Fair	(Demographics AND only one VTE feature described; OR no demographics described but VTE features well described)	1
	c. Inadequate	(No key patient characteristics well described)	0

BIAS AND CONFOUNDING

5. Was assignment of patients to study group randomized?			
	a. Adequate	(Investigators could not predict assignment)	2
	b. Partial	(Date of birth, admission date, hospital record number, or other non-random scheme for assignment OR did not state)	1
	c. Not randomized		0
	d. Unclear		0

6. Did the patient groups have any important differences on key patient characteristics? ***Demographics:*** age, gender ***VTE Features:*** **Type:** DVT, PE **Event Number:** first VTE, recurrent VTE **Cause:** idiopathic VTE, malignancy-associated temporary risk factor		
	a. Groups equivalent in all factors examined	2
	b. Groups have minor difference in 1 or 2 factors	1.5
	c. Groups have an important difference in one or more factors OR minor difference in more than two factors	1
	d. Analysis not done	0

7. Was there blinding of clinician, patients, and outcome assessors?			
	a. Excellent	(All three blinded, including all treatment arms)	2
	b. Good	(Only 2 of the 3 blinded, or some but not all of the arms)	1.5
	c. Fair	(Only 1 of the 3 blinded)	1
	d. Poor	(No blinding or not stated)	0

DESCRIPTION OF THERAPY/MANAGEMENT

8. Did the study describe details of the treatment regimen?			
	a. Adequate	(Drug, dose intensity, duration and time in therapeutic range)	2
	b. Fair	(One of the above NOT described)	1
	c. Inadequate	(More than one of above NOT described)	0

* time in therapeutic range data not required for LMWH treated patients

9.Was there a description of other treatments given to each study group? ***Treatments:*** compression stockings, aspirin, NSAIDs, oxygen			
	a. Adequate	(Other treatment fully described)	2
	b. Fair	(Some description, but information not sufficient to allow replication)	1
	c. Inadequate	(Not described)	0

OUTCOMES AND FOLLOWUP

10. Was there a description of the criteria for determining outcomes? ***Recurrence Measures:*** duplex ultrasonography, venography, MRV, V/Q scan, spiral CT scan, MRA ***Bleeding Measures:*** Major bleeding and minor bleeding defined			
	a. Adequate	(Clear definitions of each outcome AND exact techniques to assess the outcome)	2
	b. Fair	(Some description, but information not sufficient to allow replication)	1
	c. Inadequate	(No information provided)	0

11. Did the study describe adverse effects experienced by patients? ***Treatment:*** Bleeding, thrombocytopenia, osteoporosis, other			
	a. Adequate	(Bleeding and at least one other adverse effects described fully)	2
	b. Fair	(Only bleeding mentioned OR other adverse effects mentioned, but NOT described fully)	1
	c. Inadequate	(Bleeding NOT mentioned)	0

12. Did the study report the numbers of and reasons for withdrawals from the study protocol or patients otherwise lost to follow-up?		
	a. Numbers and reasons reported (or no withdrawals)	2
	b. Only numbers OR reasons reported	1
	c. Neither given	0

13. What was the greatest percentage of patients in a treatment group that withdrew from the study protocol or were lost to follow-up?		
	a. None	2
	b. < 10%	1.5
	c. 10 - 20%	1
	d. > 20%	0
	e. Not stated	0

14. What was the planned length of follow-up?		
	a. > 2 years	2
	b. 1 - 2 years	1.5
	c. 6 - 11 months	1
	d. 0 - 5 months	0

STATISTICAL QUALITY AND INTERPRETATION

15. For primary endpoints, did the study report the magnitude of difference between groups (or magnitude of association between key variables) AND an index of variability (e.g., test statistic, p value, standard error, confidence intervals)?			
	a. Adequate	(Both reported, with standard error or confidence intervals as index or variability)	2
	b. Fair	(Both reported, with only test statistic or p value as index of variability)	1
	c. Inadequate	(No information given)	0

16. Was the statistical test of all analyses clearly identified?			
	a. Adequate	(Identified for all analyses)	2
	b. Fair	(Identified for some of the analyses)	1
	c. Inadequate	(Not identified)	0

17. If groups were not comparable at study onset, was there adjustment for protocol confounders with multivariate or stratified analyses AND were confounders coded in a way to make such control adequate?			
	a. Adequate	(Adjustment AND confounders appropriately coded)	2
	b. Fair	(Adjustment BUT confounders not coded appropriately OR coding unclear)	1
	c. Inadequate	(No adjustment OR not mentioned)	0
	d. Not applicable		N/A

18. Were withdrawals, crossovers, and loss to follow-up handled appropriately in analysis?		
	a. No loss to follow-up, withdrawals, or crossovers	2
	b. Sensitivity analysis	2
	c. By intention to treat/screen	2
	d. By 'intervention received' analysis only	1
	e. By none of the above	0
	f. Unknown	0

CONFLICTS OF INTEREST

19. Did the study report identify the sources of funding and the type and degree of involvement of the funding agency?			
	a. Adequate	(Source AND type or degree of involvement OR no funding)	2
	b. Fair	(Source only)	1
	c. Inadequate	(Neither)	0

THANK YOU for your time and attention to completing this work.
Please return completed form to Mollie.

Appendix G. Quality Review Form for Key Questions 5 and 7

Johns Hopkins Evidence-Based Practice Center

VTE Project - Quality Review Form, Primary Literature - ***Diagnosis (Q5 and Q7)***

Article ID _____ First author _____ 1st Reviewer _____ 2nd Reviewer _____

Primary reasons for exclusion: (Check all that apply)

- ☐ Not in English
- ☐ Does not include human data
- ☐ Does not apply to key question
- ☐ Focuses on prevention of VTE
- ☐ No original data or results reported
- ☐ Reports only basic science
- ☐ Meeting abstract (no full article for review)
- ☐ All data reported in a subsequent publication
- ☐ Other: (specify)_____

Additional exclusions per Key Question refinements: (Check all that apply)

Question 5:

- ☐ DVT diagnosis not confirmed with imaging (US, contrast venography)
- ☐ PE diagnosis not confirmed with study (high prob V/Q, pulmonary arteriography, spiral CT, autopsy)
- ☐ No clinical model presented: does not include 2 of 3 (history, exam, laboratory testing) evaluated in combination
- ☐ Total study population < 30

Question 7:

- ☐ Does not report test characteristics of CT or MRI for diagnosis of PE (e.g., sensitivity, specificity, ROC)
- ☐ Does not use VQ scan or pulmonary arteriography as reference ("gold") standard
- ☐ Is a case report

If ANY of the above items is CHECKED - STOP: Do Not Continue; return article and form to Mollie

REPRESENTATIVENESS OF STUDY POPULATION

1. Did the study describe the setting and population from which the study sample was drawn, and the dates of the study?			
	a. Adequate	(Setting AND population described AND start and end date specified)	2
	b. Fair	(One or more of these NOT reported OR poor description)	1
	c. Inadequate	(Not specified)	0

2. Were detailed inclusion/exclusion criteria provided?			
	a. Adequate	(Detailed description of specific inclusion and exclusion criteria OR statement that all eligible patients enrolled)	2
	b. Fair	(Some description, but would be difficult to replicate based on information provided)	1
	c. Inadequate	(Minimal description or none at all)	0

3. Was information provided on excluded or non-participating patients?			
	a. Adequate	(All reasons for exclusion AND number excluded OR no exclusions)	2
	b. Fair	(Only one of above criteria specified or information not sufficient to allow replication)	1
	c. Inadequate	(None of the above criteria specified)	0

4. Does the study describe key patient characteristics at enrollment? ***Demographics*:** age, gender ***DVT/PE Risk Factors (if any)***: recent surgery, medications, prior DVT/PE, malignancy, recurrence			
	a. Adequate	(Demographic and risk factors well described)	2
	b. Fair	(Only demographics well described)	1
	c. Inadequate	(No key patient characteristics well described)	0

BIAS AND CONFOUNDING

5. Did all individuals receiving the study test also receive the reference test?			
	a. All	(All received both tests)	2
	b. Some	(Some received both tests)	1
	c. None	(No one received both tests)	0

For Q6 we want to understand the extent to which testing decisions were independent of each other. There are two ways for testing to be *dependent*: 1) the decision to perform the 2nd test can be dependent on the *results* of the 1st test 2) the decision to include a patient in the study can be based on a *referral* for testing.

6. Was the decision to obtain the reference test affected in any way by the result of the study test, or vice versa?			
	a. No	(Decision to test **not** affected by *either* 1) above *or* 2) above)	2
	b. No (implied)	(Decision to test **is** affected by *either* 1) above *or* 2) above)	1
	c. Yes	(Decision to test was affected by other test's results)	0

7. Was there blinding of study test interpretation, reference test interpretation, and clinical data? (Note: This question concerns *blinding*, not independence, of interpretations.)			
	a. Excellent	(All three blinded, including both test interpretations with each other)	2
	b. Good	(Test interpretations blinded to each other but not to clinical data)	1
	c. Fair	(Test interpretations blinded to clinical data but not to each other)	0.5
	d. Poor	(No blinding or not stated)	0

8. Was interpretation of the study test performed by two or more independent observers?			
	a. Adequate	(Multiple observers AND independent)	2
	b. Fair	(Multiple observers but NOT independent)	1
	c. Inadequate	(Neither or not stated)	0

9. Was interpretation of the reference test performed by two or more independent observers?			
	a. Adequate	(Multiple observers AND independent)	2
	b. Fair	(Multiple observers but NOT independent)	1
	c. Inadequate	(Neither or not stated)	0

DESCRIPTION OF TEST PROTOCOLS

10. Did the study describe details of the study test protocol?			
	a. Adequate	(Enough description to replicate)	2
	b. Fair	(Some description, but not enough to replicate)	1
	c. Inadequate	(No description)	0

11. Did the study describe details of the reference test protocol?			
	a. Adequate	(Enough description to replicate)	2
	b. Fair	(Some description, but not enough to replicate)	1
	c. Inadequate	(No description)	0

12. (Q5 ONLY) Does the study report the methods used to develop the clinical model being tested (e.g., pilot testing, literature-based, collective experience)?			
	a. Adequate	(3 characteristics)	2
	b. Fair	(1-2 characteristics)	1
	c. Inadequate	(None)	0
	d. Not applicable	(Does not concern Q5)	N/A

TEST INTERPRETATION

13. Were the interpretation criteria of a positive test described for the study test?			
	a. Adequate	(Enough description to replicate)	2
	b. Fair	(Some description, but not enough to replicate)	1
	c. Inadequate	(No description)	0

14. Were the interpretation criteria of a positive test described for the reference test?			
	a. Adequate	(Enough description to replicate)	2
	b. Fair	(Some description, but not enough to replicate)	1
	c. Inadequate	(No description)	0

15. Did the study report the numbers of and reasons for withdrawals from the study protocol or patients otherwise lost to follow-up?			
	a. Adequate	(Both numbers AND reasons reported, or no withdrawals)	2
	b. Fair	(Only numbers OR reasons reported)	1
	c. Inadequate	(Neither given)	0
	d. Not applicable	(No longitudinal follow-up was performed)	N/A

STATISTICAL QUALITY AND INTERPRETATION

16. Was a summary index of test performance (e.g., sensitivity/specificity, area under ROC curve) reported for the study test AND an indicator of variability (standard error, confidence interval)?			
	a. Adequate	(Both reported)	2
	b. Fair	(Test performance but no index of variability)	1
	c. Inadequate	(No information given)	0

17. If groups were not comparable at study onset, was there adjustment for potential confounders with multivariate or stratified analyses AND were confounders coded in a way to make such control adequate?			
	a. Adequate	(Adjustment AND confounders appropriately coded)	2
	b. Fair	(Adjustment BUT confounders not coded appropriately OR coding unclear)	1
	c. Inadequate	(No adjustment OR not mentioned)	0
	d. Not applicable	(Only one group being studied)	N/A

CONFLICT OF INTEREST

18. Did the study report identify the source of funding and the type and degree of involvement of the funding agency?			
	a. Adequate	(Source AND type or degree of involvement if conflict of interest possible OR no funding)	2
	b. Fair	(Source only)	1
	c. Inadequate	(Neither)	0
	d. Not applicable		N/A

THANK YOU for your time and attention to completing this work.

Appendix H. Quality Review Form for Key Questions 3b - costs

Johns Hopkins Evidence-Based Practice Center

VTE Project - Quality Review Form, Primary Literature - ***Costs (Q3b)***

Article ID _____ First author _____ 1st Reviewer _____ 2nd Reviewer _____

Primary reasons for exclusion: (Check all that apply)

☐ Not in English

☐ Does not include human data

☐ Meeting abstract (no full article for review)

☐ Involves *only* prevention

☐ Does not apply to key question

☐ No original data or results reported

☐ Is a case report (single patient)

☐ Other: (note if applies to another key question)_____

☐ Does not involve a comparison group (in an RCT or observational study) or is not a cost-effectiveness analysis

If ANY of the above items is CHECKED - STOP: Do Not Continue; return article and form to Mollie

1. Is the research question and its economic importance clearly stated?			
	a. Adequate	(States research question and the economic importance of the question)	2
	b. Fair	(States one or the other but not both)	1
	c. Inadequate	(Does not address)	0

2. Do the authors state the perspective of the analysis? (e.g. payor, physician, patient, society)			
	a. Adequate	(Perspective clearly defined)	2
	b. Fair	(Perspective could be inferred)	1
	c. Inadequate	(Perspective unclear)	0

3. Are the comparison strategies clearly described?			
	a. Adequate	(Includes the most relevant strategies, and justified if others were excluded)	2
	b. Fair	(Includes some of the relevant strategies)	1
	c. Inadequate	(Does not clearly describe)	0

4. Is the structure of the economic analysis clear? (e.g. cost-benefit, cost-effectiveness, cost-utility, cost minimization)			
	a. Adequate	(Structure is clear, replicable, and appropriate for the posed question)	2
	b. Fair	(Analysis could not be replicated due to insufficient details or is inappropriate for the question)	1
	c. Inadequate	(Does not use an acceptable form of economic analysis)	0

5. Are the costs and outcomes appropriately valued?			
	a. Adequate	(Comprehensive systematic search for data on costs and rates of outcomes OR collection of primary data to generate this information)	2
	b. Fair	(Mostly used data on costs and outcomes from the literature but did not search systematically for this data, or primary data collection was inadequate)	1
	c. Inadequate	(Majority of data on costs and outcomes was estimated)	0

6. Were allowances made for uncertainties in the analysis?

	a. Adequate	(Included a sensitivity analysis in which estimates were varied over an appropriate range; and range was chosen based on literature review)	2
	b. Fair	(Included a sensitivity analysis in which estimates were varied over an arbitrary range of values)	1
	c. Inadequate	(No sensitivity analysis)	0

7. Is it clear to what patient population the results will be applicable?			
	a. Adequate	(Clearly states what the base case is for the analyses, or defines the population in whom costs were measured)	2
	b. Fair	(Base case estimates or population is described but is inappropriate for the question or insufficiently described)	1
	c. Inadequate	(Does not)	0

8. Are the appropriate costs and benefits of each strategy presented?			
Cost-effectiveness: incremental costs per a unit measure of benefit **Cost-minimization:** all costs in all strategies **Cost-benefit:** costs of strategies and costs of outcomes in monetary units			
	a. Adequate	(Appropriately reports the results with a correct measure for the study design)	2
	b. Fair	(Describes optimal strategy but without presenting data)	1
	c. Inadequate	(Does not address optimal strategy)	0

9. Results of sensitivity analyses are appropriately interpreted and presented?			
	a. Adequate	(Authors state results and under what conditions the optimal strategies differ)	2
	b. Fair	(State the results with no comments about sub-populations or the results if parameters change)	1
	c. Inadequate	(Do not clearly state results)	0

CONFLICT OF INTEREST

10. Did the study report identify the source of funding and the type and degree of involvement of the funding			
	a. Adequate	(Source AND type or degree of involvement OR no funding)	2
	b. Fair	(Source only)	1
	c. Inadequate	(Neither)	0
	d. Not applicable		N/A

THANK YOU for your time and attention to completing this work.

Appendix I. Quality Review Form for Systematic Reviews

Quality Assessment Form for Systematic Literature Reviews

Johns Hopkins University Evidence-based Practice Center
Deep Venous Thrombosis Project

Ref #: _____ Key Question: _____ Reviewer: _____

1. Did the authors clearly state the question addressed by the overview at the beginning of the article?		
a.	Yes. The authors stated a focused clinical question about tests or treatment, AND specified a target population	2
b.	Partially.	1
c.	No	0

2. Did the authors describe the search methods used to find evidence (original research) on the primary question(s)?		
a.	Yes. Enough information was reported to permit replication	2
b	Partially.	1
c	No.	0

3. Was the search for evidence reasonably comprehensive?		
a.	Yes. Search included MEDLINE (or other electronic database), hand-searching of select journals or reference lists, AND query of 1 or more experts.	2
b	Partially. Search included MEDLINE (or other electronic database), but did not include hand-searching of journals or reference lists AND/OR did not include a query of experts.	1
c	No. Search did not include an electronic database of journals.	0
d	Can't tell.	0

4. Did the authors report on the criteria they used for deciding which studies to include in the systematic review?		
a.	Yes. Criteria were specified clearly enough to permit replication.	2
b	Partially. Criteria specified, but without enough detail to permit replication.	1
c	No. Criteria not specified.	0

5. Were the inclusion criteria appropriate (aimed at avoiding bias in the included studies)?		
a.	Yes. Inclusion criteria are likely to capture all relevant studies (e.g., included languages other than English).	2
b	Partially.	1
c	No. Inclusion criteria likely to lead to biased sampling of studies.	0
d	Cannot tell. Inclusion criteria described inadequately.	0

6. Did the authors assess study quality?		
a.	Yes. Criteria to assess study quality were specified with adequate detail to permit replication.	2
b	Partially. Criteria to assess study quality not adequately described.	1
c	No.	0

7. Was the quality assessment done appropriately?		
a.	Yes. Quality assessment was done using a validated instrument (with citation) or the authors demonstrated validity of their methods.	2
b	Partially. Authors used their own quality assessment instrument without validation, or another instrument with unknown measurement properties.	1
c	No.	0
d	Cannot tell. There was no quality assessment reported.	0

8. Did the authors demonstrate that their methodology was reproducible?		
a.	Yes. The investigators mostly (>50% of the time) agreed on selection of articles, on quality assessment, AND on the data that was extracted.	2
b	Partially. Disagreement occurred the majority of the time either on the selection of articles, quality assessment, or data extraction (but not all 3).	1
c	No. Disagreement occurred the majority of the time on the selection of articles, quality assessment, AND data extraction.	0
d	Can't tell. Authors didn't comment on reproducibility.	0

9. Did the authors discuss whether the variation in the results of the original research may be due to differences in study design or population?		
a.	Yes. Text or tables provide comparative information on most of following: study design, populations, exposures or interventions, and outcome measures	2
b	Partially.	1
c	No.	0

10. Did the authors describe the methods they used to combine the results of the relevant studies (to reach a conclusion)?		
a.	Yes. Methods were reported clearly enough to allow replication.	2
b	Partially.	1
c	No.	0

11. Were the results of the relevant studies combined appropriately relative to the primary question?		
a.	Yes. The overview included some assessment of the qualitative and quantitative heterogeneity of study results AND used an accepted pooling method (i.e., more than simple addition)	2
b	Partially.	1
c	No.	0
d	Cannot tell. No description of the methods used for combining studies.	0

12. Were the conclusions of the authors supported by the data and/or analysis reported in the overview?		
a.	Yes.	2
b	Partially.	1
c	No.	0

THANK YOU for your time and attention to completing this work. Please return completed form to Mollie.

Appendix J: Acronyms and Abbreviations

Abbreviation	Term
AC	anticoagulants
ARR	absolute risk reduction
ASA	aspirin
asymp	asymptomatic
BF	breastfeeding
bid	twice a day
ca	cancer
CA	California
CAD	Canadian dollars
CE	cost effectiveness
CI	confidence interval
CohP	cohort prospective
CohR	cohort retrospective
comp	compression
consec	consecutive
CT	computized tomography
CVA	cerebrovascular accident
d/c	discontinuation
DVT	deep venous thrombosis
dx	diagnosis
ED	emergency department
ELISA	enzyme-linked immunosorbent assay
FN	false negative
FP	false positive
FRF	French francs
f/u	followup
Gd	Gadolinium
GRE	gradient echo
hr	hour
HRT	hormone replacement therapy
ICU	intensive care unit
inpt	inpatient
INR	international normalized ratio
IPG	impedance plesthymography
IU	international units
IV	intravenous
IVC	inferior vena cava
LE	life expectancy
LMWH	low molecular weight heparin
LT	long term
LY	life year(s)
MD	physician
ME	Medicare
mo	month(s)
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
N/A	not applicable
NLG	Netherlands guilders
NNT	number needed to treat

NPV	negative predictive value
NR	non-response
NSAID	nonsteroidal anti-inflammatory drug
NSD	no significant difference
OCP	oral contraceptive pill
OR	odds ratio
outpt	outpatient
PA	pulmonary angiogram
PE	pulmonary embolism
Preg	pregnancy
PIOPED	Prospective investigation of pulmonary embolism diagnosis
postop	postoperative
PPV	positive predictive value
PRF	permanent risk factor
prosp	prospective
prox DVT	proximal deep vein thrombosis
PTP	pretest probability
pts	patients
PTT	partial thromboplastin time
QALY	quality adjusted life years
qd	every day
QOL	quality of life
RAS	risk assessment score
RCT	randomized controlled trial
ROC	receiver operating characteristic
RR	risk ratio
RRR	relative risk reduction
rx	prescription
sens	sensitivity
spec	specificity
SPECT	single-photon emission computerized tomography
SQ	subcutaneous
sx	symptom(s)
symp	symptomatic
tid	three times a day
tiw	three times per week
TN	true negative
TP	true positive
TRF	temporary risk factor
tx	treatment
u	units
UFH	unfractionated heparin
UE	upper extremity
U/S	ultrasound
USD	United States dollars
VDS	venous duplex sonography
V/Q	ventilation perfusion
vs	versus
VTE	venous thromboembolism
w/	with
w/i	within

w/o	without
wk	week(s)
yr	year(s)

Not listed above:
hx

Appendix K. Acknowledgments

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