

# Appendix 1: Literature search strategy for clinical effectiveness studies

## Guide to Search Syntax (DIALOG®)

- ! Explode the search term. Retrieve the search concept plus all narrower terms.
- ? Truncation symbol, single character. Retrieve plural and variant ending of search terms.
- " " Search phrases.
- () Proximity operator. Words must be adjacent.
- (l) Proximity operator. Links descriptors and subheadings.
- (n) Proximity operator. Words must be near each other in any order.
- (w) Proximity operator. Words must be adjacent.
- ab Search in article abstract.
- de Descriptor i.e., subject heading ( a controlled, thesaurus term).
- dt Document type.
- id Identifier (includes CAS Registry Number and natural language indexing terms).
- nd Device brand name.
- rn CAS Registry Number.
- ti Search in titles.
- tn Brand name.
- tw Text word.

DATABASES	DATES / LIMITS	SUBJECT HEADINGS/KEYWORDS
DIALOG OneSearch®  MEDLINE® BIOSIS Previews® EMBASE® PASCAL	Human	1. ((chronic OR long())term)(2w)(anticoagula? OR anti()coagula? OR warfarin) OR self(2w)(anticoagula? OR anti()coagula?) OR oral()anticoagula? OR oral()anti()coagula?)/ti,ab <i>[Textwords searched in title, abstract]</i>  2. ((oral()anticoagulant? AND (monitor? OR management OR managing OR test OR tests OR testing)) OR (oral()anti()coagulant? AND (monitor? OR management OR managing OR test OR tests OR testing)))/ti,ab <i>[Textwords searched in title, abstract]</i>  3. (Vitamin K(l)antagonists and inhibitors/de) OR (Warfarin OR Anticoagulants)/de <i>[MeSH heading for MEDLINE®]</i>  OR  (Anticoagulant Agent OR Anticoagulant Protein OR Anticoagulant Therapy OR Anticoagulation OR Antivitamin K OR Warfarin)/de <i>[EMTREE terms for EMBASE®]</i>  OR  (Warfarin OR Anticoagulant Therapy OR Anticoagulant-drug OR Anticoagulants OR Anticoagulation OR Anticoagulation therapy)/de <i>[BIOSIS Previews® thesaurus term]</i>

		<p style="text-align: center;"><i>OR</i></p> <p>(81)81()2 OR vitamin()K()antagonist? OR warfarin OR coumadin OR coumarin()derivative? OR anticoagula? OR anti()coagula? OR anti(vitamin()K)/ti,ab OR 81-81-2/id  <i>[Textwords searched in title, abstract, identifier]</i></p> <p>4. (Administration, Oral! OR 'administration and dosage')/de  <i>[MeSH heading for MEDLINE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(Oral Administration OR Oral Drug Delivery)/de  <i>[BIOSIS Previews® thesaurus term]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>Oral Drug Administration/de  <i>[EMTREE terms for EMBASE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(oral OR orally)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>5. (International Normalized Ratio OR Prothrombin Time OR Blood Coagulation Tests OR Whole Blood Coagulation Time)/de  <i>[MeSH heading for MEDLINE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(International Normalized Ratio OR Prothrombin OR Prothrombin Time OR Blood Clotting OR Blood Coagulation OR Clotting Time)/de  <i>[BIOSIS Previews® thesaurus term]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(Blood Clotting Test OR Blood Clotting Time OR Prothrombin OR Prothrombin Time)/de  <i>[EMTREE terms for EMBASE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(International()Normali?ed()Ratio? OR INR OR prothrombin? OR PT()monitor? OR PT()system? OR PT()measure? OR PT()test OR PT()tests OR PT()testing OR PT()device? OR coagulomet?)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>6. (Ambulatory Care Facilities! OR Self Care! OR Point-of-Care Systems OR Monitoring, Ambulatory! OR Ambulatory Care! OR Home Care Services OR Long-Term Care OR Outpatients)/de  <i>[MeSH heading for MEDLINE®]</i></p>
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		<p><i>OR</i></p> <p>(Autoregulation OR Drug Self-Administration OR Home Care OR Long-term Care OR Long-term Follow-up OR Outpatient Care OR Outpatient Treatment OR Self-Care)/de  <i>[BIOSIS Previews® thesaurus term]</i></p> <p><i>OR</i></p> <p>(Ambulatory Care! OR Drug Self Administration OR Home Care OR Home Monitoring OR Long Term Care OR Outpatient Care OR Self Care! OR Self Monitoring OR Autoregulation)/de  <i>[EMTREE terms for EMBASE®]</i></p> <p><i>OR</i></p> <p>(self())testing OR self()test OR self()tests OR self()tested OR self()monitor? OR self()managing OR self()manage? OR self()control? OR self()administer? OR home()testing OR home()test OR home()tests OR home()monitor? OR home()managing OR home()manage? OR home()control? OR home()administer? OR home()device? OR point()of()care OR POC()test? OR POC()monitor? OR POC()device? OR near()patient()test? OR monitor?(n)ambulator? OR outpatient(2n)monitor? OR monitor?(2w)outpatients OR ambulatory()care) OR outpatient()control OR outpatient(2n)care OR care(2w)outpatients OR outpatient()health()service? OR home(2n)care)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>7. TN, ND=(ProTime OR Pro()Time OR CoaguChek? OR CoaguCheck? OR Inratio OR Avocet? OR TAS()PT()NC OR Harmony()INR OR Rubicon)  <i>[Brand names in EMBASE®]</i></p> <p><i>OR</i></p> <p>(ProTime OR Pro()Time OR CoaguChek? OR CoaguCheck? OR Inratio OR Avocet? OR TAS()PT()NC OR Harmony()INR OR Rubicon(3n)prothrombin)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>8. (Controlled Clinical Trials! OR Epidemiologic Research Design!)/de  <i>[MeSH headings for MEDLINE®]</i></p> <p><i>OR</i></p> <p>dt=(Multicenter Study OR Randomized Controlled Trial OR Controlled Clinical Trial)  <i>[Document type in MEDLINE®]</i></p> <p><i>OR</i></p> <p>(Multicenter Study OR Randomized Controlled Trial OR Randomized Clinical Trial OR Randomized Trial OR Evidence-Based Medicine)/de  <i>[BIOSIS Previews® thesaurus terms]</i></p>
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		<p><i>OR</i></p> <p>(Major Clinical Study OR Multicenter Study OR Controlled Study! OR Randomized Controlled Trial OR Evidence Based Medicine!)/de <i>[EMTREE terms for EMBASE®]</i></p> <p><i>OR</i></p> <p>(random? OR sham? OR placebo? OR sing!?) (blind? OR dumm? OR mask?) OR doubl?() (blind? OR dumm? OR mask?) OR tripl?() (blind? OR dumm? OR mask?) OR trebl?() (blind? OR dumm? OR mask?) OR control?() (study OR studies OR trial?) OR RCT? ? OR (multicent? OR multi()cent?()) (study OR studies OR trial?)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>9. dt=Meta-Analysis <i>[Document type in MEDLINE®]</i></p> <p><i>OR</i></p> <p>(Meta-Analysis OR Technology Assessment, Biomedical!)/de <i>[MeSH headings for MEDLINE®]</i></p> <p><i>OR</i></p> <p>(Meta Analysis OR Systematic Review OR Biomedical Technology Assessment)/de <i>[EMTREE terms for EMBASE®]</i></p> <p><i>OR</i></p> <p>Meta-Analysis/de <i>[BIOSIS Previews® thesaurus term]</i></p> <p><i>OR</i></p> <p>(meta()analy? OR metaanaly? OR met()analy? OR metanaly? OR health()technology()assessment? OR meta()regression? OR metaregression? OR mega()regression? OR systematic?() (literature()review? OR review? OR overview?) OR methodologic?() (literature()review? OR review? OR overview?) OR quantitative() (review? OR overview? OR syntheses?) OR research() (integration? OR overview?) OR integrative(2w) (review? OR overview?) OR collaborative() (review? OR overview?) OR pool?() analy? OR data()synthes? OR data()extraction? OR data()abstraction? OR handsearch? OR hand()search? OR mantel()haenszel OR peto OR der()simonian OR dersimonian OR fixed()effect? OR latin()square?)/ti,ab <i>[Textwords searched in title, abstract]</i></p>
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		<p>10. (((1 OR (3 AND 4)) AND 5 AND 6) OR (2 AND 6) OR 7) AND (8 OR 9)</p> <p><i>Search performed on 2 July 2005; monthly alerts set up on MEDLINE®, EMBASE® and BIOSIS Previews® and were ongoing until 11/08/2006</i></p> <p><i>Total Hits = 489 Records (414 'clinical' results + 75 sys. review /meta-analysis results)</i></p>
Cochrane Library Issue 2 2005; Issues 1, 2, 3 2006		<p>Same MeSH and keywords as per MEDLINE® search, excluding study design filter. Appropriate syntax used.</p> <p><i>Initial search performed on 16 June 2005 and updated with subsequent database updates. Last update performed on 20/07/2006.</i></p>
PubMed	Human	<p>Same MeSH and keywords as per MEDLINE® search. Appropriate syntax used.</p>
Websites of health technology assessment (HTA) and related agencies; trial registries; other databases		<p>AHRQ; National Research Register; University of York NHS Centre for Reviews and Dissemination – CRD databases; LILACS etc.</p>

## APPENDIX 2: Literature search strategy for economic studies

DATABASES	DATES / LIMITS	SUBJECT HEADINGS/KEYWORDS
DIALOG OneSearch®  MEDLINE® BIOSIS Previews® EMBASE® PASCAL	Human	<ol style="list-style-type: none"> <li>1. ((chronic OR long()term)(2w)(anticoagula? OR anti()coagula? OR warfarin) OR self(2w)(anticoagula? OR anti()coagula?) OR oral()anticoagula? OR oral()anti()coagula?)/ti,ab  <i>[Textwords searched in title, abstract]</i></li>   <li>2. ((oral()anticoagulant? AND (monitor? OR management OR managing OR test OR tests OR testing)) OR (oral()anti()coagulant? AND (monitor? OR management OR managing OR test OR tests OR testing)))/ti,ab  <i>[Textwords searched in title, abstract]</i></li>   <li>3. (Vitamin K(1)antagonists and inhibitors/de) OR (Warfarin OR Anticoagulants)/de  <i>[MeSH heading for MEDLINE®]</i>   <i>OR</i>             (Anticoagulant Agent OR Anticoagulant Protein OR Anticoagulant Therapy OR Anticoagulation OR Antivitamin K OR Warfarin)/de  <i>[EMTREE terms for EMBASE®]</i>   <i>OR</i>             (Warfarin OR Anticoagulant Therapy OR Anticoagulant-drug OR Anticoagulants OR Anticoagulation OR Anticoagulation therapy)/de  <i>[BIOSIS Previews® thesaurus term]</i>   <i>OR</i>             (81()81()2 OR vitamin()K()antagonist? OR warfarin OR coumadin OR coumarin()derivative? OR anticoagula? OR anti()coagula? OR anti(vitamin()K)/ti,ab OR 81-81-2/id  <i>[Textwords searched in title, abstract, identifier]</i></li>   <li>4. (Administration, Oral! OR 'administration and dosage')/de  <i>[MeSH heading for MEDLINE®]</i>   <i>OR</i>             (Oral Administration OR Oral Drug Delivery)/de  <i>[BIOSIS Previews® thesaurus term]</i>   <i>OR</i>             Oral Drug Administration/de  <i>[EMTREE terms for EMBASE®]</i></li> </ol>

		<p><i>OR</i></p> <p>(oral OR orally)/ti,ab [Textwords searched in title, abstract]</p> <p>5. (International Normalized Ratio OR Prothrombin Time OR Blood Coagulation Tests OR Whole Blood Coagulation Time)/de [MeSH heading for MEDLINE®]</p> <p><i>OR</i></p> <p>(International Normalized Ratio OR Prothrombin OR Prothrombin Time OR Blood Clotting OR Blood Coagulation OR Clotting Time)/de [BIOSIS Previews® thesaurus term]</p> <p><i>OR</i></p> <p>(Blood Clotting Test OR Blood Clotting Time OR Prothrombin OR Prothrombin Time)/de [EMTREE terms for EMBASE®]</p> <p><i>OR</i></p> <p>(International()Normali?ed()Ratio? OR INR OR prothrombin? OR PT()monitor? OR PT()system? OR PT()measure? OR PT()test OR PT()tests OR PT()testing OR PT()device? OR coagulomet?)/ti,ab [Textwords searched in title, abstract]</p> <p>6. (Ambulatory Care Facilities! OR Self Care! OR Point-of-Care Systems OR Monitoring, Ambulatory! OR Ambulatory Care! OR Home Care Services OR Long-Term Care OR Outpatients)/de [MeSH heading for MEDLINE®]</p> <p><i>OR</i></p> <p>(Autoregulation OR Drug Self-Administration OR Home Care OR Long-term Care OR Long-term Follow-up OR Outpatient Care OR Outpatient Treatment OR Self-Care)/de [BIOSIS Previews® thesaurus term]</p> <p><i>OR</i></p> <p>(Ambulatory Care! OR Drug Self Administration OR Home Care OR Home Monitoring OR Long Term Care OR Outpatient Care OR Self Care! OR Self Monitoring OR Autoregulation)/de [EMTREE terms for EMBASE®]</p> <p><i>OR</i></p> <p>(self()testing OR self()test OR self()tests OR self()tested OR self()monitor? OR self()managing OR self()manage? OR self()control? OR self()administer? OR home()testing OR home()test OR home()tests OR home()monitor? OR home()managing OR home()manage? OR home()control? OR home()administer? OR home()device? OR point(of)care OR POC()test? OR</p>
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		<p>POC()monitor? OR POC()device? OR near()patient()test? OR monitor?(n)ambulator? OR outpatient(2n)monitor? OR monitor?(2w)outpatients OR ambulatory()care) OR outpatient()control OR outpatient(2n)care OR care(2w)outpatients OR outpatient()health()service? OR home(2n)care)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>7. TN, ND=(ProTime OR Pro()Time OR CoaguChek? OR CoaguCheck? OR Inratio OR Avocet? OR TAS()PT()NC OR Harmony()INR OR Rubicon)  <i>[Brand names in EMBASE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(ProTime OR Pro()Time OR CoaguChek? OR CoaguCheck? OR Inratio OR Avocet? OR TAS()PT()NC OR Harmony()INR OR Rubicon(3n)prothrombin)/ti,ab  <i>[Textwords searched in title, abstract]</i></p> <p>8. (Economics OR "Costs and Cost Analysis"! OR "Value of Life" OR Economics, Medical! OR Economics, Hospital! OR Economics, Nursing OR Economics, Pharmaceutical OR "Fees and Charges"! OR Budgets OR Models, Economic! OR Markov Chains OR Monte Carlo Method OR Decision Trees OR "Quality of Life" OR Patient Satisfaction OR Quality-Adjusted Life Years)/de  <i>[MeSH headings for MEDLINE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(Health economics! OR Economic Evaluation! OR Pharmacoeconomics! OR Economic Aspect! OR Quality Adjusted Life Year OR "Quality of Life"!)/de  <i>[EMTREE terms for EMBASE®]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(Economic Impact OR Economic Value OR Pharmacoeconomics OR Health Care Cost OR Economic Factors OR Economics OR Cost Analysis OR Cost OR Economic Analysis OR Cost-Effectiveness OR Costs OR "Quality of Life" OR Health Care Cost OR Cost Savings OR Cost-Benefit Analysis OR Hospital Costs OR Medical Costs OR Quality-of-Life)/de  <i>[BIOSIS Previews® thesaurus terms]</i></p> <p style="text-align: center;"><i>OR</i></p> <p>(econom? OR cost OR costly OR costing OR costed OR costs OR price OR prices OR pricing OR priced OR discount OR discounts OR discounted OR discounting OR expenditure OR expenditures OR budget? OR afford? OR pharmacoeconomic? OR pharmaco(1n)economic? OR decision(1n)(tree? OR analy? OR model?) OR (value OR values OR valuation)(2n)(money OR monetary OR life OR lives) OR QOL OR QOLY OR QOLYs OR HRQOL OR QALY OR QALYs OR quality(1n)life OR willingness(1n)pay OR quality(1n)adjusted()life()year?)/ti,ab  <i>[Textwords searched in title, abstract]</i></p>
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		<p>9. (((1 OR (3 AND 4)) AND 5 AND 6) OR (2 AND 6) OR 7) AND 8</p> <p><i>Search performed on 2 July 2005; monthly alerts set up on MEDLINE®, EMBASE® and BIOSIS Previews® and were ongoing until 11/08/2006.</i></p> <p><i>Total Hits = 137 Unique Records (i.e. records remaining after 'clinical' records from 1-A search NOT'd out)</i></p>
Cochrane Library Issue 2, 3 2005; 1, 2, 3, 2006		<p>Same MeSH and keywords as per MEDLINE® search, excluding study design filter. Appropriate syntax used.</p> <p><i>Initial search performed on 16 June 2005 and updated with subsequent database updates. Last update performed on 20/07/2006.</i></p>
PubMed	Human	<p>Same MeSH and keywords as per MEDLINE® search. Appropriate syntax used.</p>
OHE-IFPMA Database Ltd.  HEED: Health Economic Evaluations Database July 2005		<p>self-monitoring OR point of care OR oral anticoagulat* OR ProTime OR CoaguChek OR Inratio OR Avosure OR "TAS PT NC" OR "Harmony INR" OR prothrombin OR near patient[all fields], <i>0 Unique Relevant Results</i></p>
Websites of health economics research groups		<p>Health Economics Research Group (HERG); Health Economics Research Unit (HERU); etc.</p>

## Appendix 3: Clinical review data extraction and quality assessment form

Date:	Reviewer's initials:	ID number:	
Article identification: <i>(author, year)</i> Full citation: Geographic location: Time period: Setting: <i>(e.g., hospital-based, clinic-based, community-based, referral criteria or process, other)</i> Declared conflict of interest: Source(s) of funding:			
<b>Study characteristics</b>			
Purpose or objective(s) of study <i>(include among whom)</i> :			
Design: <i>(RCT, randomized cross-over, Zelen-design RCT, prospective RCT-retrospective controls)</i>			
Method of randomization:			
Blinding: <i>(patients, investigator, assessor)</i>			
Sample size: <i>(n≥20 patients, 10/group)</i>			
Sampling procedure: <i>(consecutive, selective, random, unreported, other)</i>			
Participation rate: <i>(total eligible for inclusion, total randomized, withdrawals or dropouts and reasons, total completing trial)</i>			
Exclusion criteria:			
<b>Baseline patient characteristics</b>			
Inclusion Criteria	POC Testing Patient Group	Reference Patient Group	
Mean age: <i>(years)</i> Gender: <i>(male or female (%))</i> Ethnicity: <i>(%)</i> Mean weight: <i>(kg)</i> Dietary modifications: <i>(if any)</i> Functional capacity: <i>(mental, manual dexterity, vision)</i> Indication: <i>(prosthetic heart valve, atrial fibrillation, venous thromboembolism, acute myocardial infarction, stroke, peripheral arterial occlusion, deep-vein thrombosis)</i> Severity and duration of condition: Anticoagulation therapy: <i>(drug, duration)</i> Notes: <i>(calculations, if any)</i>			
Test description	POC testing (clinic, health practitioner, patient)	Reference (usual care, venipuncture testing)	Total (if given)
Description of technique: <i>(fingerstick sample run on CoaguCheck, ProTime, venipuncture sample on in-hospital or in-laboratory device, other)</i> Details: <i>(POC performed by anticoagulation clinic, nurse, nurse or practitioner or pharmacists, patient, self-management or self-control) (INR based on venipuncture by anticoagulation clinic or individual practitioner)</i>			
Manufacturer and modifications (if any): <i>(CoaguCheck, ProTime, in-hospital or in-laboratory device other, ISI of reagent strips)</i>			

Target therapeutic range: (2 to 3 most indications, 2.5 to 3.5 valve replacement)			
Frequency of monitoring:			
Regulatory status:			
Cost:			
Failure rate of test: (plus reasons if available; if unspecified, verify number of subjects with test results)			
Sensitivity: (true (+)/true (+)+false (-))			
Specificity: (true (-)/true (-)+false (+))			
Notes: (calculations, if any)			

Clinical data extraction	POC testing patient group (clinic, health practitioner, patient)	Reference test patient group (usual care, venipuncture)
Time in therapeutic range as defined in study: (%)		
Time above therapeutic range: (%)		
Time below therapeutic range: (%)		
Quality of life: (Short-Form 36)		
Psychosocial implications:		
Ethical implications:		
Notes: (calculations, if any)		

Adverse events	POC Testing Patient Group (clinic, health practitioner, patient)	Reference Test Patient Group (usual care, venipuncture)
Total number of major hemorrhages: (resulting in death, or intracranial, retroperitoneal, intraocular, intraspinal, pericardial drop in hemoglobin of at least 2.0 g, or need for transfusion of $\geq 2$ units of packed RBCs or bleeding index $> 2$ )		
Deaths		
Intracranial		
Retroperitoneal		
Intraocular		
Intraspinal		
Pericardial		
Drop in hemoglobin of at least 2.0 grams per decilitre		
Transfusion of $\geq 2$ units of packed RBCs		
Bleeding index $> 2$		
Total number of objectively confirmed thromboembolic events: (venous and atrial thromboembolic complications, DVT, PE, RIND, CVA, TP, stroke and valve thrombosis, and TIAs, as determined by physician)		
DVT		
PE		
RIND		
CVA		

TP		
Stroke		
TIA		
Valve thrombosis		
Total number of patients with major hemorrhage:		
Total number of patients with confirmed thromboembolic events:		
Number of participants withdrawn from trial due to adverse events:		
Description of adverse events:		
Notes: (calculations, if any)		

<b>Assessment of study quality</b>		
<b>Randomization</b>	<b>Yes, No, Unclear</b>	<b>Score</b>
Was the study described as randomized? <i>A trial reporting that it is "randomized" receives one point.</i>		
Trials describing an appropriate method of randomization (table of random numbers, computer-generated) receive an additional point. Appropriate=1		
If the report describes the trial as randomized and uses an inappropriate method of randomization (date of birth, hospital numbers), a point is deducted. Inappropriate=0		
<b>Blinding</b>	<b>Yes, No, Unclear</b>	<b>Score</b>
Was the study described as double-blind? A trial reporting that it is "double-blind" receives one point. Yes=1, no=0		
Trials describing an appropriate method of double-blinding (identical placebo, active placebo) receive an additional point. Appropriate=1		
If the report describes a trial as double-blind and uses an inappropriate method (comparison of tablets versus injection with no dummy), a point is deducted. Inappropriate=-1		
Was the treatment allocation masked from the participants?		
Was the treatment allocation masked from the investigators?		
Was the treatment allocation masked from outcome assessment?		
<b>Withdrawals and dropouts</b>	<b>Yes, No, Unclear</b>	<b>Score</b>
Was there a description of withdrawals and dropouts? A trial reporting the number and reasons for withdrawals or dropouts receives one point. If there is no description, no point is given. Yes=1, no=0		
<b>Total score (for above categories) (0 to 2=low, 3 to 5=high)</b>	<b>Low or High</b>	<b>Score</b>
<b>Adequacy of allocation concealment</b>	<b>Adequacy Level Adequate/Inadequate/Unclear</b>	
Central randomization; numbered or coded bottles or containers; drugs prepared by a pharmacy, serially numbered, opaque, sealed envelopes. Adequate		
Alternation; reference to case record number or date of birth. Inadequate		
Allocation concealment is not reported or fits neither category. Unclear		
Notes:		

<b>Potential biases</b> (mark with ✓ or ? if it applies)			
selection <i>systematic (non-random) differences between those selected for study and those not selected</i>	performance <i>systematic differences in study in how interventions delivered</i>	measurement <i>systematic differences in study in how variables measured (or how subjects classified)</i>	attrition (loss to follow-up) <i>systematic differences between those analyzed and those who withdrew or were lost from study</i>
<b>Describe potential biases and estimated impact on results:</b>			
Reporting of study details: (mark) notes:	complete	incomplete	
Completeness of clinical information: (mark) notes:	complete	incomplete	
<b>Limitations of study:</b> (e.g., regarding test sensitivity or specificity, uninterpretable data, study design, potential biases, surprising results)			
<b>Population targeted by authors:</b>			
Results appear applicable or generalizable to authors' target:	yes	no	unclear
Results appear applicable or generalizable to another target: if so, which target(s):	yes	no	unclear
<b>Conclusions</b> made by authors based on data: (in words, related to objectives on page 1)			
Consistent with data or analysis? (mark)	yes	no	

CVA=cerebrovascular accident ;DVT=deep vein thrombosis; PE=pulmonary embolism; RIND=reversible ischemic neurological deficit; TIA= transient ischemic attack; TP=thrombophlebitis.

## Appendix 4: Excluded full-text clinical articles

29 reports excluded because:

Study design inappropriate for review (seven articles and four reviews)

Andrew M, Ansell J, Becker D, Becker R, Triplett D, Shepherd A. Multicenter trial of accurate home self-testing in oral anticoagulant patients with a novel whole blood system. *Blood* 1996;88(10 Suppl 1 part 1-2):179A.

Becker R, Andrew M, Ansell J, Becker D, Triplett D, Shepherd A. Multicenter trial of accurate home self-testing in oral anticoagulant patients with a novel whole blood system. *J Am Coll Cardiol* 1997;29(2 Suppl A):525A.

Biasiolo A, Rampazzo P, Furnari O, Filippi B, Pengo V. Comparison between routine laboratory prothrombin time measurements and fingerstick determinations using a near- patient testing device (Pro-Time). *Thromb Res* 2000;97(6):495-8.

Caliezi C, Niederer A, Wuillemin WA. Die Patienten-Selbstkontrolle der oralen Antikoagulation [Patient self-management of oral anticoagulation]. *Ther Umsch Rev Ther* 2003;60(1):59-62.

Cosmi B, Palareti G, Moia M, Pengo V, Testa S. Uso domiciliare di un monitor portatile per la determinazione del tempo di protrombina (CoaguCheck) nei pazienti in terapia con anticoagulanti orali. Studio prospettico multicentrico [Home use of an ambulatory monitor for the determination of prothrombin time (CoaguCheck) in patients treated with oral anticoagulants. Multicenter prospective study]. *Minerva Cardioangiol* 1999;47(12):598-9.

Watzke HH, Forberg E, Svolba G, Jimenez-Boj E, Kringinger B. A prospective controlled trial comparing weekly self-testing and self-dosing with the standard management of patients on stable oral anticoagulation. *Thromb Haemost* 2000;83(5):661-5.

White RH, McCurdy SA. Home prothrombin time monitoring after the initiation of warfarin therapy. A randomized, prospective study. *Ann Intern Med* 1989;111:730-7.

### Reviews (4)

de Solà-Morales Serra O, Elorza Ricart JM. Coagulómetros portátiles: una revisión sistemática de la evidencia científica del autocontrol del tratamiento anticoagulante oral [Portable coagulometers: a systematic review of the evidence on self-management of oral anticoagulant treatment]. *Med Clin (Barc)* 2005;124(9):321-5.

Odegaard KJ. Egenkontroll i antikoagulasjonsbehandling--en metaanalyse [Self-management in anticoagulation--a meta-analysis]. *Tidsskr Nor Lægeforen* 2004;124(22):2900-3.

Siebenhofer A, Berghold A, Sawicki PT. Systematic review of studies of self-management of oral anticoagulation. *Thrombosis & Haemostasis* 2004;91(2):225-32.

Fitzmaurice DA, Gardiner C, Kitchen S, Mackie I, Murray ET, Machin SJ. An evidence-based review and guidelines for patient self-testing and management of oral anticoagulation. *Br J Haematol* 2005;131(2):156-65.

### Intervention inappropriate for review (5)

Barreira R, Ribeiro J, Farinha M, Martins R, Rodrigues I, Mendes FC. Monitorização da terapêutica com anticoagulantes orais: Consulta de anticoagulação médico assistente [Monitoring therapy with oral anticoagulants: Anticoagulation clinics vs assistant physician]. *Acta Med Port* 2004;17(6):413-6.

Fitzmaurice DA, Murray ET, Gee KM, Allan TF, Hobbs FD. A randomised controlled trial of patient self management of oral anticoagulation treatment compared with primary care management. *J Clin Pathol* 2002;55(11):845-9.

Gardiner C, Williams K, Mackie IJ, Machin SJ, Cohen H. Patient self-testing is a reliable and acceptable alternative to laboratory INR monitoring. *Br J Haematol* 2005;128(2):242-7.

Koertke H, Minami K, Boethig D, Breymann T, Seifert D, Wagner O, et al. INR self-management permits lower anticoagulation levels after mechanical heart valve replacement. *Circulation* 2003;108 Suppl 1:1175-8.

Jackson SL, Peterson GM, Vial JH, Jupe DML. Improving the outcomes of anticoagulation: an evaluation of home follow-up of warfarin initiation. *J Intern Med* 2004;256(2):137-44.

### Population inappropriate for review (1)

Caprini JA, Sehgal LR, Oyslender M, Kudrna JC, Williams RE, Measday MA, et al. A novel system to manage anticoagulation in hip replacement patients employing patient self-testing and a telemonitoring system. *Blood* 2003;102(11):325a.

### Outcome measures inappropriate for review (1)

Murray E, Fitzmaurice D, McCahon D, Fuller C, Sandhur H. Training for patients in a randomised controlled trial of self management of warfarin treatment. *BMJ* 2004;328(7437):437-8.

### Protocol only, study incomplete (3)

McCahon D, Fitzmaurice DA, Murray ET, Fuller CJ, Hobbs Richard FD, Allan TF, et al. SMART: self-management of anticoagulation, a randomised trial [ISRCTN19313375]. *BMC Fam Pract* 2003;4(1):11.

Völler H, Glatz J, Taborski U, Bernardo A, Dovifat C, Burkard G, et al. Hintergrund und Prüfplan der Studie zum Selbstmanagement der Antikoagulation bei Patienten mit nichtvalvularem Vorhofflimmern (SMAAF-Studie) [Background and evaluation plan of a study on self- management of anticoagulation in patients with non-valvular atrial fibrillation (SMAAF Study)]. *Z Kardiol* 2000;89(4):284-8.

Matchar DB, Jacobson AK, Edson RG, Lavori PW, Ansell JE, Ezekowitz MD, et al. The impact of patient self-testing of prothrombin time for managing anticoagulation: rationale and design of VA cooperative study #481 - The Home INR Study (THINRS). *J Thromb Thrombolysis* 2005;19(3):163-72.

### Duplicates of excluded studies (3)

Fitzmaurice DA, Hobbs FDR, Rose PE, Murray ET. The haematological primary/secondary care interface. A randomised controlled trial comparing primary care oral anticoagulant management utilising computerised decision support (DSS) and near patient testing (NPT), with traditional management. *Br J Haematol* 1996;93(Suppl 2):9.

Gerinnungs-Selbstkontrolle nach Klappenersatz. Stabile Antikoagulation erlaubt Absenken der Intensität [Coagulation self-control after valve replacement. Stable anticoagulation permits lowering of the intensity]. *MMW Fortschritte der Medizin* 2004;146(14):44.

Williams E, Gardiner C, Mackie IJ, Machin SJ, Cohen H. Preliminary data from the Medical Devices Agency (MDA) study of the CoaguCheck S in a patient self-testing environment. *Br J Haematol* 2003;121(Suppl 1):7.

#### Duplicates of included studies (5)

Fitzmaurice DA, Hobbs FDR, Rose PE, Murray ET. A randomised controlled trial comparing primary care oral anticoagulant management utilising computerised decision support (DSS) and near patient testing (NPT) versus routine care: final results. *Br J Haematol* 1997;97(Suppl 1):79.

Gadisseur APA, Kaptein AA, Breukink-Engbers WGM, van der Meer FJM, Rosendaal FR. Patient self-management of oral anticoagulant care vs. management by specialized anticoagulation clinics: positive effects on quality of life. *J Thromb Haemost* 2004;2(4):584-91.

Gadisseur Alain PA, Kaptein AA, Breukink-Engbers Mimi GM, Meer Felix JM, Rosendaal FR. Patient self-management of oral anticoagulant care versus management by specialized anticoagulation clinics: Positive effects on Quality of Life. *Blood* 2003;102(11):321a.

Körtke H, Minami K, Breymann T, Seifert D, Baraktaris A, Wagner O, et al. INR-Selbstmanagement nach mechanischem Herzklappenersatz: ESCAT (Early Self-Controlled Anticoagulation Trial) [INR self-management after mechanical heart valve replacement: ESCAT (Early Self-Controlled Anticoagulation Trial)]. *Z Kardiol* 2001;90 Suppl 6:118-24.

Sawicki PT, Gläser B, Kleespies C, Stubbe J, Schmitz N, Kaiser T. Long-term results of patients' self-management of oral anticoagulation. *J Clin Basic Cardiol* 2003;6(1-4):59-62. Available: <http://www.kup.at/kup/pdf/3927.pdf> (accessed 2005 Nov 11).

## Appendix 5: Characteristics of clinical trials

Author	Country	Intervention Group	Control Group	Observation Period	Mean Intervention	Age Control	Gender Intervention Group	(M/F) Control Group	Indication
Cromheecke <i>et al.</i> <sup>54</sup>	Netherlands	SM	ACC	3 months	42	42	28/17	25/19	AF, MV, VTE
Fitzmaurice <i>et al.</i> <sup>55</sup>	UK	SM	PC or HACC	12 months	64	66	(400/217)*	(400/217)*	AF, MV, VTE, O
Gadisseur <i>et al.</i> <sup>57</sup> **	Netherlands	SM STPOC	ACC ACC	26 weeks 26 weeks	53.9 54.8	62 62	36/11 40/12	110/51 110/51	AF, MV, VTE, O AF, MV, VTE, O
Horstkotte <i>et al.</i> <sup>58</sup>	Germany	SM	PC	NR	NR	NR	NR	NR	MV
Khan <i>et al.</i> <sup>59</sup> **	UK	STPOC	ACC and education	6 months	71	73	26/14	19/20	AF
Koertke <i>et al.</i> <sup>60</sup> † Koertke <i>et al.</i> <sup>61</sup>	Germany	SM	PC	up to 51 months	(62.5)*	(62.5)*	(394/206)*	(394/206)*	MV
Menendez-Jandula <i>et al.</i> <sup>62</sup>	Spain	SM	ACC	up to 17 months	61 to 65	63 to 66	190/178	201/168	AF, MV, VTE, O
Shiach <i>et al.</i> <sup>64</sup>	UK	CPOC	HACC	6 months	NR	NR	NR	NR	NR
Sidhu <i>et al.</i> <sup>65</sup>	Ireland	SM	HACC or PC	2 years	61.0	60.8	27/24	19/30	MV
Beyth <i>et al.</i> <sup>67</sup> ‡	USA	STPOC	PC	up to 6 months	74.9	74.5	74/89	95/67	AF, MV, VTE, O
Claes <i>et al.</i> <sup>68</sup> **‡	Belgium	STPOC	PC and education	6 months	(70.2)*	(70.2)*	(455/379)*	(455/379)*	52% AF, MV, VTE, O
Fitzmaurice <i>et al.</i> <sup>56</sup> **‡	UK	NPOC	PC	12 months	NR	NR	NR	NR	AF, MV, VTE, O
Sawicki <i>et al.</i> <sup>63</sup> ‡	Germany	SM	ACC or PC	6 months	55	55	64/26	62/27	>80% MV
Sunderji <i>et al.</i> <sup>69</sup> ‡	Canada	SM	PC	up to 8 months	57.6	62.3	44/25	54/16	64% MV, 29% AF, VTE
Voller <i>et al.</i> <sup>66</sup> ‡	Germany	SM	PC	up to 19 months	64.6	64.1	72/29	62/39	AF

\*gender or age in ( ) is for overall study; not reported for control or intervention group; \*\*multiple comparisons, but for analysis and figures in this table, used routine care as control group; †used both papers to obtain data used in the analysis; ‡studies included patients who had OAC therapy for <6 months; ACC=specialized anticoagulation clinic; AF=atrial fibrillation; CPOC=MD in clinic dosed, based on POC result; HACC=hospital anticoagulation clinic; MV=mechanical valve; NR=not reported; O=others; PC=primary care; PCPOC=primary care with POC used for INR determination; NPOC=nurse dosed in a clinic with INRs determined by POC; SM=self-testing with POC and dosing by patient; STPOC=self- or family-member testing with POC, but clinic provided dosing; VTE=venous thromboembolism

## Appendix 6: Outcome data from eligible trials

Author	Patient Years of Observation		Time in Range		Major Hemorrhage		Major TEE		Minor TEE		Deaths		Quality Score
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Cromheecke <i>et al.</i> <sup>54</sup>	12.5	12.5	NR	NR	0	0	0	0	0	1	NR	NR	2
Fitzmaurice <i>et al.</i> <sup>55</sup>	318	264	70% (68.1 to 72.4)	68% (65.2 to 70.6)	4	4	3	3	1	0	5	11	3
Gadisseur <i>et al.</i> <sup>57</sup>	25	74.6	66.9% (62.7 to 71.0)	63.5% (59.7 to 67.3)	0	1	0	0	0	0	NR	NR	2
	21.8	74.6	68.6% (63.7 to 73.6)	63.5% (59.7 to 67.3)	2	1	0	0	0	0	NR	NR	2
Horstkotte <i>et al.</i> <sup>58</sup>	NR	NR	NR	NR	NR	NR	0.92/year	3.33/year	NR	NR	NR	NR	1
Khan <i>et al.</i> <sup>59</sup>	20	20	71.1%±14.5%	63.2% ±25.9%	1	0	0	NR	0	2	NR	NR	3
Menendez-Jandula <i>et al.</i> <sup>62</sup>	368	369	64.3%±14.3%	64.9% ±19.9%	4	7	3	12	1	8	6	15	2-obj**
Shiach <i>et al.</i> <sup>64</sup>	9.5	10	60.9%±26.4%	63.4% ±23%	NR	NR	NR	NR	NR	NR	0	0	3-obj**
Sidhu <i>et al.</i> <sup>65</sup>	67	85.1	76.5% SD NR	63.8% SD NR	1	0	1	4	not defined	not defined	0	4	3
Beyth <i>et al.</i> <sup>67*</sup>	42.5	29	58.5% SD NR	34.2% SD NR	8	17	13	20	1	1	21	26	2
Claes <i>et al.</i> <sup>68*</sup>	72.9	213	NR	NR	5	9	4	13	0	0	NR	NR	3-obj**
Fitzmaurice <i>et al.</i> <sup>56*</sup>	87.3	165.7	69% (66 to 73)	62% (53 to 70)	1	0	2	6	0	4	3	6	2
Koertke <i>et al.</i> <sup>60†*</sup>	973	943	78.3% SD NR	60.5% SD NR	17	25	12	20	NR	NR	NR	NR	3
Koertke <i>et al.</i> <sup>61</sup>													
Sawicki <i>et al.</i> <sup>63*</sup>	44.4	43.9	NR	NR	1	1	0	2	1	0	1	1	3
Sunderji <i>et al.</i> <sup>69*</sup>	45.4	46.0	71.8%±5.5%	63% ±5.8%	0	1	0	2	0	0	0	0	3
Voller <i>et al.</i> <sup>66*</sup>	37.3	40.3	67.8%±17.6%	58.5% ±19.8%	2	0	0	1	0	0	NR	NR	1

\*studies included patients who had OAC therapy for <6 months; \*\* (obj)=paper stated objective criteria for diagnosis of thromboembolic events; †used both papers to obtain data used in the analysis; NR=not reported; SD=standard deviation; TEE=thromboembolic event.

## Appendix 7: Frequency of INR measurements

Author	Treatment Arm	Frequency of INR Measurements
Beyth <i>et al.</i> <sup>67</sup>	POC	3 times in first week; weekly for first month; monthly thereafter
	control	NR
Claes <i>et al.</i> <sup>68</sup>	POC	18 days (median)
	control	18 days (median)
Cromheecke <i>et al.</i> <sup>54</sup>	POC	1 to 2 weeks
	control	1 to 2 weeks
Fitzmaurice <i>et al.</i> <sup>55</sup>	POC	12.4 days (mean)
	control	37.9 days (mean)
Fitzmaurice <i>et al.</i> <sup>56</sup>	POC	NR
	control	NR
Gadisseur <i>et al.</i> <sup>57</sup>	POC+self-management	Weekly
	POC+clinic management	Weekly
	training but routine care	NR
	Zelen group	NR
Horstkotte <i>et al.</i> <sup>58</sup>	POC	3 days
	control	NR
Khan <i>et al.</i> <sup>59</sup>	POC	Weekly
	control (education+routine care)	NR
	Zelen group	NR
Koertke <i>et al.</i> <sup>60-61</sup>	POC	approximately 2 weeks
	control	approximately 10 weeks
Menéndez-Jándula <i>et al.</i> <sup>62</sup>	POC	Weekly
	control	4 weeks, or 1 to 2 weeks when INR out of target range
Sawicki <i>et al.</i> <sup>63</sup>	POC	1 or 2 times per week
	control	2 weeks
Shiach <i>et al.</i> <sup>64</sup>	POC	NR
	control	NR
Sidhu <i>et al.</i> <sup>65</sup>	POC	frequency changed throughout study to at 3 months, 5.2 days; at 6 months, 6.6 days; at 12 months, 7.3 days; at 24 months, 7.8 days
	control	29.2 days
Sunderji <i>et al.</i> <sup>69</sup>	POC	9.3 days (mean)
	control	17.5 days (mean)
Völler <i>et al.</i> <sup>66</sup>	POC	NR
	control	NR

## APPENDIX 8: Withdrawals

Author	Treatment Arm	Number of Patients Randomized	Number of Withdrawals	Description of Withdrawals
Beyth <i>et al.</i> <sup>67</sup>	POC	163	31	31 patients (19%) declined to participate in POC; additional 36 (22%) did not withdraw but were monitored conventionally
	control	162	NR	
Claes <i>et al.</i> <sup>68</sup>	POC	834	NR	
	control		NR	
Cromheecke <i>et al.</i> <sup>54</sup>	POC	50 (crossover study)	1	1 patient could not self-manage because of progressive visual impairment
	control	50	0	
Fitzmaurice <i>et al.</i> <sup>55</sup>	POC	337	139	10 patients (3%) did not attend training, 80 (24%) did not complete training, 3 discontinued warfarin, 1 withdrew consent; during intervention, 34 (14%) did not complete intervention, 7 discontinued warfarin, 4 moved away
	control	280	19	1 patient withdrew permission for data collection, 15 discontinued warfarin, 1 began to self-monitor immediately after randomization, 2 moved away
Fitzmaurice <i>et al.</i> <sup>56</sup>	POC	122	20	3 patients moved away, 3 too ill or non-compliant, 8 returned to hospital clinic, 6 completed OAT therapy
	control	245	26	6 patients moved away, 20 completed OAT therapy
Gadisseur <i>et al.</i> <sup>57</sup>	POC + self-management	47	21 at training	21 withdrawals at training; before randomization, 9 patients could not use CoaguChek device properly, 8 patients had problems with self-dosing, 2 patients had differences >20% between their measurements and laboratory measurements, 2 patients did not agree with randomization process; any withdrawals after randomization NR
	POC + clinic management	52		
	Training but routine care	60		
	Zelen group	161	NR	
Horstkotte <i>et al.</i> <sup>58</sup>	POC	75	1	NR
	control	75	2	NR
Khan <i>et al.</i> <sup>59</sup>	POC	44	4	1 patient unable to perform self-monitoring competently at home; 3 patients discontinued OAT
	control (education + routine care)	41	2	2 patients discontinued OAT
	Zelen group	40	NR	

Koertke <i>et al.</i> <sup>60-61</sup>	POC	305	unclear	
	control	295	unclear	
Menéndez-Jándula <i>et al.</i> <sup>62</sup>	POC	368	79 (21.5%)	58 (16%) declined before training; 10 (3%) unable to pass examination; 11 withdrawals during study period
	control	369	9 (2.4%)	NR
Sawicki <i>et al.</i> <sup>63</sup>	POC	90	6	5 patients refused to participate; 1 patient stopped OAT
	control	89	6	6 patients refused to participate
Shiach <i>et al.</i> <sup>64</sup>	POC	23	7	4 patients could not have venous samples drawn easily; 3 patients provided 1 INR test in 6-month period
	control	23		
Sidhu <i>et al.</i> <sup>65</sup>	POC	51	17	7 patients declined training because of distance from training centre (4), lack of confidence in ability to manage OAT dosing (2), lack of confidence in performing finger-pricks (1); 3 patients considered to be unsuitable because of difficulty with blood sampling or managing dosing; during follow-up, 3 patients abandoned self-monitoring because of difficulty in obtaining blood samples, 2 preferred general practitioner management, 1 had technical difficulties with the POC device, 1 practised self-management for a year, then returned to general practitioner management because of difficulty obtaining strips
	control	49	none	
Sunderji <i>et al.</i> <sup>69</sup>	POC	70	17	13 patients withdrew immediately after randomization: withdrew consent (1), had difficulty with POC device (5), failed competency test (2), preferred physician management (4), deemed unsuitable by physician (1); 4 patients withdrew during study: difficulty with blood collection (1), failure to follow study protocol (2), minor bleeding requiring change in target INR that no longer met inclusion (1)
	control	70	3	3 patients discontinued OAT
Völler <i>et al.</i> <sup>66</sup>	POC	101	NR	
	control	101	NR	

## Appendix 9: Quality assessment of full economic studies

Study design	de Solà-Morales <sup>79</sup>	Lafata <sup>77,78</sup>
Research question is stated	yes	yes
Economic importance of research question is stated	yes	not clear
Viewpoint(s) of analysis clearly stated and justified	yes	yes
Rationale for choosing alternative programs or interventions compared stated	yes	yes
Alternatives being compared clearly described	yes	yes
Form of economic evaluation used stated	yes	yes
Choice of economic evaluation justified in relation to questions addressed	yes	yes
<b>Data collection</b>		
Source(s) of effectiveness estimates used stated	yes	yes
Details of design and results of effectiveness study given (if based on 1 study)	not applicable	yes
Details of method of synthesis or meta-analysis of estimates given (if based on overview of effectiveness studies)	not clear	not applicable
Primary outcome measure(s) for economic evaluation stated	yes	yes
Methods to value health states and other benefits stated	no	yes
Details of subjects from whom valuations obtained given	not applicable	not applicable
Productivity changes (if included) reported separately	not applicable	not applicable
Relevance of productivity changes to study question discussed	not applicable	not applicable
Quantities of resources reported separately from unit costs	yes	yes
Methods for estimation of quantities and unit costs described	yes	yes
Currency and price data recorded	yes	yes
Details of price adjustments for inflation or currency conversion given	yes	no
Details of model used given	yes	yes
Choice of model used and key parameters on which it is based justified	yes	yes
<b>Analysis and interpretation of results</b>		
Time horizon of costs and benefits stated	yes	yes
Discount rate(s) stated	yes	yes
Choice of rate(s) justified	no	no
Explanation given if costs or benefits not discounted	not applicable	not applicable
Statistical test and confidence intervals given for stochastic data	no	no
Approach to sensitivity analysis given	yes	yes
Choice of variables for sensitivity analysis justified	yes	yes
Ranges over which variables varied stated	not clear	yes
Relevant alternatives compared	yes	yes
Incremental analysis reported	yes	yes
Major outcomes presented in disaggregated and aggregated forms	yes	yes
Answer to study question given	yes	yes
Conclusions follow from data reported	yes	yes
Conclusions accompanied by appropriate caveats	yes	yes
Sum of “no” and “not clears”	5	4

## Appendix 10: Quality assessment of cost comparison economic studies

Study	Inputs Included	Physical Measures and Unit Costs Reported Separately	Well Defined Answerable Question	Timelines of Study
Ansell <sup>17</sup>	Total costs for materials, procedures, and labor calculated per test. Labour costs calculated from time standards for nursing, secretarial, and receptionist activities. Financial data for wages and benefits obtained from hospital finance and nursing administration. Laboratory costs associated with standard testing obtained from clinical pathology department's cost accounting system. Coumatrak PT testing costs determined through calculation of actual cost of materials plus instrument depreciation.	yes	yes	20 OAT patients using usual or POC testing every other week for 8 weeks in cross-over design
Cheung <sup>80</sup>	Costs for materials, procedures, transportation, and labour summed for laboratory and POC testing.	yes	yes	2 years
Jacobson <sup>81</sup>	Direct operational costs (sum of human resources costs); direct costs of POC test supplies, quality control, and equipment from Roche.	yes	yes	total turnaround time defined as time from initial blood draw (stamped on laboratory result sheet) to time of patient notification of test results; per test data extrapolated to a year.
Taborski <sup>9</sup>	Costs considered were those covered by government-controlled health insurance funds, including outpatient visits and acute inpatient treatment and rehabilitation for serious complications of treatment. Direct monitoring costs, and costs for treating minor and serious complications, used to calculate overall therapy costs.	yes	yes	1 patient-year

## Appendix 11: Economic Data Extraction Form

<b>Economic Data Extraction Form</b>	
<b>Reviewer</b>	
<b>Author</b>	
<b>Year</b>	
<b>Title</b>	
<b>RevMan ID</b>	
<b>Declared Financial Support or Affiliation</b>	
<b>Study Population</b>	
<b>Study Perspective</b>	
<b>Intervention and Comparators</b>	
<b>Study Design</b>	
<b>Geographic Location</b>	
<b>Clinical Outcomes and Source</b>	
<b>Currency and Currency Year</b>	
<b>Estimate of Cost Effectiveness or Relative Cost</b>	
<b>Conclusions</b>	

## Appendix 12: Parameters used in Economic Model

Parameter	Value	Source Details
<b>Population</b>		
Population initiating chronic warfarin therapy	100	
<b>Clinical Effectiveness Parameters</b>		
Time outside therapeutic range:		study meta-analysis
Usual care	39%	
POC device	31%	
Time in therapeutic range:		study meta-analysis
Usual care	61%	
POC device	69%	
First thromboembolic events (TE) (number of TEs per 100 patient-years)		study meta-analysis
Usual care		
Fatal	1.55	
Non-fatal	3.90	
POC device		
Fatal	0.61	
Non-fatal	1.53	
Recurrent TEs (number of TEs per 100 patient-years)		study meta-analysis
Usual care		
Fatal	3.1	
Non-fatal	7.79	
POC device		
Fatal	1.22	
Non-fatal	3.07	
Percent of patients off therapy with prior events who have TE in subsequent years:		European Atrial Fibrillation Trial Study Group <sup>90</sup>
Total	17%	
Severity distribution of subsequent TEs:		Fihn <sup>109</sup>
Fatal	1%	Fihn <sup>109</sup>
Non-fatal	99%	
TE disability		Wilkinson <sup>84</sup> Bonita <sup>85</sup> Dorman <sup>86</sup>
Percent of non-fatal TEs that cause permanent disability	60%	Tennant <sup>87</sup> Dighe <sup>88</sup>
Percent of patients with permanently disabling TE who continue therapy	50%	Lafata <sup>78</sup>
First bleeding events (Number of bleeds per 100 patient-years)		study meta-analysis
Usual care		
Fatal	1.09	
Non-fatal	2.72	
POC device		
Fatal	0.73	
Non-fatal	1.84	

Recurrent bleeding events (number of bleeds per 100 patient-years)		study meta-analysis
Usual care		
Fatal	2.18	
Non-fatal	5.43	
POC device		
Fatal	1.46	
Non-fatal	3.68	
Percent of patients off therapy with prior event who bleed in subsequent years:		European Atrial Fibrillation Trial Study Group <sup>90</sup>
Total	1%	
Severity distribution of bleeds		
Fatal	20%	Fihn <sup>109</sup>
Non-fatal	80%	Fihn <sup>109</sup>
Bleed disability		
Percent of non-fatal bleeds that cause permanent disability	10%	White <sup>89</sup>
Percent of patients with permanently disabling bleed who continue therapy	50%	Lafata <sup>78</sup>
<b>Cost Parameters: Resource Utilization</b>		
Equipment and personnel		
Number of POC monitors required:		
POC anticoagulation clinic	1	Lafata <sup>78</sup>
POC patient self-testing	100	corresponds to 100 patients in cohort
Number of nurses required to monitor patients:		
POC anticoagulation clinic	1	Lafata <sup>78</sup>
POC patient self-testing	1	Lafata <sup>78</sup>
Caregivers		
Percent of patients with caregivers attending clinic monitoring visits	30%	Lafata <sup>78</sup>
Percent of patients with caregivers assisting in home monitor test	9%	Murphy <sup>98</sup>
Training		
Nursing time to train patient <sup>†</sup> on monitor (hours)	1.5	Lafata <sup>78</sup>
Patient travel <sup>‡</sup> distance for training on monitor (round trip miles)	26	Lafata <sup>78</sup>
Patient travel <sup>†</sup> time for training on monitor (round trip minutes)	52	based on 2 minutes per mile travelled (or 1.24 minutes per kilometre travelled)
Patient <sup>†</sup> wait time for training session (minutes)	7	Lafata <sup>78</sup>
Monitoring		
Number of PT-INR performed per year per patient:		
Usual care		(PW, unpublished observations, 2006)
POC anticoagulation clinic	20	Ansell <sup>96</sup>
POC patient self-testing	23	

Percent of time MD consulted about PT-INR test result:	52	Bernardo <sup>97</sup>
Usual care	90%	Lafata <sup>78</sup>
POC anticoagulation clinic	10%	Ansell <sup>17</sup>
POC patient self-testing	10%	Ansell <sup>17</sup>
MD consult time per test: (minutes)		
Usual care	2	Lafata <sup>78</sup>
POC anticoagulation clinic	2	Ansell <sup>17</sup>
POC patient self-testing	2	Ansell <sup>17</sup>
Nursing time per test: (minutes)		
Usual care	13	Ansell <sup>17</sup>
POC anticoagulation clinic	15	Ansell <sup>17</sup>
POC patient self-testing	8	Ansell <sup>17</sup>
Patient <sup>†</sup> time per test: (minutes)		
Usual care	17	Ansell <sup>17</sup>
POC anticoagulation clinic	20	Ansell <sup>17</sup>
POC patient self-testing	15	Ansell <sup>17</sup>
Patient travel distance <sup>‡</sup> for PT-/INR testing (round trip miles)	26	Lafata <sup>78</sup>
Patient <sup>†</sup> travel time for PT-INR testing (round trip minutes)	52	based on 2 minutes per mile travelled (or 1.24 minutes per kilometre travelled)
Thromboembolic event related resource use		
Percent of TEs that result in emergency room visits:		
Fatal	90%	Lafata <sup>78</sup>
Non-fatal	100%	Lafata <sup>78</sup>
Number of emergency room visits per TE:		
Fatal	1	Lafata <sup>78</sup>
Non-fatal	1	Lafata <sup>78</sup>
Percent of TEs that result in inpatient stay:		
Fatal	90%	Lafata <sup>78</sup>
Non-fatal	100%	Lafata <sup>78</sup>
Number of inpatient days per TE:		
Fatal	3	Lafata <sup>78</sup>
Non-fatal	11	Lafata <sup>78</sup> Mitchell <sup>110</sup> Holloway <sup>111</sup>
Percent of TEs that result in inpatient nursing facility stay:		
Non-fatal		
Temporarily disabling	30%	Lafata <sup>78</sup>
Permanently disabling	63%	Lafata <sup>78</sup>
Number of inpatient nursing facility days per TE:		
Non-fatal		
Temporarily disabling	30	short-term stay <sup>78</sup>
Permanently disabling	365	long-term stay <sup>78</sup>
Bleed event related resource use		
Percent of bleed events that result in emergency room visits:		

Fatal	90%	Lafata <sup>78</sup>
Non-fatal	100%	Lafata <sup>78</sup>
Number of emergency room visits per bleed event:		
Fatal	1	Lafata <sup>78</sup>
Non-fatal	1	Lafata <sup>78</sup>
Percent of bleed events that result in inpatient stay:		
Fatal		
Non-fatal	90%	Lafata <sup>78</sup>
Number of inpatient days per bleed event:	100%	Lafata <sup>78</sup>
Fatal		
Non-fatal	7	Lafata <sup>78</sup>
	12	Lafata <sup>78</sup> Mitchell <sup>110</sup>
Percent of bleed events that result in inpatient nursing facility stay:		Holloway <sup>111</sup>
Non-fatal		
Temporarily disabling		
Permanently disabling	10%	Lafata <sup>78</sup>
Number of inpatient nursing facility days per bleed event:	20%	Lafata <sup>78</sup>
Non-fatal		
Temporarily disabling		
Permanently disabling	30	short-term stay <sup>78</sup>
	365	long-term stay <sup>78</sup>
<b>Cost Parameters:* Resource Valuation</b>		
MD average hourly earnings rate	\$75.05 (2005)**	Physicians, dentists and veterinarians 2003 Source: Statistics Canada, Ottawa, Survey of Labour and Income Dynamics (SLID), 2003. <sup>112</sup> \$71.83 (2003)
Nursing and trainer average hourly earnings rate	\$33.89 (2005)**	Nurse supervisors and registered nurses 2003 Source: Statistics Canada, Ottawa, Survey of Labour and Income Dynamics (SLID), 2003. <sup>112</sup> \$32.43 (2003)
Patient and caregiver hourly wage rate	\$19.33	Average wage for all professions, Oct. 2005 Statistics Canada <sup>113</sup>
Cost per travel mile	\$0.77	at 0.62 miles=1.0 kilometre and cost of \$0.48 per travel kilometre (average rate for regions from Treasury Board of Canada rates, Dec. 2005) <sup>114</sup>
Cost of laboratory INR test	\$6.49	(Robin Greig, Stanton Territorial Health Authority, Yellowknife, NT: personal communication, 2006 Aug. 06)

Cost of CoaguChek S monitor	\$995.00	CoaguChek Jan. 2005 (and in effect for 2006) <sup>10</sup> retail price
Cost of CoaguChek cartridges and lancets (per test)	\$6.92	CoaguChek Jan. 2005 (and in effect for 2006) <sup>10</sup> retail price (strips \$325.00 for 48, lancets \$7.49 for 50)
Cost of ProTime machine	\$1,895.00 (pricing subject to change)	(Katrin Jung: personal communication, 2006 Aug. 18)
Cost of ProTime cuvettes and collectors (per test)	\$8.25 (pricing subject to change)	\$206.25 for box of 25 ProTime reagent cuvettes and Tenderlett collectors (Katrin Jung: personal communication, 2006 Aug. 18)
Cost per outpatient visit	\$101.43	Average of consultation and limited/repeat consultation for hematology, Ontario Schedule of benefits, Oct. 2005 <sup>115</sup>
Cost of emergency room visit	\$468	Health Cost in Alberta 2005 <sup>116</sup> ACCS Group #2002
Cost per day of hospital stay	\$975.93 (2005)**	For nonspecific cerebrovascular disorders CMG code 015, Health Costing in Alberta 2003 <sup>117</sup> \$934 (2003)
Cost per day of inpatient physician services	\$56.10	Ontario Oct. 2005: non-emergency hospital in-patient services, consultation <sup>115</sup>
Cost per day of nursing facility stay	\$161.2 (2005)**	Long-term care for standard accommodation, Alberta 2001 <sup>118</sup> \$105 (2001)+ accommodation fee=\$116.05 (2005)+\$45.15 (2005)=\$161.2 (2005);** \$45.15 accommodation fee=average of semi-private (\$42) and private (\$48.50)
Discount rate	baseline 0.05 (5%); sensitivity analysis at 0.0 (0%) and 0.03 (3%)	CADTH Guidelines for Economic Evaluation of Health Technologies: Canada <sup>99</sup>
Quality of life parameters		
Permanently disabling events	0.50	77,78,91-95
Temporarily disabling events	0.75	77,78,91-95

\*Costs and prices in Canadian dollars unless otherwise indicated; \*\*Canadian inflation index adjustment;<sup>119</sup>; †time for caregiver assumed equal to time for patient; ‡caregiver assumed to travel with patient; TE=thromboembolism.

## Appendix 13: Life-Table

An abridged life-table was obtained for Ontario 1996-1997.<sup>120</sup> The data for males and females were merged to get overall deaths per thousand. The data were for five-year age groups, so to get data for each year, a spline extrapolation was done using PROC EXPAND in SAS.

Age (years)	Deaths per 1,000
0 to 1	5.335
1 to 4	1.065
5	0.11
6	0.11
7	0.11
8	0.11
9	0.11
10	0.11
11	0.11
12	0.12
13	0.18
14	0.25
15	0.31
16	0.38
17	0.44
18	0.46
19	0.47
20	0.48
21	0.49
22	0.50
23	0.50
24	0.50
25	0.50
26	0.50
27	0.50
28	0.53
29	0.57
30	0.61
31	0.65
32	0.70
33	0.75
34	0.81
35	0.86

Age (years)	Deaths per 1,000
36	0.92
37	0.98
38	1.08
39	1.18
40	1.28
41	1.39
42	1.49
43	1.62
44	1.75
45	1.88
46	2.01
47	2.16
48	2.42
49	2.69
50	2.96
51	3.23
52	3.53
53	4.02
54	4.53
55	5.05
56	5.57
57	6.11
58	6.83
59	7.58
60	8.32
61	9.07
62	9.87
63	11.00
64	12.18
65	13.36
66	14.55
67	15.83
68	17.72

Age (years)	Deaths per 1,000
69	19.70
70	21.69
71	23.68
72	25.74
73	28.27
74	30.87
75	33.48
76	36.08
77	38.98
78	43.63
79	48.58
80	53.53
81	58.47
82	63.59
83	69.73
84	76.04
85	82.34
86	88.65
87	95.20
88	103.20
89	111.44
90	119.69
91	127.93
92	136.14
93	144.14
94	152.10
95	160.07
96	168.03
97	176.00
98	183.97
99	191.93
100	193.32

## Appendix 14: Probabilistic Sensitivity Analysis: Deterministic and Stochastic ICER Results

Comparison	Perspective	Deterministic ICER Result	Stochastic ICER Result (Forecast mean)*	Threshold Analysis
Usual care to CoaguChek® in anticoagulation clinic	health care provider (excluding nursing home costs)	(\$2,720)	(\$2,713)	probability<\$0=63%
"	health care provider (including nursing home costs)	(\$18,081)	(\$18,063)	probability<\$0=99%
"	societal	\$10,808	\$12,466	probability<\$0=37% probability<\$50,000=86%
Usual care to CoaguChek® in patient self-testing	health care provider (excluding nursing home costs)	\$72,955	\$72,990	probability<\$50,000=2%
"	health care provider (including nursing home costs)	\$57,595	\$57,640	probability<\$50,000=26%
"	societal	(\$7,104)	(\$110)	probability<\$0=52%
Usual care to ProTime® in anticoagulation clinic	health care provider (excluding nursing home costs)	\$2,437	\$2,438	probability<\$50,000=100%
"	health care provider (including nursing home costs)	(\$12,923)	(\$12,922)	probability<\$0=94%
"	societal	\$15,966	\$15,930	probability<\$50,000=82%

ICER=Incremental cost effectiveness ratio; \*10,000 iterations run for each Monte Carlo simulation; brackets indicate negative values (cost savings).

## Appendix 15: Probability Sensitivity Analysis: Stochastic Parameters

	Parameter	Expected Value	Distribution
1	Percent of life threatening TEs that cause permanent disability	60%	beta (55.7, 37.8)
2	Percent of patients with permanently disabling TE who continue therapy	50%	beta (3, 3)
3	Percent of life-threatening hemorrhages that cause permanent disability	10%	beta (9, 89.3)
4	Percent of patients with disabling hemorrhage who continue therapy	50%	beta (3, 3)
	Number of tests performed per year per patient		
5	Usual care	20	normal (20, 2)
6	POC in anticoagulation clinic	23	normal (23, 2)
7	POC in patient self-testing	52	normal (52, 5)
	Patient time per test (minutes)		
8	Usual care	17	gamma (7.5, 2) shape 8.5 scale 2
9	POC in anticoagulation clinic	20	gamma (9, 2) shape 10 scale 2
10	POC in patient self-testing	15	gamma (6.5, 2) shape 7.5 scale 2

POC=point of care device; TE=thromboembolism; normal distributions characterized by means and standard deviations; beta and gamma distributions characterized by alpha and beta.

## Appendix 16: Disaggregated Economic Results

Disaggregated results are presented below for five years, per 100-patient cohort, for the anticoagulation management strategies analyzed.

### CoaguChek® Health Outcomes

	Usual Care (UC)	Point of care (POC) device	Difference: POC–UC
<b>Thromboembolic Events</b>			
Fatal	6.89	6.40	(0.49)
Other	19.09	17.73	(1.37)
Total	25.98	24.12	(1.86)
<b>Hemorrhagic Events</b>			
Fatal	6.16	5.99	(0.17)
Other	15.47	15.05	(0.42)
Total	21.63	21.04	(0.59)
<b>Life Years</b>			
Total life-years of cohort	406.26	407.83	1.57
Non-disabled life-years	370.51	374.19	3.68
Disabled life-years	35.76	33.65	(2.11)
Quality-adjusted life-years (QALY)	387.97	390.61	2.64

### CoaguChek® Cost Outcomes (\$)

	Usual Care (UC)	POC in Anti-coagulation Clinic (POC clinic)	POC in Patient Self-test (POC PST)	Difference: POC clinic–UC	Difference: POC PST– UC
<b>Monitoring costs</b>					
HC provider	139,005	156,099	356,131	17,095	217,126
Patients and caregivers	296,333	372,696	125,319	76,363	(171,015)
Total	435,338	528,795	481,449	93,457	46,111
<b>Event-related costs to HC providers</b>					
Excluding NH costs	489,271	464,986	464,986	(24,286)	(24,286)
Including NH costs	1,071,129	1,0006,241	1,006,241	(64,888)	(64,888)
Total costs HC provider					
Excluding NH costs	628,276	621,085	821,116	(7,191)	192,840
Including NH costs	1,210,134	1,162,340	1,362,371	(47,793)	152,238
Total costs to patient and caregiver	296,333	372,696	125,319	76,363	(171,015)
<b>Grand total</b>					
Excluding NH costs	924,609	993,781	946,435	69,172	21,826
Including NH costs (societal perspective)	1,506,467	1,535,036	1,487,690	28,569	(18,777)

HC=health care; NH=nursing home; PST=patient self-test; UC=usual care.

## CoaguChek<sup>®</sup> Incremental Cost Effectiveness Ratios (\$ cost per QALY)

Perspective	POC clinic–Usual Care	POC PST–Usual Care
HC provider	(2,720)	72,955
HC provider and NH	(18,081)	57,595
Societal	10,808	7,104

HC=health care; NH=nursing home; PST=patient self-test; UC=usual care.

## ProTime<sup>®</sup> Health Outcomes

	Usual Care (UC)	Point of Care Device (POC )	Difference: POC–UC
Thromboembolic Events			
Fatal	6.89	6.40	(0.49)
Other	19.09	17.73	(1.37)
Total	25.98	24.12	(1.86)
Hemorrhagic Events			
Fatal	6.16	5.99	(0.17)
Other	15.47	15.05	(0.42)
Total	21.63	21.04	(0.59)
Life-Years			
Total life-years of cohort	406.26	407.83	1.57
Non-disabled life–years	370.51	374.19	3.68
Disabled life–years	35.76	33.65	(2.11)
Quality-adjusted life-years (QALY)	387.97	390.61	2.64

POC=point of care; UC=usual care.

## ProTime<sup>®</sup> Cost Outcomes

	Usual Care (UC)	POC in Anticoagulation Clinic (POC clinic)	Difference: POC clinic –UC
Monitoring costs			
HC provider	139,005	169,733	30,728
Patients and caregivers	296,333	372,696	76,363
Total	435,338	542,429	107,091
Event related costs to HC providers			
Excluding NH costs	489,271	464,986	(24,286)
Including NH costs	1,071,129	1,006,241	(64,888)
Total costs HC provider			
Excluding NH costs	628,276	634,719	6,443
Including NH costs	1,210,134	1,175,974	(34,160)
Total costs to patient and caregiver	296,333	372,696	76,363
Grand total			
Excluding NH costs	924,609	1,007,414	82,805
Including NH costs	1,506,467	1,548,670	42,203

HC=health care; NH=nursing home; UC=usual care.

## ProTime<sup>®</sup> Incremental Cost Effectiveness Ratios (\$ cost per QALY)

Perspective	POC clinic–Usual Care
HC provider excluding NH	2,437
HC provider and NH	(12,923)
Societal	15,966

HC=health care; NH=nursing home; UC=usual care.