

Web References [cited as w1, w2, etc in text]

1. Peterson P, Boysen G, Gofriedsen J, Andersen ED, Anderson B: Placebo controlled, randomized trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation: the Copenhagen AFASAK Study. *Lancet* 1989;1:175-179.
2. Stroke Prevention in Atrial Fibrillation (SPAF) Investigators. Stroke Prevention in Atrial Fibrillation Study: final results. *Circulation* 1991; 84:527-539.
3. The Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF) Investigators. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1990; 323:1505-1511.
4. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C: Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *J Am Coll Cardiol* 1991; 18:349-355.
5. Ezekowitz MD, Bridgers SL, James KE, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation (SPINAF). *N Engl J Med* 1992; 327:1406-1412
6. European Atrial Fibrillation (EAFT) Study Group. Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. *Lancet* 1993; 342:1255-1262
7. Diener HC, Cunha L, Forbes C, et al. European Stroke Prevention Study (ESPS) 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci* 1996; 143:1-13.
8. Posada IS, Barriales V: Alternate – day dosing of aspirin in atrial fibrillation. LASAF Pilot Study Group. *Am Heart J* 1999; 138:137-143.
9. Benavente O, Hart R, Koudstaal P, Laupacis A, et al. Antiplatelet therapy for preventing stroke in patients with nonvalvular atrial fibrillation and no previous history of stroke or transient ischemic attacks. In: Warlow C, Van Gijn J, Sandercock P, eds. *Stroke Module of the Cochrane Database of Systematic Reviews*. Oxford: The Cochrane Collaboration; 1999. CD-ROM.
10. Lip GYH, Hart RG, Conway DS. Antithrombotic therapy for atrial fibrillation. *BMJ* 2002;325:1022-5.
11. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: Stroke Prevention in Atrial Fibrillation II Study. *Lancet* 1994; 343:687-691.
12. Gullov AL, Koefoed BG, Petersen P, et al. Fixed mididose warfarin and aspirin alone and in combination vs adjusted-dose warfarin for stroke prevention in atrial fibrillation: Second Copenhagen Atrial Fibrillation, Aspirin, and Anticoagulation Study. *Arch Intern Med* 1998; 158:1513-1521.
13. Hellemons BS, Langenberg M, Lodder J, Vermeer F, Schouten HJ, Lemmens T, van Ree JW, Knottnerus JA. Primary prevention of arterial thromboembolism in non-

- rheumatic atrial fibrillation in primary care: randomised controlled trial comparing two intensities of coumarin with aspirin. *BMJ*. 1999;319(7215):958-64.
14. van Walraven C, Hart RG, Singer DE, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. *JAMA* 2002;288:2441-8.
 15. Atrial Fibrillation Investigators. Adjusted-dose warfarin vs low-intensity, fixed-dose warfarin plus aspirin for high risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomized clinical trial *Lancet* 1996; 348:633-638
 16. Pengo V, Zasso A, Barbero F, et al. Effectiveness of fixed mididose warfarin in the prevention of thromboembolism and vascular death in nonrheumatic atrial fibrillation. *Am J Cardiol* 1998;82:433-7.
 17. Lechat P, Lardoux H, Mallet A, et al. FFAACS (Fluindione, Fibrillation Auriculaire, Aspirin et Contraste Spontane) Investigators. Anticoagulant (fluindione)-aspirin combination in patients with high-risk atrial fibrillation. A randomized trial (Fluindione, Fibrillation Auriculaire, Aspirin et Contraste Spontane; FFAACS). *Cerebrovasc Dis* 2001;12:245-52.
 18. Perez-Gomez F, Alegria E, Berjon J et al. NASPEAF Investigators. Comparative effects of antiplatelet, anticoagulant, or combined therapy in patients with valvular and nonvalvular atrial fibrillation: a randomized multicenter study. *J Am Coll Cardiol* 2004;44:1557-66.
 19. Falk RH. Reconsidering combined antiplatelet and anticoagulant therapy in atrial fibrillation. *J Am Coll Cardiol*. 2004;44(8):1567-9.
 20. Morocutti C, Amabile G, Fattapposta F, et al. Indobufen versus warfarin in the secondary prevention of major vascular events in nonrheumatic atrial fibrillation. SIFA (Studio Italiano Fibrillazione Atriale) Investigators. *Stroke* 1997;28:1015-21.
 21. Diener HC, Lowenthal A. Letter to the Editor: Reply to Dr G. Hart and Dr O. Benavente (University of Texas). *J Neurol Sci* 1997;153: 112.
 22. Atrial Fibrillation Investigators. Risk factors for stroke and efficiency of antithrombotic therapy in atrial fibrillation analysis of pooled data from five randomized controlled trials. *Arch Intern Med* 1994; 154:1449-1457.
 23. Stroke Prevention in Atrial Fibrillation investigators. Risk factors for thromboembolism during aspirin therapy in patients with atrial fibrillation: The Stroke Prevention in Atrial Fibrillation study. *J Stroke Cerebrovascular Dis* 1995;5:147-157.
 24. Lip GYH. Thromboprophylaxis for atrial fibrillation. *Lancet* 1999;353:4-6.
 25. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA* 2001;285:2864-70.
 26. Wang TJ, Massaro JM, Levy D, et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA* 2003;290:1049-56.

27. Gage BF, van Walraven C, Pearce L, Hart RG, Koudstaal PJ, Boode BS, Petersen P. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation*. 2004; 110(16):2287-92.
28. 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;328:437-8.
29. 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;128:242-7.
30. Jackson SL, Peterson GM, Vial JH, Jupe DM. Improving the outcomes of anticoagulation: an evaluation of home follow-up of warfarin initiation. *J Intern Med* 2004;256:137-44.
31. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71-86
32. DiMarco JP, regory Flaker G, Albert L, Waldo AL, et al. Factors affecting bleeding risk during anticoagulant therapy in patients with atrial fibrillation: Observations from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Study. *Am Heart J* 2005;149:650- 6.
33. Silber S, Albertsson P, Aviles FF, Camici PG, Colombo A, Hamm C, et al. Guidelines for percutaneous coronary interventions: the task force for percutaneous coronary interventions of the European society of cardiology. *Eur Heart J* 2005;26:804-47.
34. Evans A, Perez I, Yu G, Kalra L. Secondary stroke prevention in atrial fibrillation: lessons from clinical practice. *Stroke* 2000;31:2106-11.
35. Evans A, Perez I, Yu G, Kalra L. Should stroke subtype influence anticoagulation decisions to prevent recurrence in stroke patients with atrial fibrillation? *Stroke* 2001;32:2828-32.
36. Go AS. Efficacy of anticoagulation for stroke prevention and risk stratification in atrial fibrillation: translating trials into clinical practice. *Am J Manag Care* 2004;10(3 Suppl):S58-65.
37. Go AS, Hylek EM, Chang Y, Phillips KA, Henault LE, Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *JAMA* 2003;290:2685-92.
38. Hylek EM, Go AS, Chang Y, et al. Effect of intensity of oral anticoagulation on stroke severity and mortality. *N Engl J Med* 2003;349:1019-1026
39. Mant JW, Richards SH, Hobbs FD, et al. Midlands Research Consortium of General Practice. Protocol for Birmingham Atrial Fibrillation Treatment of the Aged study (BAFTA): a randomised controlled trial of warfarin versus aspirin for stroke prevention in the management of atrial fibrillation in an elderly primary care population. *BMC Cardiovasc Disord* 2003;3:9.

40. Ansell J, Hirsh J, Poller L, Bussey H, Jacobson A, Hylek E. The pharmacology and management of the vitamin K antagonists: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126(3 Suppl):204S-233S. Erratum in: *Chest*. 2005 Jan;127(1):415-6.
41. Levine MN, Raskob G, Beyth RJ, et al. Hemorrhagic complications of anticoagulant treatment: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126(3 Suppl):287S-310S.
42. Haustein KO. Pharmacokinetic and pharmacodynamic properties of oral anticoagulants, especially phenprocoumon. *Semin Thromb Hemost* 1999; 25:5-11.
43. Tabrizi AR, Zehnbauer BA, Borecki IB, et al. The frequency and effects of cytochrome P450 (CYP) 2C9 polymorphisms in patients receiving warfarin. *J Am Coll Surg* 2002; 194:267-73.
44. Tabrizi AR, Zehnbauer BA, Borecki IB, et al. Role of dietary vitamin K intake in chronic oral anticoagulation: prospective evidence from observational and randomized protocols. *Am J Med* 2004; 116:651-6.
45. McCormick D, Gurwitz JH, Goldberg RJ, et al. Prevalence and quality of warfarin use for patients with atrial fibrillation in the long-term care setting. *Arch Intern Med* 2001; 161:2458-63.
46. Fang MC, Stafford RS, Ruskin JN, Singer DE. National trends in antiarrhythmic and antithrombotic medication use in atrial fibrillation. *Arch Intern Med* 2004; 164:55-60.
47. Jones M, McEwan P, Morgan CL, Peters JR, Goodfellow J, Currie CJ. Evaluation of the pattern of treatment, level of anticoagulation control, and outcome of treatment with warfarin in patients with non-valvar atrial fibrillation: a record linkage study in a large British population. *Heart* 2005;91:472-7.
48. Nadar S, Begum N, Kaur B, Sandhu S, Lip GYH. Patients' understanding of anticoagulant therapy in a multiethnic population. *J R Soc Med* 2003, 96:175-9.
49. Bungard TJ, Ghali WA, Teo KK, McAlister FA, Tsuyuki RT. Why do patients with atrial fibrillation not receive warfarin? *Arch Intern Med* 2000; 160:41-6.
50. Lip GYH, Kamath S, Jafri M, Mohammed A, Bareford D. Ethnic differences in patient perceptions of atrial fibrillation and anticoagulation therapy: the West Birmingham Atrial Fibrillation Project. *Stroke* 2002; 33:238-42.

Web Table 1. Summary of the main randomised antithrombotic trials in atrial fibrillation

Trial	Number of patients	IINR range/aspirin dose	Annual event rate per 100	% Relative risk reduction (95% CI)	% Absolute risk reduction per year	P Value
OAC versus control						
			OAC	Control		
AFSAK I ^{w1}	671	2.8 -4.2	2.7	6.2	56	2.6
SPAF I ^{w2}	421	2.0-4.5	2.3	7.4	67	4.7
BAATAF ^{w3}	420	1.5-2.7	0.4	3.0	86	2.4
CAFA ^{w4}	378	2.0-3.0	3.4	4.6	26	1.2
SPINAF ^{w5}	571	1.4-2.8	0.9	4.3	79	3.3
EAFT ^{w6}	439	2.5-4.0	8.5	16.5	47	8.4
Aspirin versus control						
			Aspirin	Control		
AFSAK I ^{w1}	672	75mg	5.2	6.2	16	1.0
SPAF I ^{w2}	1120	325mg	3.6	6.3	42	2.7
EAFT ^{w6}	782	300mg	15.5	19.0	17	3.5
ESPS II ^{w7}	211	50mg	13.8	20.7	33	6.9
LASAF ^{w8}	195	125mg/day	2.2	2.6	15	0.4
	181	125mg/alter-nate days	0.7	2.2	68	1.5
UK-TIA ^{w9}	28	300mg			17	
	36	1200mg			14	
OAC versus aspirin						
			OAC	Aspirin		
AFSAK I ^{w1}	671	75mg	2.7	5.2	48	2.5
SPAF II ^{w11}		325mg				<0.05
≤75 years	715		1.3	1.9	33	0.6
>75 years	385		3.6	4.8	27	1.2
EAFT ^{w6}	455	300mg	NA	NA	40	0.008
AFSAK II ^{w12}	339	300mg	3.4	2.7	21	0.7
PATAF ^{w13}	272	150mg	2.5	3.1	19	0.6

CI, confidence interval; OAC, oral anticoagulant; RRR, relative risk reduction; ARR, absolute risk reduction