Supplementary Material

METHODS

Search Strategy

An updated systematic search of the three databases was conducted for the period of March 1, 2013 to December 18, 2013, with the objective of capturing new subgroup analyses from phase 3 trials of dabigatran, rivaroxaban, and apixaban. No limits in terms of publication date or language were included in this search strategy.

Data Extraction

A total of 43 variables were extracted using a standardized data abstraction form developed in Microsoft Excel (Table A-1). In addition, data for the outcomes of interest, if available, were extracted from the trials that compared a new oral anticoagulant versus warfarin in patients with CHADS$_2$ score $\geq 2$ at baseline. In addition, edoxaban data were extracted from the clinical study report or post hoc analysis of ENGAGE AF-TIMI 48 (Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis In Myocardial Infarction study 48) if needed.

Statistical Methods

The mixed Poisson regression model specific to this analysis can be described as follows:
\[ y_{ij} \sim \text{Poisson}(\lambda_{ij}E_{ij}) \]

\[ \log(\lambda_{ij}) = t_j + s_i \]

where

- \( y_{ij} \) is the number of events that occurred among the patients who received treatment \( j \) in study \( i \)
- \( \lambda_{ij} \) is the risk of events among the patients who received treatment \( j \) in study \( i \)
- \( E_{ij} \) is the exposure time contributed by the patients who received treatment \( j \) in study \( i \), generally given in the format of person-years
- \( t_j \) is the mean logarithm of risk for treatment \( j \)
- \( s_i \) are random study effects following a normal distribution with mean zero and unknown variance that account for the correlation between \( y_{ij} \) and \( y_{ij'} \) for \( j \neq j' \) when treatment groups come from the same study

It therefore follows that the risk of event due to treatment \( i \) is \( \lambda_i = \exp(t_i) \), and the risk ratio (RR) of treatment \( a \) versus treatment \( b \) is defined as \( \lambda_a/\lambda_b = \exp(t_a-t_b) \).

In this model, we assumed that risk is constant over the follow-up period. Suppose there are 1,000 person-years from one treatment \( j \) and study \( i \) after 1 year follow-up, then the mean of observed number of events is \( 1,000\lambda_{ij} \). If we follow up the patients for another 1.2 years and have a total of 2,000 person-years, then the mean number of events should be \( 2,000\lambda_{ij} \). This assumption is not true when the chance of events is varied according to the exposure time (e.g., for a type of adverse event that occurs immediately after the first treatment).
For each outcome analyzed using a model based on the Poisson distribution, the risk for specified treatment was estimated by \( \exp(\beta_1) \) with 95% confidence interval (CI) and the \( \text{RR} \) was estimated by \( \exp(\beta_1 - \beta_2) \) with 95% CI. The estimated risk, \( \text{RR} \), and 95% CI are presented in the tables and forest plots. For consistency, person-years were derived by the ratio of number of events versus risk, even if person-years were provided separately.

**RESULTS**

**Systematic Review and Summary of Included Trials**

Of the 1,357 records identified in the initial literature search, 51 publications met the inclusion criteria. Eleven additional publications were identified from an updated systematic search of the literature. A total of 33 publications were identified as relevant. Of them, four phase 3 trials that compared a new oral anticoagulant versus warfarin and two publications\(^1\)\(^2\) of these trials evaluating outcomes by CHADS\(_2\) score were included in this meta-analysis. The four phase 3 trials were ARISTOTLE (apixaban),\(^3\) ROCKET-AF (rivaroxaban),\(^4\) RE-LY (dabigatran),\(^5\) and ENGAGE AF-TIMI 48 (edoxaban).\(^6\) The PRISMA checklist is presented in table A-2 and a list of excluded publications is presented in table A-3.

The average age of patients was similar among trials, as were the proportion of women recruited and the percentage or patients with prior myocardial infarction. However, there were a number of differences across these four trials in trial design, patients enrolled, and populations analyzed:
The ARISTOTLE, ROCKET-AF, and ENGAGE AF-TIMI 48 trials were double-blind, double-dummy trials. In contrast, in the RE-LY trial, the assignments to dabigatran or warfarin were not concealed, and warfarin was administered as an open-label treatment.

The RE-LY trial publication based all efficacy and safety analyses on the intention-to-treat (ITT) principle. In the ARISTOTLE trial publication, efficacy analyses were conducted on the ITT population and safety analyses on the on-treatment population. Analyses of efficacy in the ROCKET-AF trial publication were conducted on the ITT population only for the primary efficacy endpoint, and on a per-protocol population to demonstrate non-inferiority, with superiority and safety analyses run on the on-treatment population. In the ENGAGE AF-TIMI 48 trial, efficacy analyses were conducted on the ITT/modified ITT (mITT) overall study period and on-treatment populations, and safety analyses were conducted on the safety population during the on-treatment and overall study periods.

Median follow-up ranged from 1.8 years in ARISTOTLE to 2.8 years in ENGAGE AF-TIMI 48.

Subjects were enrolled in the ARISTOTLE, ENGAGE AF-TIMI 48, and RE-LY trials if they had a CHADS\textsubscript{2} score of ≥ 1, whereas ROCKET-AF enrolled a higher-risk population (CHADS\textsubscript{2} score ≥ 2). At baseline, the mean CHADS\textsubscript{2} score for the ROCKET-AF trial was 3.4, compared with 2.1 for both RE-LY and ARISTOTLE.

A larger proportion of patients with previous stroke or transient ischemic attack, with heart failure, or with diabetes were enrolled in ROCKET-AF than in the other trials.
- The mean percentage of time in which the international normalized ratio was in the therapeutic range of 2.0-3.0 for warfarin was 64% in the RE-LY trial, 62% in the ARISTOTLE trial, 55% in the ROCKET-AF trial, and 65% in the ENGAGE AF-TIMI 48 trial.
Table A-1. Data Abstraction Form

| Worksheet                     | Fields                                                                 |
|-------------------------------|------------------------------------------------------------------------|
| Study characteristics         | ▪ Record number<br>▪ Reference<br>▪ Follow-up duration; study duration<br>▪ Study design<br>▪ Study phase<br>▪ Intention-to-treat analysis<br>▪ Inclusion criteria<br>▪ Exclusion criteria<br>▪ Concomitant medications at baseline |
| Baseline characteristics by arm | ▪ Record number<br>▪ Age<br>▪ Female (% patients)<br>▪ BP<br>▪ Type of AF<br>▪ Diabetes (% patients)<br>▪ Hypertension (% patients)<br>▪ CHADS<sub>2</sub> score<br>▪ Creatinine clearance<br>▪ VKA naïve (% patients)<br>▪ Definition of VKA naïve<br>▪ Comments |
| Treatments per arm            | ▪ Record number<br>▪ Treatment group<br>▪ Number randomized<br>▪ Dosing schedule<br>▪ Time in therapeutic range (% patients)<br>▪ Dyspepsia, n (%)<br>▪ Lost to follow-up, n (%)<br>▪ Discontinuations, n (%) |
| Worksheet | Fields |
|-----------|--------|
| Outcomes per arm<sup>a</sup> | ▪ Record number  
▪ Composite of stroke and systemic embolism  
▪ Systemic embolism  
▪ Ischemic stroke  
▪ Hemorrhagic stroke  
▪ All-cause death  
▪ Cardiovascular mortality  
▪ MI  
▪ Composite of major bleeding or clinically relevant nonmajor bleeding  
▪ Major bleeding<sup>b</sup>  
▪ Major gastrointestinal bleeding  
▪ Clinically relevant non-major bleeding  
▪ Fatal bleeding  
▪ Intracranial hemorrhage |

Abbreviations: AF, atrial fibrillation; BP, blood pressure; CHADS<sub>2</sub>, stroke risk factor scoring system in which 1 point is given for history of congestive heart failure, hypertension, age ≥ 75 years, and diabetes, and 2 points are given for history of stroke or transient ischemic attack; CI, confidence interval; ITT, intention to treat; MACE, major adverse cardiac event; MI, myocardial infarction; TIA, transient ischemic attack; VKA, vitamin K antagonist.

<sup>a</sup> For each treatment arm, definition, type of analysis (e.g., ITT, per-protocol population), total number of patients analyzed, number of patients with events, and event rate (%/patient-year) were extracted for each outcome. In addition, hazard ratios between treatment groups with CIs, standard errors, and <i>P</i> values were also extracted.

<sup>b</sup>The Subcommittee on Control of Anticoagulation, of the Scientific and Standardization Committee of the ISTH, endorses the following criteria for major bleeding in non-surgical patients: (i) fatal bleeding, and/or (ii) symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, or pericardial, or intramuscular with compartment syndrome, and/or (iii) bleeding causing a fall in hemoglobin level of 20 g L<sup>-1</sup> (1.24 mmol/L<sup>-1</sup>) or more, or leading to a transfusion of two or more units of whole blood or red cells.
Table A-2. PRISMA Checklist

| Section/topic          | # | Checklist item                                                                                                                                                                                                 | Reported on page # |
|------------------------|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| **TITLE**              |   |                                                                                                                                                                                                              |                    |
| Title                  | 1 | Identify the report as a systematic review, meta-analysis, or both.                                                                                                                                         | 1                  |
| **ABSTRACT**           |   |                                                                                                                                                                                                              |                    |
| Structured summary     | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1                  |
| **INTRODUCTION**       |   |                                                                                                                                                                                                              |                    |
| Rationale              | 3 | Describe the rationale for the review in the context of what is already known.                                                                                                                                | 2-3                |
| Objectives             | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).                                                       | 4-6                |
| **METHODS**            |   |                                                                                                                                                                                                              |                    |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.                                        | NA                 |
| Eligibility criteria   | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.                                 | 4                  |
| Information sources    | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.                                         | 4                  |
| Search                 | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.                                                                               | 4                  |
| Study selection        | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).                                                      | 4                  |
| Data collection process| 10| Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.                                      | 5                  |
| Data items             | 11| List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.                                                                            | 5-6                |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 5 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 6-7 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$), for each meta-analysis. | 6-7 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 6-7 |

**RESULTS**

| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 4 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 5 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 8-10 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 8-10 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 10 |

**DISCUSSION**

| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 11-13 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 12-13 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 14 |
FUNDING

| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. |

NA= not available;
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097. Available at www.prisma-statement.org. Accessed on 29 July 2015.

Table A-3. Excluded Studies and Reasons for Exclusion

| Reference | Ref ID | Reason |
|-----------|-------|--------|
| Level 1 Screening (n = 1,101) | | |
| Embolic complications in atrial fibrillation. Data of the Studio Italiano Fibrillation Atriale (SIFA)], G Chir 1995 Mar;16(3):137-9. | 464 | Study Design |
| [INR self monitoring: large study shows no prognostic value], MMW Fortschr Med 2008 Nov 20;150(47):14. | 191 | Intervention/Comparators |
| Aalbers J, Bryer A, Klug E. FDA committee unanimously recommends approval of dabigatran etexilate for stroke prevention in atrial fibrillation. Cardiovasc J Afr 2010 Nov;21(6):341. | 129 | Study Design |
| Aalbers J, Wagenaar P, Klug E. New anti-coagulant therapies set to revitalise clinical haemotology practice. Cardiovasc J Afr 2010 Nov;21(6):323-6, 337. | 130 | Study Design |
| Aalbers J, Wagenaar P, Klug E. New anti-coagulant therapies set to revitalise clinical haemotology practice: Annual meeting of the Southern African Society of Thrombosis and Haemostasis. Cardiovascular Journal of Africa 2010;21(6):323-6+337. | 734 | Study Design |
| Aalbers J. New anticoagulants offer consistent stroke-reduction benefit in atrial fibrillation. Cardiovascular Journal of Africa 2012;23(3):168. | 612 | Study Design |
| Aalbers J. Rivaroxaban equals warfarin treatment in atrial fibrillation patients at high risk of stroke. Cardiovasc J Afr 2010 Nov;21(6):342-3. | 128 | Intervention/Comparators |
| Abdelhafiz AH, Myint MP, Tayek JA, Wheeldon NM. Anemia, hypoalbuminemia, and renal impairment as predictors of bleeding complications in patients receiving anticoagulation therapy for nonvalvular atrial fibrillation: a secondary analysis. Clin Ther 2009 Jul;31(7):1534-9. | 175 | Study Design |
| Abdelhafiz AH, Wheeldon NM. Results of an open-label, prospective study of anticoagulant therapy for atrial fibrillation in an outpatient anticoagulation clinic. Clinical Therapeutics 2004;26(9):1470-8. | 946 | Intervention/Comparators |
| Abi nasr I, Mansencal N, Dubourg O. Management of atrial fibrillation in heart failure in the elderly. International Journal of Cardiology 2008;125(2):178-82. | 843 | Study Design |
| Abrol R, Page RL. Azimilide dihydrochloride: A new class III anti-arrhythmic agent. Expert Opinion on Investigational Drugs 2000;9(11):2705-15. | 1060 | Study Design |
| Reference | Ref ID | Reason |
|-----------|--------|--------|
| ACTIVE-W: warfarin beats clopidogrel/aspirin in atrial fibrillation. Cardiovasc J S Afr 2006 Mar;17(2):91. | 260 | Intervention/Comparators |
| Ad N, Henry L, Schlauch K, Holmes SD, Hunt S. The CHADS score role in managing anticoagulation after surgical ablation for atrial fibrillation. Annals of Thoracic Surgery 2010;90(4):1257-62. | 736 | Study Design |
| Adam SS, McDuffie JR, Ortel TL, Nagi A, Williams JW. 2012 Apr. | 41 | Study Population |
| Adams Jr HP. 10 Most Commonly Asked Questions about which Antiplatelet Agent to Prescribe. Neurologist 2003;9(6):318-22. | 971 | Study Design |
| Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. Lancet 1996 Sep 7;348(9028):633-8. | 448 | Intervention/Comparators |
| Agarwal S, Bennett D, Smith DJ. Predictors of warfarin use in atrial fibrillation patients in the inpatient setting. Am J Cardiovasc Drugs 2010;10(1):37-48. | 155 | Intervention/Comparators |
| Aghaibwe SO, Okeke C, Okonkwo O. Janssen pharmaceuticals' xarelto. Pharm.Times 77. 2011. | 648 | Study Design |
| Ageno W, Crowther M, Steidl L, Ultori C, Mera V, Dentali F, et al. Low dose oral vitamin K to reverse acenocoumarol-induced coagulopathy: A randomized controlled trial. Thrombosis and Haemostasis 2002;88(1):48-51. | 1013 | Study Population |
| Aguirre FV, McMahon RP, Mueller H, Kleiman NS, Kern MJ, Desvigne-Nickens P, et al. Impact of age on clinical outcome and postlytic management strategies in patients treated with intravenous thrombolytic therapy: Results from the TIMI II study. Circulation 1994;90(1):78-86. | 1148 | Study Design |
| Ahmad Y, Lip GYH, Apostolakis S. New oral anticoagulants for stroke prevention in atrial fibrillation: Impact of gender, heart failure, diabetes mellitus and paroxysmal atrial fibrillation. Expert Review of Cardiovascular Therapy 2012;10(12):1471-80. | 521 | Study Design |
| Ahrens I, Bode C. Oral anticoagulation with edoxaban. Focus on current phase III clinical development. Hamostaseologie 2012;32(3):212-5. | 34 | Study Design |
| Ahrens I, Lip GY, Peter K. What do the RE-LY, AVERROES and ROCKET-AF trials tell us for stroke prevention in atrial fibrillation? Thromb Haemost 2011 Apr;105(4):574-8. | 122 | Study Design |
| Aizawa Y, Kohsaka S, Suzuki S, Atarashi H, Kamakura S, Sakurai M, et al. Comparison of antiarrhythmics used in patients with paroxysmal atrial fibrillation: Subanalysis of J-RHYTHM study. Circulation Journal 2010;74(1):71-6. | 776 | Intervention/Comparators |
| Akdeniz B, Badak O, Baris N, Aslan O, Kirimli O, Goldeli O, et al. Left atrial appendage-flow velocity predicts cardioversion success in atrial fibrillation. Tohoku Journal of Experimental Medicine 2006;208(3):243-50. | 897 | Study Design |
| Akdeniz B, Turker S, Ozturk V, Badak O, Okan T, Aslan O, et al. Cardioversion under the guidance of transseosophageal echocardiography in persistent atrial fibrillation: Results with low molecular weight heparin. International Journal of Cardiology 2005;98(1):49-55. | 934 | Intervention/Comparators |
| Reference | Ref ID | Reason |
|-----------|-------|--------|
| Akins PT, Feldman HA, Zoble RG, Newman D, Spitzer SG, Diener HC, et al. Secondary stroke prevention with ximelagatran versus warfarin in patients with atrial fibrillation: pooled analysis of SPORTIF III and V clinical trials. Stroke 2007 Mar;38(3):874-80. | 241 | Intervention/Com parators |
| Al Suwaidi J, Zubaid M, Al-Mahmeed WA, Al-Rashdan I, Amin H, Bener A, et al. Impact of fasting in Ramadan in patients with cardiac disease. Saudi Medical Journal 2005;26(10):1579-83. | 916 | Study Population |
| Albage A, van der Linden J, Lindblom D, Kenneback G, Nygren AT, Svedenhag J, et al. The maze operation for treatment of atrial fibrillation. Scandinavian Cardiovascular Journal 2000;34(5):480-5. | 1058 | Intervention/Com parators |
| Albers GW, Atwood JE, Hirsh J, Sherman DG, Hughes RA, Connolly SJ. Stroke prevention in nonvalvular atrial fibrillation. Ann Intern Med 1991 Nov 1;115(9):727-36. | 492 | Study Design |
| Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001;119(1 SUPPL.):194S-206S. | 1051 | Study Design |
| Albers GW, Diener HC, Frison L, Grind M, Nevinson M, Partridge S, et al. Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. JAMA 2005 Feb 9;293(6):690-8. | 296 | Intervention/Com parators |
| Albers GW. Antithrombotic therapy for prevention and treatment of ischemic stroke. Journal of Thrombosis and Thrombolysis 2001;12(1):19-22. | 1024 | Study Design |
| Albers GW. Atrial fibrillation and stroke: Three new studies, three remaining questions. Archives of Internal Medicine 1994;154(13):1443-8. | 1146 | Study Design |
| Alex J, Guvendik L. Evaluation of ventral cardiac denervation as a prophylaxis against atrial fibrillation after coronary artery bypass grafting. Annals of Thoracic Surgery 2005;79(2):517-20. | 932 | Study Population |
| Alexander R, Ferretti AC, Sorensen JR. Stop the nonsense not the anticoagulants: a matter of life and death. N Y State Dent J 2002 Nov;68(9):24-6. | 349 | Study Design |
| Alexander W, Connolly S, Arnesen H. European Society of Cardiology: Apixaban or aspirin in decreasing stroke risk (The AVERROES Trial). P and T 2010;35(10):580-1. | 737 | Intervention/Com parators |
| Algra A, Koundstaal PJ, Van Gijn J. Secondary prevention after cerebral ischaemia: Monotherapy with acetylsalicylic acid still first choice? Nederlands Tijdschrift voor Geneeskunde 1998;142(6):277-80. | 1103 | Intervention/Com parators |
| Al-Khadra AS, Salem DN, Rand WM, Udelson JE, Smith JJ, Konstam MA. Warfarin anticoagulation and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction. J Am Coll Cardiol 1998 Mar 15;31(4):749-53. | 438 | Intervention/Com parators |
| Al-Khatib SM, Hafley G, Harrington RA, Mack MJ, Ferguson TB, Peterson ED, et al. Patterns of management of atrial fibrillation complicating coronary artery bypass grafting: Results from the PRoject of Ex-vivo Vein graft ENgineering via Transfection IV (PREVENT-IV) Trial. Am Heart J 2009 Nov;158(5):792-8. | 166 | Intervention/Com parators |
| Al-Khatib SM, Pieper KS, Lee KL, Mahaffey KW, Hochman JS, Pepine CJ, et al. Atrial fibrillation and mortality among patients with acute coronary syndromes without ST-segment elevation: Results from the PURSUIT trial. American Journal of Cardiology 2001;88(1):76-9. | 1044 | Study Population |
| Reference | Ref ID | Reason |
|-----------|--------|--------|
| Almroth H, Hoglund N, Boman K, Englund A, Jensen S, Kjellman B, et al. Atorvastatin and persistent atrial fibrillation following cardioversion: A randomized placebo-controlled multicentre study. European Heart Journal 2009;30(7):827-33. | 808 | Intervention/Comparators |
| Alonso-Coello P, Zhou Q, Guyatt G. Home-monitoring of oral anticoagulation vs. dabigatran: An indirect comparison. Thrombosis and Haemostasis 2012;108(4):647-53. | 564 | Intervention/Comparators |
| Alreja G, Chandrasekaran D, Trikalinos T, Rothberg M. Oral anticoagulants for secondary prophylaxis of stroke in coronary artery disease and cerebrovascular accident. J Am Coll Cardiol 2011;57(14):E1509. | 701 | Study Population |
| Amabile G, Matteoli S, Fattapposta F, Lavezzari M, Trappolini M, Heiman F, et al. [Italian Study on Atrial Fibrillation (SIFA): status report]. Cardiologia 1993 Dec;38(12 Suppl 1):327-32. | 475 | Intervention/Comparators |
| Amin A. New oral anticoagulants for stroke prevention in atrial fibrillation: An update for managed care and hospital decision-makers. Formulary 2012;47(8):299-305. | 522 | Study Design |
| Amin AN, Lin J, Thompson S, Wiederkehr D. Inpatient and outpatient occurrence of deep vein thrombosis and pulmonary embolism and thromboprophylaxis following selected at-risk surgeries. Ann Pharmacother 2011 Sep;45(9):1045-52. | 87 | Study Design |
| Andersen LV, Lip GY, Lindholt JS, Frost L. Upper limb arterial thromboembolism: A systematic review on incidence, risk factors, and prognosis including a meta-analysis of risk-modifying drugs. J Thromb Haemost 2013 Feb 25. | 2 | Study Population |
| Anderson DC, Buckingham T, Hart RG, Kelley RE, Litin SC, McBride R, et al. Design of a multicenter randomized trial for the stroke prevention in atrial fibrillation study. Stroke 1990;21(4):538-45. | 1165 | Study Design |
| Anderson DC. Progress report of the Stroke Prevention in Atrial Fibrillation Study. Stroke 1990 Nov;21(11 Suppl):III12-III17. | 498 | Study Design |
| Anderson J, O’Donnell M. Clinical trials of new anticoagulants. Vnitrni Lekarstvi 2006;52(SUPPL. 1):123-6. | 895 | Study Design |
| Antiplatelet agents for stroke patients. MeReC Bulletin 2003;14(2):5-8. | 975 | Study Design |
| Antonielli E, Pizziuti A, Gandolfo N, Sclavo M, Tanga M, Riva G, et al. Short-term anticoagulation before electrical cardioversion of chronic atrial fibrillation. Giornale Italiano di Cardiologia 1997;27(8):803-10. | 1108 | Intervention/Comparators |
| Apixaban in other situations? Prescrire Int 2012 Sep;21(130):203. | 25 | Study Design |
| Apixaban superior to warfarin in preventing stroke or systemic embolism. Australian Journal of Pharmacy 2012;93(1104):93. | 601 | Study Design |
| Apostolakis S, Lane DA, Guo Y, Buller H, Lip GY. Performance of the HEMORR(2)HAGES, ATRIA, and HAS-BLED bleeding risk-prediction scores in patients with atrial fibrillation undergoing anticoagulation: the AMADEUS (evaluating the use of SR34006 compared to warfarin or acenocoumarol in patients with atrial fibrillation) study. J Am Coll Cardiol 2012 Aug 28;60(9):861-7. | 28 | Intervention/Comparators |
| Apostolakis S, Marin F, Lip GYH. Antiplatelet therapy in stroke prevention. Adv.Cardiol. 47, 141-154, 2012. | 580 | Study Design |
| Reference                                                                 | Ref ID | Reason            |
|--------------------------------------------------------------------------|--------|-------------------|
| Appadu B, Morosan M. Drugs affecting coagulation. Anaesthesia and Intensive Care Medicine 2013;14(1):32-8. | 518    | Study Design      |
| Aramendi JI, Mestres CA, Campos V, Martínez-Leon J, Pontes C, Munoz G, et al. Triflusals versus oral anticoagulation for primary prevention of thromboembolism after bioprosthetic valve replacement (TRAC): Rationale and design for a prospective, randomized, co-operative trial. Interactive Cardiovascular and Thoracic Surgery 2003;2(2):170-4. | 992    | Study Design      |
| Aramendi JI, Mestres CA, Martínez-Leon J, Campos V, Munoz G, Navas C. Triflusals versus oral anticoagulation for primary prevention of thromboembolism after bioprosthetic valve replacement (trac): prospective, randomized, co-operative trial. Eur J Cardiothorac Surg 2005 May;27(5):854-60. | 294    | Study Design      |
| Archer SL, James KE, Kvernen LR, Cohen IS, Ezekowitz MD, Gornick CC. Role of transesophageal echocardiography in the detection of left atrial thrombus in patients with chronic nonrheumatic atrial fibrillation. Am Heart J 1995 Aug;130(2):287-95. | 460    | Intervention/Comparators |
| Arentz T, Weber R, Burkle G, Herrera C, Blum T, Stockinger J, et al. Small or large isolation areas around the pulmonary veins for the treatment of atrial fibrillation? Results from a prospective randomized study. Circulation 2007 Jun 19;115(24):3057-63. | 228    | Intervention/Comparators |
| Ariesen MJ, Algra A, Koudstaal PJ, Rothwell PM, Van Walraven C. Risk of Intracerebral Hemorrhage in Patients with Arterial Versus Cardiac Origin of Cerebral Ischemia on Aspirin or Placebo: Analysis of Individual Patient Data from 9 Trials. Stroke 2004;35(3):710-4. | 964    | Intervention/Comparators |
| Arnold M, Nedeltchev K, Mattle HP. [Anticoagulation and antiaggregation in neurological patients]. Ther Umsch 2003 Jan;60(1):33-5. | 343    | Study Design      |
| Arnold M, Nedeltchev K, Mattle HP. Antiplatelet agents and anticoagulation in the neurological patient. Therapeutische Umschau 2003;60(1):33-5. | 998    | Study Design      |
| Asher CR, Klein AL. Transesophageal echocardiography to guide cardioversion in patients with atrial fibrillation: ACUTE trial update. Cardiac Electrophysiology Review 2003;7:387-91. | 1188   | Intervention/Comparators |
| Asher CR, Klein AL. Transesophageal echocardiography to guide electrical cardioversion in atrial fibrillation. Cleveland Clinic Journal of Medicine 2002;69(9):713-8. | 1009   | Intervention/Comparators |
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**Level 2 Screening (n = 57)**

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