Drug Efficacy (NNT) table

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Hypertension								
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and age > 80 years	Total mortality	2 years	333	666	High risk is defined as patients with a previous history of stroke Cardiovascular mortality and morbidity includes fatal and non-fatal MI, sudden cardiac death, aneurysms, congestive heart failure, fatal and non-fatal stroke and transient ischaemic attacks Total mortality is death from all causes NB the evidence base to support the NNT for impact on mortality in the over 80 years is very limited	34
			Cardiovascular mortality and morbidity	2 years	35	70		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and high risk* and age > 80 years	Total mortality	2 years	333	666		
			Cardiovascular mortality and morbidity	2 years	16	32		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and age > 60 years	Total mortality	4.5 years	83	374		
			Cardiovascular mortality and morbidity	4.5 years	23	104		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and high risk* and age > 60 years	Total mortality	4.5 years	33	149		
			Cardiovascular mortality and morbidity	4.5 years	9	41		

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Heart Failure								
Spironolactone 25 mg daily	Placebo	Patients with heart failure Patients had NYHA class IV heart failure in the 6 months prior to enrolment, but were NYHA class III or IV at the time of enrolment	Prevent one death (all causes)	24 months (mean duration of follow-up)	9	18	Mean age of patients was 65 years. Spironolactone also reduced the frequency of hospitalisation for heart failure and produced a significant improvement in the symptoms of heart failure. Patients in the trial were on an ACE inhibitor (if tolerated) and a diuretic. 10% of patients were also on a beta-blocker.	35
Beta-blocker (bisoprolol titrated to target dose of 10 mg/day)	Placebo	Patients with moderate to severe heart failure NYHA class III or IV and LVEF </=0.35	Prevent one death (all causes)	1.3 years (mean duration of follow-up)	18	24	Mean age of patients was 61 years, 83% of whom were NYHA class III. Current treatment had to include a diuretic and an ACE inhibitor although other vasodilators were allowed if patients were intolerant of ACE inhibitors. 96% of patients were on ACE inhibitors.	36
Beta-blocker (carvedilol titrated to target dose of 25 mg twice daily)	Placebo	Patients with severe heart failure NYHA class IV and LVEF < 0.25	Prevent one death (any cause)	10.4 months (mean duration of follow-up)	18	16	Mean age of patients was 63 years. Conventional therapy included diuretics and an ACEI or ARB. 97% of patients were on ACE inhibitor or ARB.	37

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Beta-blocker (Metoprolol modified-release titrated to a target dose of 200 mg/day)	Placebo	Patients with mild to severe heart failure NYHA class II to IV and LVEF </=0.40	Prevent one death (all causes)	12 months (mean duration of follow-up)	28	28	Mean age of patients was 64 years. Optimum standard therapy was defined as any combination of ACE inhibitors, Angiotensin receptor blockers and diuretics. 97% of patients were on an ACE inhibitor or Angiotensin receptor blocker.	38
Beta-blocker (nebivolol titrated to a target dose of 10 mg/day)	Placebo	Patients >70 years old with mild-severe heart failure NYHA class I to IV irrespective of LVEF	Prevent one death (all causes)	21 months (mean duration of follow-up)	44	78	Median age of patients was 75 years. 64% of patients had a LVEF of </=0.35. >95% of enrolled patients were NYHA class II or III. 87% of patients were on an ACE inhibitor or Angiotensin receptor blocker.	39
ACE inhibitor (ramipril 10 mg/day)	Placebo	Patients at high-risk of cardiovascular disease without LVSD or heart failure High-risk of cardiovascular disease defined as: history of coronary heart disease, stroke, peripheral vascular disease or diabetes plus one other cardiovascular risk factor (see comments)	Prevent one death (any cause)	60 months	54	270	Mean age of enrolled patients was 66 years. >50% of patients had a history of MI. Cardiovascular risk factors: hypertension, elevated total cholesterol, low HDL, smoker, microalbuminuria. Ramipril reduced the risk of myocardial infarction, stroke, coronary revascularisation and heart failure. There are no data to support ARBs for this indication.	40

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Angiotensin II receptor antagonist (telmisartan 80 mg/day)	Placebo	Patients intolerant of ACE Inhibitors with established cardiovascular disease: coronary artery, peripheral vascular or cerebrovascular disease, or diabetes with end organ damage Patients with heart failure were excluded	Prevent one of a composite of cardiovascular death, MI or stroke	56 months (median duration of follow-up)	55	258	Mean age of patients was approximately 67 years. Death rate (of any cause) was higher in treatment group than placebo group. When hospitalisations for cardiac failure were added to the composite endpoint as a primary outcome, the results were non-significant. Study concluded that telmisartan did not significantly reduce cardiovascular death.	41
ACE inhibitor (enalapril 2.5 to– 40 mg/day (up-titrated as tolerated))	Placebo	Patients with severe heart failure NYHA class IV Co-morbidities included coronary heart disease, previous MI , hypertension and diabetes	Prevent one death (any cause)	188 days (mean follow-up)	7	3	Mean age of patients was 70 years. Symptomatic improvement was observed i.e. a significant improvement in NYHA classification. NB Patient numbers in the study were low (n=253).	42
ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with heart failure NYHA class I – IV and LVEF ≤0.35	Prevent one death (any cause)	41.4 months (mean follow-up)	22	76	Mean age of patients was 61 years, approximately 80% were male. Less than 2% were NYHA Class IV. Treatment also reduced hospital admissions for heart failure. Mortality benefit appears to be most marked in the first 24 months.	43

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ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with heart failure and chronic kidney disease NYHA class I - IV and LVEF ≤0.35 and eGFR <60 mL /min /1.73m2	Prevent one death (any cause)	41.4 months (mean follow-up)	29	101	Mean age of patients was 64 years. Approximately 75% were male.	44
ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with asymptomatic heart failure NYHA class I and LVEF ≤0.35	Prevent one death (any cause)	34 months (mean follow-up)	88	251	Mean age of enrolled patients was 60 years. Treatment reduced the incidence of congestive heart failure and related hospital admissions.	45
Angiotensin receptor blocker (candesartan 4 to 32 mg/day)	Placebo	Patients with intolerance to ACE inhibitors with symptomatic heart failure NYHA Class II-IV and ejection fraction ≤0.4	Prevent one death (cardiovascular cause) or hospital admission for chronic heart failure	33.7 months	14	40	Mean age of enrolled patients was approximately 66 years. Patients were already taking other drugs as part of therapy for heart failure. Approximately 70% had heart failure of ischaemic cause.	46
			Prevent one death		34	94		
ACE inhibitor and indapamide (perindopril 4 mg/day and idapamide 2.5 mg/day)	Placebo	Patients who had a history of stroke or TIA in the last 5 years	Prevent one stroke (any cause)	3.9 years (mean duration of follow-up)	17	68	Mean age of patients was 64 years. 70% of patients in the trial had ischaemic stroke. There were similar reductions in the risk of stroke in hypertensive v. non-hypertensive patients.	47

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Cerebrovascular/ Cardiovascular Disease								
Warfarin (target INR 2 - 3)	Aspirin 75 mg daily	Age > 75 years with AF	1st occurrence of fatal or non-fatal disabling stroke (ischaemic or haemorrhagic), other intracranial haemorrhage or clinically significant arterial embolism	2.7 years (mean duration of follow-up)	20	54	Mean age of patients prescribed warfarin was 81.5 years. 73% of patients had a CHADS2 score of 1-2. 67% of patients on warfarin remained on this treatment for the complete duration of the trial.	48
Direct Acting Oral Anticoagulants (DOACs) There are no studies comparing DOACs against placebo. The NNT and NNH data in the table are based on comparative studies against warfarin, not against placebo. Great care is required in interpreting this data. It is of limited use to guide a decision on whether or not to continue with a DOAC. In addition it should be noted that these studies were equivalence/non-inferiority studies against warfarin, so the validity of extrapolating the results could be questioned. However, these data are included as a useful representation of the potential relative risks and benefits between warfarin and the individual agents.								
Apixaban 5 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score > 3 (30%))	Stroke or systemic embolism	1.8 years	167	301	Median age 70yrs (63-76). Treating 167 patients with apixaban instead of warfarin for 1.8 years might prevent one stroke or systemic embolism **Note: warfarin group were within therapeutic range only 66% of the time.**	49
Apixaban 5 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score > 3 (30%))	Major bleeding	1.8 years			NNH of 67 with respect to major bleeding, so treating 67 patients with apixaban instead of warfarin for 1.8 years might prevent one major bleeding episode.	

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Dabigatran 110 mg or 150 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score 3-6 (33%)) Approx age 71 years	Stroke or systemic embolism	2 years	**333** (for 110 mg twice daily dose) **91** (for 150 mg twice daily dose)	**666** (for 110 mg twice daily dose) **182** (for 150 mg twice daily dose)	Approximate average age 71 yrs. This means that treating 333 (110mg) or 91 (150mg) patients with dabigatran instead of warfarin for 2 years might prevent one stroke or systemic embolism (depending on the dose used). **Note: warfarin group were within therapeutic range only 64% of the time.**	50
Dabigatran 110 mg or 150 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score 3-6 (33%))	Major bleeding	2 years			NNH, with respect to major bleeding, treating 83 (110mg) or 250 (150mg) patients with dabigatran instead of warfarin for 2 years might prevent one major bleeding episode (depending on the dose used).	
Edoxaban 30 mg or 60 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.8 (CHADS2 score 4-6 (23%))	Stroke or systemic embolism	2.8 years	**167** (for 60 mg daily dose)	**468** (for 60 mg daily dose)	Median age 72 years (range 64-78) This means that treating 167 patients with edoxaban instead of warfarin for 2.8 years might prevent one stroke or systemic embolism. **Note, however, that the warfarin group were within**	51

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Edoxaban 30 mg or 60 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.8 (CHADS2 score 4-6 (23%))	Major bleeding	2.8 years			**therapeutic range only 68% of the time.** NNH, with respect to major bleeding, treating 67 patients with edoxaban instead of warfarin for 2.8 years might prevent one major bleeding episode.	
Rivaroxaban 20 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 3.5 (CHADS2 score > 3 (10%)) Median age 73 years (range 65-78)	Stroke or systemic embolism	1.9 years	**200**	**380**	Median age 73 years (range 65-78) This means that treating 200 patients with rivaroxaban instead of warfarin for 1.9 years might prevent one stroke or systemic embolism. **Note, however, that the warfarin group were within therapeutic range only 55% of the time.**	52
Rivaroxaban 20 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 3.5 (CHADS2 score > 3 (10%))	Major or clinically relevant non major bleeding	1.9 years			NNH, with respect to major bleeding, treating 260 (in favour of warfarin) patients with rivaroxaban instead of warfarin for 1.9 years might cause one major bleeding episode.	

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Aspirin	Placebo or no treatment	Primary prevention of CVD Individuals without history of occlusive disease	Serious vascular event (MI, stroke or vascular death).	Mean 5.8 years	246	1428	Age range in trials was 19-94 years Patients had hypertension or coronary risk factors without overt disease.	53
Aspirin or other antiplatelet*	Placebo or no treatment	Secondary prevention of CVD in patients with history of stroke or TIA	Serious vascular event (non-fatal MI, non-fatal stroke or vascular death).	29 -31 months	28-40	68 – 94	*Antiplatelets included aspirin (most widely studied), clopidogrel, dipyridamole, and other antiplatelets not commonly used in UK practice.	54, 55
Antiplatelet*	Placebo or no treatment	Secondary prevention in patients at high risk of cardiovascular events (previous MI, acute MI, previous stroke/TIA, and other high risk (excluding acute stroke)).	Serious vascular event (non-fatal MI, non-fatal stroke or vascular death).	26 months	15	32	*Antiplatelets include aspirin (most widely studied), clopidogrel, dipyridamole, and other antiplatelets not commonly used in UK practice.	54
Aspirin & dipyridamole	Placebo	Secondary prevention of CVD in patients with arterial vascular disease (coronary artery disease, MI, angina, retinopathy, nephropathy, PAD, stroke, TIA, amaurosis fugax)	Vascular event (non-fatal MI, non-fatal stroke or vascular death).	30 months	25	163	Mean age of patients 54 years.	56

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Aspirin & dipyridamole	Aspirin	Secondary prevention of CVD in patients with arterial vascular disease (coronary artery disease, MI, angina, retinopathy, nephropathy, PAD, stroke, TIA, amaurosis fugax)	Vascular event (non-fatal MI, non-fatal stroke or vascular death).	29 months	50	121	Mean age of patients 55 years	57
Clopidogrel or ticlopidine	Aspirin	Secondary prevention of CVD in patients with history of ischaemic stroke or TIA.	Stroke (all types)	22 months	100	184	Mean age of patients was 63 years Ticlopidine is not available in the UK but has similar mode of action to clopidogrel	58
			Stroke, MI or vascular death	28 months	100	223		
Statin (Simvastatin 40 mg daily, atorvastatin 80 mg daily, pravastatin 40 mg daily)	Placebo	Secondary prevention of CVD in patients with history of ischaemic or haemorrhagic stroke or TIA.	Ischaemic or haemorrhagic stroke	48 months	100	400-420		59
			Serious vascular events (non-fatal stroke, non-fatal myocardial infarction, vascular death) and all-cause mortality including sudden deaths	41- 44 months	20	68-74		

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Diabetes								
Intensive sulphonylurea with insulin to achieve fasting plasma glucose less than 6.0mmol/L	Conventional treatment with diet to aim for fasting blood glucose less than 15mmol/L (Metformin and/or sulphonyl-urea could be added, or patients changed to insulin if target not achieved)	Newly diagnosed type 2 diabetes patients between 25-65 years	Any diabetes end point	10 years (median duration of follow-up)	20	200	Mean age of patients was 54 years (range 25-65). Any diabetes-related endpoint: sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, digital amputation, vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye, or cataract extraction. Diabetes related death was death due to: myocardial infarction, stroke, peripheral vascular disease, renal disease, hyperglycaemia or hypoglycaemia, and sudden death. Reduction in micro-vascular events were mostly retinal. Median HbA_{1c} over 10 years 7.0% in intensive group versus 7.9% in conventional group. Intensive group had more hypo-glycaemic episodes per year and higher weight gain than conventional group.	60
			Diabetes related death		91	910		
			Micro-vascular complications		36	360		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Metformin to achieve fasting blood glucose <6.0mmol/l (maximum dose 2550mg) Glibenclamide added if target not achieved and changed to insulin if required	Diet alone to achieve fasting blood glucose <15mmol/l. sulphonyl-urea or metformin or insulin could be added	Newly diagnosed type 2 diabetes patients - between 25-65 years Overweight defined as >120% ideal body weight	Any diabetes end point	10.7 years (median duration of follow-up)	7	80	Mean age of patients was 53 years; mean weight 87kg ; BMI 31. Any diabetes-related endpoint: As above. Median HbA_{1c} during 10 years was 7.4% in metformin group and 8.0% in conventional group. Hypoglycaemic episodes were higher in metformin group but lower than the sulfonylureas group. Hypoglycaemia rates increased over time in insulin group as higher doses were required.	61
			Diabetes related death		19	203		
			Microvascular disease		45	481		
Intensive control of glucose by including Gliclazide mr to existing medication to achieve a HbA_{1c} of 6.5% or less.	Hypo-glycaemia agents chosen by the treating physician	Patients with type 2 diabetes mellitus at least 55 years old with a history of major macro-vascular or micro-vascular disease or at least one other risk factor for vascular disease	Major microvascular or macrovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke)	5 years (median)	53	263	Mean HbA_{1c} in control group was 7.3% and intensive (gliclazide mr) arm was 6.5% after 5 years follow up. Microvascular benefits were mostly due to reduction in nephropathy. No significant effect on major macrovascular events alone. Severe hypoglycaemia occurred in 2.7% of patients on intensive therapy compared with 1.5% of patients in the standard therapy group (NNH=80).	62
			Major micro-vascular events (new or worsening nephropathy or retinopathy).		67	333		

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Osteoporosis										
Alendronate 10 mg tablets	Placebo	Post-menopausal women a) For primary prevention average T-score was within 2 standard deviations of the mean for bone density b) For secondary prevention in women who had experienced previous vertebral compression fractures	Rate of vertebral, non-vertebral or hip fractures (as below) over a 5 year period	60 months (5 years)	As per age range (left column) below		As per age range (left column) below		Age range 42-85 but >62 for secondary prevention These NNTs apply to the first 5 years of treatment only.	63
			Vertebral secondary prevention		65-74	16	65-69	80		
					70-74	13	70-74	65		
					75-79	9	75-79	45		
					80-84	12	80-84	60		
					85-89	11	85-89	55		
					90+	8	90+	40		
			Non-vertebral secondary prevention		65-69	52	65-69	260		
					70-74	39	70-74	195		
					75-79	36	75-79	180		
					80-84	27	80-84	135		
					85-89	24	85-89	120		
					90+	12	90+	60		
			Hip secondary prevention		65-69	21	65-69	105		
					70-74	86	70-74	430		
					75-79	36	75-79	180		
					80-84	21	80-84	105		
					85-89	9	85-89	45		
					90+	8	90+	40		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)		Annualised NNT		Comments	Ref
Alendronate	Placebo	Postmenopausal women a) For primary prevention average T-score was within 2 standard deviations of the mean for bone density b) For secondary prevention women who had experienced previous vertebral compression fractures	Rate of vertebral, non-vertebral or hip fractures (as below) over a 5 year period Vertebral primary prevention	60 months (5 years)					Age range 42-85 but >62 for secondary prevention. These NNTs apply to the first 5 years of treatment only. All patients received calcium and vitamin D.	63
					65-69	148	65-69	740		
					70-74	123	70-74	615		
					75-79	67	75-79	335		
					80-84	97	80-84	485		
					85-89	89	85-89	445		
					90+	47	90+	235		
			Non-vertebral primary prevention		65-69	104	65-69	520		
					70-74	67	70-74	335		
					75-79	59	75-79	295		
					80-84	42	80-84	210		
					85-89	32	85-89	160		
					90+	12	90+	60		
			Hip primary prevention		65-69	23	65-69	118		
					70-74	118	70-74	590		
					75-79	50	75-79	250		
					80-84	27	80-84	135		
					85-89	11	85-89	55		
					90+	9	90+	45		