Adjusted dose Warfarin vs. placebo

Trial	Inclusion criteria	Exclusion criteria
AFASAK I- 1989	18 years ECG- verified chronic AF	Previous anticoagulation therapy for more than 6 months, cerebrovascular events within the past month, contraindications for aspirin, warfarin; pregnancy or breast feeding; heart surgery with valve replacement; rheumatic heart disease.
SPAF I- 1991	Adults ECG- verified AF. Previous history of stroke or TIA more than two years before entry were eligible	Transient, self limited AF, mitral stenosis, prosthetic heart valve, congestive heart failure, myocardial infarction within previous 3 months, chronic renal failure, thrombocytopenia, requirement for warfarin.
BAATAF 1990	Adults with chronic sustained or intermittent AF	Transient AF during an acute illness or if cardioversion was planned. ECG evidence or intracardiac thrombus, severe congestive heart failure or prosthetic heart valves. Stroke within previous 6 months, TIA
CAFA- 1991	Age >= 19 years, chronic AF for >=1 month or paroxysmal AF occurring at least three times in the previous 3 months, absence of mitral valve prothesis and absence of mitral valve stenosis	Requirement for anticoagulation, medical contraindication for anticoagulation, stroke or TIA within 1 year, requirement for antiplatelet drug therapy, hyperthyroidism, uncontrolled hypertension, myocardial infarction
SPINAF- 1992	Male veterans of any age with AF. Both patients who had no clinical evidence of a previous stroke and those who had had a clinically evident cerebral infarction at least one month before entry into the study were enrolled	Intermittent AF, definite indication for anticoagulation or antiplatelet agents, contraindication to anticoagulation
EAFT 1993	Pts. >25 years who had a TIA or minor ischaemic stroke in the previous 3 months and AF confirmed in ECG at the time and no evidence of rheumatic valvular disease. Pts with AF secondary to other disorders such as hyperthyroidism were excluded.	Contraindication to or absolute indication to aspirin, on NSAI, had other sources of cardiac embolism such as prosthetic valves, cardiac aneurysm, atrial myxoma or disorders of blood coagulation.

Antiplatelet vs. placebo/no treatment

Trial	Inclusion criteria	Exclusion criteria
AFASAK I- 1989	18 years ECG- verified chronic AF	Previous anticoagulation therapy for more than 6 months, cerebrovascular events within the past month, contraindications for aspirin, warfarin; pregnancy or breast feeding; heart surgery with valve replacement; rheumatic heart disease.
SPAF I- 1991	Adults ECG- verified AF. Previous history of stroke or TIA more than two years before entry were eligible	Transient, self limited AF, mitral stenosis, prosthetic heart valve, congestive heart failure, myocardial infarction within previous 3 months, chronic renal failure, thrombocytopenia, requirement for warfarin.
EAFT 1993	Pts. >25 years who had a TIA or minor ischaemic stroke in the previous 3 months and AF confirmed in ECG at the time and no evidence of rheumatic valvular disease. Pts with AF secondary to other disorders such as hyperthyroidism were excluded.	Contraindication to or absolute indication to aspirin, on NSAI, had other sources of cardiac embolism such as prosthetic valves, cardiac aneurysm, atrial myxoma or disorders of blood coagulation.
ESPS II	>18 years and had experienced a TIA or a completed ischemic stroke within the preceding 3 months	Recent history of peptic ulcer or other GI bleeding, intolerance to study medication, any condition requiring aspirin or anticoagulants or life-threatening condition.
LASAF 1999	Patients with primary AF	General contraindications for the use of aspirin, accepted indication for the use of oral anticoagulants, indication for antiplatelet treatment before entry into the study such as previous episodes of angina, myocardial infarction or TIA
JAST 2006	Patients with chronic or intermittent AF.	Prosthetic heart valve, rheumatic heart disease, mitral valve disease, uncontrolled hypertension, hyperthyroidism, severe heart failure, previous intracranial bleeding or GI hemorrhage within 6 months
SAFT 2003	>= 60 years old with ECG documentation of AF in the preceding 4 weeks	Prosthetic valve, valvular diseases, previous stroke or TIA and other requirements for or contraindications to aspirin or warfarin therapy. Heart failure, bradycardia, severe hypertension, chronic obstructing lung disease, primary liver disorder, bleeding disorder. Patients with ischaemic heart disease receiving aspirin.

Adjusted-dose warfarin vs. antiplatelet treatment

Trial	Inclusion criteria	Exclusion criteria
AFASAK I- 1989	18 years ECG- verified chronic AF	Previous anticoagulation therapy for more than 6 months, cerebrovascular events within the past month, contraindications for aspirin, warfarin; pregnancy or breast feeding; heart surgery with valve replacement; rheumatic heart disease.
SPAF II	Adults ECG- verified AF. Previous history of stroke or TIA more than two years before entry were eligible	Transient, self limited AF, mitral stenosis, prosthetic heart valve, congestive heart failure, myocardial infarction within previous 3 months, chronic renal failure, thrombocytopenia, requirement for or contraindications to aspirin or warfarin
EAFT 1993	Pts. >25 years who had a TIA or minor ischaemic stroke in the previous 3 months and AF confirmed in ECG at the time and no evidence of rheumatic valvular disease. Pts with AF secondary to other disorders such as hyperthyroidism were excluded.	Contraindication to or absolute indication to aspirin, on NSAI, had other sources of cardiac embolism such as prosthetic valves, cardiac aneurysm, atrial myxoma or disorders of blood coagulation.
AFASAK II	>18 years old with nonvalvular chronic AF	Lone AF in patients < 60 years old, thromboembolic event within the last 6 months, mitral stenosis, contraindications for aspirin or warfarin, warfarin therapy based on other medical conditions, requirement for permanent NSAIDs, TIA or stroke within 6 months, pregnancy and breastfeeding
PATAF 1999	Patients >=60 years old with ECG confirmed AF or intermittent AF	Treatable cause of AF, previous stroke, rheumatic valvular disease, myocardial infarction or cardiovascular surgery in past year, cardiomyopathy, chronic heart failure.
Vemmos et al 2006	>75 years of age with ECG confirmed chronic or intermittent AF within the prior 12 months	Previous stroke or systemic embolism, valvular disease, treatable cause of AF (hyperthyroidism), other source of cardiac emboli, contraindications to oral anticoagulants.
WASPO 2007	>80 and <90 years old ambulant and had permanent AF.	One or more falls or syncopal episode within the last 12 months; epileptiform seizures, alchololic liver disease, previous history of thromboembolism (stroke, TIA, systemic embolus), GI or genitourinary bleeding in the previous 6 months, previous intracranial haemorrhage.
SIFA 1997	>30 years old with chronic or paroxysmal AF who had had	Rheumatic AF or had undergone cardioversion, intracardiac thrombosis

	a TIA or ischaemic stroke (with no evidence of haemorrhage on CT), in the previous 2 weeks.	or tumour, congestive heart failure, prosthetic valves, AMI, contraindication to study drugs.
NASPEAF 2004	(this study includes pts with valvular and non-valvular AF) Patients with chronic or documented AF - high-risk: nonvalvular AF and prior embolism and patients with mitral stenosis with and without prior embolism - intermediate risk: all others	Patients at low risk according to SPAF III stratification or <60 years. Mechanical valve prosthesis, stroke in previous 6 months, creatinine >3 mg/dl, alcoholism, hypertension.
ACTIVE- W 2006	ECG evidence of AF and at least one of the following: >=75 years-old, on treatment for systemic hypertension, previous stroke, TIA, or non-CNS systemic embolus, left ventricular dysfunction. Pts 55-74 years-old with none of the above were required to have either diabetes mellitus requiring drug therapy or previous coronary heart disease.	Exclusion criteria: contraindicactions for clopidogrel or oral anticoagulant, peptic ulcer, previous intracerebral haemorrhage, thrombocytopenia or mitral stenosis.
SPAF III 1996	Adults with AF with no prosthetic heart valves, mitral stenosis or contraindications to aspirin or warfarin and who had one or more high-risk features: Impaired left ventricular function, systolic blood pressure > 160 mm Hg, previous stroke, TIA or systemic embolism, female and over 75 years	Pts. who had taken part in previous SPAF studies or similar clinical trials. Pts who had had a non-disabling stroke or TIA were eligible after 30 days of the insult.
BAFTA 2007	>= 75 years old, ECG confirmed AF	Rheumatic heart disease, major non-traumatic haemorrhage, intracranial haemorrhage, oesophageal varices, peptic ulcer, long-term use of NSAIDs, factors known to increase the risk of stroke
Hu et al 2006	Aged 40-80 years old; standard diagnosis for AF ; subjects with detailed ECG records and ultrasound cardiogram inspections confirming a lack of rheumatic valve disease.	Subjects with serious illness predicted time-to-live of < two years; subjects who do not agree to be selected or do not agree with follow ups; subjects with AF caused by reversible illness including MI, acute myocarditis, untreated hyperparathyroidism and electrophysiology, angiography, and pacemaker operations, as well as recent heart surgery, where after treatment the AF never re-occurred; subjects with persistent AF which has not reoccurred after medication or cardioversion; subjects with ultrasound cardiogram verified rheumatic valve disease; subjects with artificial valve transplant; subjects with lone

		fibrillation; subjects with systolic blood pressure or diastolic pressure ≥ 180/100mm Hg (1mm Hg = 0.133kPa); subjects with thrombus in the heart and infectious endocarditis; subjects within 1 month of an acute heart attack; subjects with non-heart related factors (previously had a transient ischemic attack or stroke; intracranial bleeding, or bleeding in the digestive, urinary, or reproductive tract within 6 months; allergic to warfarin or aspirin; serious liver or kidney disease, chronic kidney function decline, or serum creatine > 3.0mg/dl; aminotransferase three times or more higher than the referential value; other thrombosis diseases requiring warfarin to be taken; require long-term oral taking of non-steroid anti-inflammatory drugs; require antiplatelet agents, anticoagulant drugs, or thrombolytic drugs outside of the experiment; malignant tumour; confirmed or possible blood system disease (not including mild or intermediate anemia); thrombocytopenia, blood platelet < 100,000/ml
Lu et al 2006	Diagnosis of persistent AF with ECG or dynamic ECG (two ECGs in a period of half a year)	Subjects with ultrasound cardiogram confirmed heart valvular disease; subjects with acute cerebrovascular accidents, serious injuries, or major operations within the past half-year; critical illness of the liver, kidney, or blood

Ximelagatran vs. placebo

Trial	Inclusion criteria	Exclusion criteria
ESTEEM 2003	Symptoms of ischaemic chest pain within the past 14 days; raised biochemical marker of myocardial damage, new ischaemic ECG changes and at least one of the following risk factors: <=65 years old, diabetes mellitus, previous MI, known multivessel coronary disease, previous ischaemic stroke, peripheral arterial occlusive disease, symptomatic congestive heart failure, or left ventricular ejection fraction of less than 40%, presumed new left bundle branch block, ST-segment depression of 0.1 mV or greater associated	Percutaneous coronary intervention in the past 4 months or within 60 days of randomisation; conditions known to increase the risk of bleeding, need for treatment with other oral antiplatelet or anticoagulant drugs, recent stroke, renal dysfunction, known liver disease

	with the index vent, or a history of hypertension.	

Ximelagatran vs. adjusted dose warfarin

Trial	Inclusion criteria	Exclusion criteria
SPORTIF II	>= 18 years old with ECG verified AF, plus at least one of the defined risk factors for stroke.	Stroke and/or systemic embolism within the previous 2 years, conditions associated with increased risk of bleeding, presence of mechanical heart valves, myocardial infarction within previous 3 months
SPORTIF III	>=18 years old, ECG verified AF and one or more risk factor for stroke: hypertension, >=75 years old, previous stroke, left ventricular dysfunction	Mitral stenosis, stroke within previous 30 days or TIA within 3 days, conditions associated with increased risk of bleeding, planed cardioversion, planned major surgery
SPORTIF V	>=18 years old, ECG verified AF and one or more risk factor for stroke: hypertension, >=75 years old, previous stroke, left ventricular dysfunction	Mitral stenosis, stroke within previous 30 days or TIA within 3 days, conditions associated with increased risk of bleeding, planed cardioversion, planned major surgery

Dabigatran with or without aspirin vs. adjusted-dose warfarin

Trial	Inclusion criteria	Exclusion criteria
PETRO 2007	Patients with AF with high risk of thromboembolic events. Documented AF with coronary artery disease plus >=1 of the following: hypertension requiring medical treatment, diabetes mellitus, heart failure, previous stroke or TIA, or age >75 years. After entry of approximately half of the patients, the requirement for coronary artery disease was removed to facilitate recruitment	Mitral stenosis, prosthetic valves, planed cardioversion, recent (<=1 month) MI, recent stroke or TIA, major haemorrhage, renal impairment , abnormal liver function

Idraparinux vs. adjusted-dose warfarin

Trial	Inclusion criteria	Exclusion criteria
Amadeus 2008	ECG AF confirmed and indication for long-term anticoagulation based on the presence of at least one of the following risk factors: previous ischaemic stroke, TIA, systemic embolism, hypertension requiring treatment, >75 years old or age 65-75 with either diabetes or coronary artery disease.	Exclusion criteria: contraindication or requirement to anticoagulation.

Adjusted-dose anticoagulation plus aspirin or triflusal vs. adjusted-dose anticoagulation

Trial	Inclusion criteria	Exclusion criteria
FFAACS 2001	Patients with present permanent or paroxysmal nonvalvular AF with a high risk defined: - history of thromboembolic event or - >65 years old and at least: a history of hypertension, recent episode of congestive heart failure	Patients with mitral stenosis, uncontrolled hypo- or hyperthyroidism, chronic alcoholism, history of severe haemorrhages, injuries at risk of bleeding.
NASPEAF 2004	(this study includes pts with valvular and non-valvular AF) Patients with chronic or documented AF - high-risk: nonvalvular AF and prior embolism and patients with mitral stenosis with and without prior embolism - intermediate risk: all others	Patients at low risk according to SPAF III stratification or <60 years. Mechanical valve prosthesis, stroke in previous 6 months, creatinine >3 mg/dl, alcoholism, hypertension.

Clopidogrel plus aspirin vs. aspirin

Trial	Inclusion criteria	Exclusion criteria
ACTIVE-A 2009	ECG evidence of AF and at least one of the following: >=75 years-old, on treatment for systemic hypertension, previous stroke, TIA, or non-CNS systemic embolus, left ventricular dysfunction. Pts 55-74 years-old with none of the above were required to have either diabetes mellitus requiring drug therapy or previous coronary heart disease.	Requirement for vit K antagonist or clopidogrel or had risk factors for haemorrhage: peptic ulcer, intracerebral haemorrhage, thrombocytopenia, alcohol abuse.
CHARISMA	>=45 years of age with one of the following conditions: multiple atherothrombotic risk factors, documented coronary disease, cerebrovascular disease, or documented symptomatic peripheral arterial disease.	Patients on oral antithrombotic medications or NSAIDs on a long term basis. Patients who were scheduled to undergo a revascularisation were not allowed to enrol until the procedure had been completed

Adjusted-dose warfarin vs low-dose, fixed-dose warfarin

Trial	Inclusion criteria	Exclusion criteria
AFASAK II	>18 years old with nonvalvular chronic AF	Lone AF in patients < 60 years old, thromboembolic event within the last 6 months, mitral stenosis, contraindications for aspirin or warfarin, warfarin therapy based on other medical conditions, requirement for permanent NSAIDs, TIA or stroke within 6 months, pregnancy and breastfeeding
MWNAF 1998	>60 years old with chronic AF	Uncontrolled systolic hypertension, chronic renal failure, chronic liver failure, alcoholism, major bleeding in preceding 6 months, heart failure, planned cardioversion, previous cerebral ischaemia, recent myocardial infarction
Vemmos et al 2006	>75 years of age with ECG confirmed chronic or intermittent AF within the prior 12 months	Previous stroke or systemic embolism, valvular disease, treatable cause of AF (hyperthyroidism), other source of cardiac emboli, contraindications to oral anticoagulants.

Adjusted-dose warfarin vs low-intensity, adjusted warfarin

Trial	Inclusion criteria	Exclusion criteria
PATAF 1999	Patients >=60 years old with ECG confirmed AF or intermittent AF	Treatable cause of AF, previous stroke, rheumatic valvular disease, myocardial infarction or cardiovascular surgery in past year, cardiomyopathy, chronic heart failure.
JNAFESP 2000	<80 years-old with definite or possible cardioembolic stroke or TIA due to NVAF at 1 to 6 months before entry	Intracardiac thrombus, left ventricular aneurysm, congestive heart failure, MI, hyperthyroidism, intracerebral haemorrhage, pregnancy, cancer
Pengo et al, 2010	Patients with non-valvular AF documented by two ECGs at least 15 days apart over 75 years of age.	Uncontrolled blood pressure, chronic renal failure, chronic alcoholism and psychiatric disorders, previous cerebral ischemia (stroke or TIA), major bleeding in the preceding 6 months, congestive heart failure (NYHA class III-IV), a life expectancy of less than 12 months, programmed pharmacological or electrical cardioversion, recent acute MI (less than 1 month), history of valvular heart disease or dilated cardiomyopathy, antiplatelet therapy, and other indications of oral anticoagulation.

Aspirin vs. low- or fixed-dose anticoagulation

Trial	Inclusion criteria	Exclusion criteria
AFASAK II	>18 years old with nonvalvular chronic AF	Lone AF in patients < 60 years old, thromboembolic event within the last 6 months, mitral stenosis, contraindications for aspirin or warfarin, warfarin therapy based on other medical conditions, requirement for permanent NSAIDs, TIA or stroke within 6 months, pregnancy and breastfeeding
PATAF 1999	Patients >=60 years old with ECG confirmed AF or intermittent AF	Treatable cause of AF, previous stroke, rheumatic valvular disease, myocardial infarction or cardiovascular surgery in past year, cardiomyopathy, chronic heart failure.
Vemmos et al 2006	>75 years of age with ECG confirmed chronic or intermittent AF within the prior 12 months	Previous stroke or systemic embolism, valvular disease, treatable cause of AF (hyperthyroidism), other source of cardiac emboli, contraindications to oral anticoagulants.

Aspirin or triflusal plus low-, or fixed-dose anticoagulation vs. aspirin or triflusal

Trial	Inclusion criteria	Exclusion criteria
AFASAK II	>18 years old with nonvalvular chronic AF	Lone AF in patients < 60 years old, thromboembolic event within the last 6 months, mitral stenosis, contraindications for aspirin or warfarin, warfarin therapy based on other medical conditions, requirement for permanent NSAIDs, TIA or stroke within 6 months, pregnancy and breastfeeding
NASPEAF 2004	(this study includes pts with valvular and non-valvular AF) Patients with chronic or documented AF	Patients at low risk according to SPAF III stratification or <60 years. Mechanical valve prosthesis, stroke in previous 6 months, creatinine >3

	- high-risk: nonvalvular AF and prior embolism and patients with mitral stenosis with and without prior embolism - intermediate risk: all others	mg/dl, alcoholism, hypertension.

Dabigatran with or without aspirin vs. adjusted-dose warfarin

Trial	Inclusion criteria	Exclusion criteria
RE-LY	Patients with AF documented on ECG performed at screening or within 6 months beforehand and at least one of the following characteristics: previous stroke or TIA, a LVEF of < 40%, NYHA class II or higher heart failure symptoms within 6 months before screening, and an age of at least 75 years or an age of 65 to 74 years plus diabetes mellitus, hypertension, or coronary artery disease.	Presence of severe heart-valve disorder, stroke within 14 days or severe stroke within 6 months before screening, a condition that increased the risk of haemorrhage, a creatinine clearance of less than 30 ml per minute, active liver disease, and pregnancy.

Apixaban vs. aspirin

Trial	Inclusion criteria	Exclusion criteria
AVERROES	Patients ≥50 years and had AF documented in the 6 months before enrolment or by 12-lead electrocardiography on the day of screening. Patients also had to have at least one of the following risk factors for stroke: prior stroke or TIA, an age of 75 years or older, arterial hypertension (receiving treatment), diabetes mellitus (receiving treatment), heart failure (NYHA class 2 or higher at the time of enrolment), a LVEF of 35% or less, or documented peripheral-artery disease. Patients could not be receiving vit. K antagonist therapy, either because it had already been demonstrated to be unsuitable for them or because it was expected to be unsuitable.	Presence of conditions other than AF for which the patient required long-term anticoagulation, valvular disease requiring surgery, a serious bleeding event in the previous 6 months or high risk of bleeding, current alcohol or drug abuse or psychosocial issues, life expectancy of less than 1 year, severe renal insufficiency, an alanine aminotransferase or aspartate aminotransferase level greater than 2 times the upper limit of the normal range or a total bilirubin more than 1.5 times the upper limit of the normal range, and allergy to aspirin.