CLINICAL QUESTIONS – STABLE ANGINA

Questions	Population (and subgroups)	Intervention	Comparison	Outcomes
Q1) What is the clinical /cost effectiveness of nicorandil for the management of angina? Preferred: Double blind RCTs Minimum number of participants n=50 >60% patients with stable angina 3 month follow up Adverse event data to be sourced from RCTs only	Adults with a diagnosis of stable angina including people with diabetes, South Asians, women, minimal coronary heart disease Patients who have recurrence of anginal symptoms following revascularisation.	 Potassium channel activator: Nicorandil 	In patients taking or not taking background therapies (same baseline combinations in both arms), Nicorandil vs. placebo Nicorandil vs. other antianginal monotherapy: • Beta blockers • CCB • LA nitrates • ivabradine • ranolazine • trimetazidine	Note: some shorter term outcomes such as ECG changes included in newer drugs Mortality @ longest available evaluation time point (preferred 5yr, 10 yr) Preferred outcomes : All cause mortality Cardiac mortality Other outcomes: Cardiovascular mortality Angina frequency @ longest available evaluation time point (preferred 1yr, 5yr, 10yr) Preferred outcomes : Angina incidence reported in diaries GTN usage Angina severity @ longest available evaluation time point (preferred 1yr, 5yr, 10yr, not below 3m)

Questions	Population (and	Intervention	Comparison	Outcomes
				CCS score
				Exercise tolerance (based on repeat of baseline ETT at a min of 3m follow up) Preferred outcomes : Change in total exercise time
				Major cardiac events @ longest available evaluation timepoint (preferred 1yr, 5yr, 10yr)
				Preferred outcome: Nonfatal MI
				Hospitalisation @ 6m -1yr
				Revascularisation @ 1yr, 5yr, 10yr if available
				Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation timepoint (preferred 1y, 5y, 10y)
				Adverse events

Questions	Population (and subgroups)	Intervention	Comparison	Outcomes

Questions	Population (and	Intervention	Comparison	Outcomes
	subgroups)			
				Note: these outcomes are
Q2) What is the	Adults with a diagnosis			primarily short-term outcomes
clinical /cost	of stable angina	Short acting nitrate by buccal,	 Nitrate spray 	Immediate improvement in exercise
effectiveness of		lingual or sublingual	vs. nitrate tablet	tolerance – within 30 mins of
short acting	including people with	administration	 Nifedipine vs 	intervention
drugs for the	diabetes, South	Glyceryl trinitrate – tablet,	placebo	

management of anginal symptoms? Preferred : Double blind RCTs Minimum n=50 >60% stable angina Adverse event data to be sourced from RCTs only	Asians, women, refractory angina (prophylaxis), minimal coronary heart disease Patients who have recurrence of anginal symptoms following revascularisation.	spray •Nifedipine capsule by sublingual/buccal administration	 Nifedipine vs nitrate spray Nifedipine vs nitrate tablet 	Preferred outcome : Change in total exercise time Other outcomes : Change in time to ST depression Change in time to onset of symptoms Change in time to stopping exercise Change in workload Frequency of angina (and prophylaxic use) Preferred outcomes: Time to relief of pain Incidence of angina post-
				Incidence of angina post- intervention Others Pain severity Duration of pain important adverse events (headache and syncope)

		Ivabradine	Placebo	Note: some shorter term
Q 3) What is the	Adults with a diagnosis		CCB	outcomes such as ECG changes

clinical /cost	of stable angina		B blockers	included in newer drugs
newer drugs for the management of angina?	including people with diabetes, South Asians, women, minimal coronary beart		Combinations	Mortality @ longest available evaluation time point (preferred 5yr, 10 yr) Preferred outcomes :
Preferred: Double blind	disease	Ranolazine	Placebo CCB	All cause mortality Cardiac mortality
RCTs	Patients who have		B blockers	
Minimum number	recurrence of anginal		Nitrates	Other outcomes:
of participants n=50	symptoms following revascularisation.		Combinations	Cardiovascular mortality
>60% patients with stable angina 3 month follow up Adverse event data to be sourced from RCTs only				Angina frequency @ longest available evaluation time point (preferred 1yr, 5yr, 10yr) Preferred outcomes : Angina incidence reported in diaries GTN usage
				Exercise tolerance Preferred outcomes : Change in total exercise time
				Major cardiac events @ longest available evaluation timepoint (preferred 1yr, 5yr, 10yr)
				Preferred outcome: Nonfatal MI

		Hospitalisation @ 6m -1yr
		Revascularisation @ 1yr, 5yr, 10yr if available
		Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation timepoint (preferred 1y, 5y, 10y)
		Adverse events

Q4) What is the	Adults with a diagnosis	What is best drug to use first?		Mortality all cause @ longest
comparative	of stable angina	B blocker	ССВ	available evaluation time point
clinical /cost				(preferred 5yr, 10 yr)
effectiveness of	including people with	Are 2 drugs better than one?	?	Preferred outcomes :
standard	diabetes, South	B blocker	B blocker+ CCB	
antianginal drugs	Asians, women,	ССВ	B blocker + CCB	Cardiac mortality @ longest
(calcium channel	minimal coronary heart			available evaluation time point
blockers, long	disease	What is benefit of adding lor	ng acting nitrate?	(preferred 5yr, 10 yr)
acting nitrates)		B blocker + CCB	B Blocker + nitrate	
for the		B blocker + CCB	B blocker + CCB +	Angina frequency @ longest
management of			nitrate	available evaluation time point
angina?				(preferred 1yr, 5yr, 10yr)
		ССВ	CCB + nitrates	Preterred outcomes :

Preferred :	B blocker	CCB + nitrates	Angina incidence reported in diaries
Double blind	ССВ	B Blocker + nitrate	GTN usage
RCTs	CCB + B blocker	CCB+ nitrate	
Minimum n=50			Major cardiac events @ longest
>60% stable			available evaluation time point
angina	Beta blockers		(preferred 1yr, 5yr, 10yr)
Minimum Follow	atenolol, propranolol,		
Up = 3m	bisoprolol, metoprolol,		Preferred outcome:
Adverse event	nadolol,		Nonfatal MI
data to be sourced			
from RCTs only	Calcium channel blockers		Hospitalisation @ 6m -1yr
	amlodipine, diltiazem,		
	felodipine, nifedipine,		Revascularisation @ 1yr, 5yr, 10yr if
	verapamil)		available
	Long opting pitrotop		Quality of Life eq EQ-5D, SE-36
	Long acting mitates		HAD, etc @ longest available
	Isosorbide mononitrate		evaluation timepoint (preferred 1y,
			5y, 10y)

Q 5) What is the clinical/cost effectiveness of aspirin or clopidogrel to alleviate angina symptoms and to improve long term outcomes? Preferred: Double blind RCTs Minimum number of participants n=50 >60% patients with stable angina	Adults with a diagnosis of stable angina • including people with diabetes, South Asians, women, minimal coronary heart disease.	 (1) Aspirin (acetylsalicylic acid) + standard antianginal drugs (2) Clopidogrel, ticlopidine + standard antianginal drugs 	Aspirin +standard anginal treatment vs. standard anginal treatment Clopidogrel ,ticlodipine+ standard anginal treatment vs. standard anginal treatment Aspirin + clopidogrel,ticlodipine + standard anginal treatment vs. standard anginal treatment vs.	Mortality @ longest available evaluation time point (preferred 5yr, 10 yr) Preferred outcomes : All cause mortality Cardiac mortality Other outcomes: Cardiovascular mortality Major cardiac events @ longest available evaluation time point (preferred 1yr, 5yr, 10yr) Preferred outcome: Nonfatal MI

Minimum 1yr				Hospitalisation @1yr
follow up				
Adverse event				Revascularisation @ 1yr, 5yr, 10yr if
data to be sourced				available
from RCTS only				Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation timepoint (preferred 1y, 5y, 10y)
				Adverse events
		(1) ACE inhibitors (in	ACE or ARB vs.	
Q 6) What is the	Adults with a diagnosis	addition to standard anti-	Standard anti-anginal	Mortality @ longest available
clinical /cost	of stable angina	anginal treatment) captopril,	treatment (without	evaluation timepoint (preferred 5yr,
effectiveness of		cilazapril, enalapril,	ACE/without ARB)	10 yr)
ACE INNIDITORS	including people with diabetes. South	moevipril, imidapril, ilsinopril,		Preferred outcomes :
management of	Asians women	quinapril ramipril		All cause mortality
angina?	minimal coronary heart	trandolapril		Cardiac mortality
	disease.			
Preferred:		(2) ARBs (in addition to		Other outcomes:
Double blind		standard anti-anginal		Cardiovascular mortality
RCTs		treatment) candasartan,		
Minimum number		valsartan, losartan,		Major cardiac events @ longest
of participants		irbesartan, eprosartan,		available evaluation timepoint
n=50		olmesartan, telmisartan		(preferred 1yr, 5yr, 10yr)

>60% patients with stable angina Minimum 1yr follow up Adverse event data to be sourced from RCTs only				Preferred outcome: Nonfatal MI Hospitalisation @1yr Revascularisation @ 1yr, 5yr, 10yr if available Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation time point (preferred 1y, 5y, 10y) Adverse events
Q7) What is the clinical /cost effectiveness of using statin therapy in patients with normal coronary arteries (syndrome X)?	For statins: Patients with typical symptoms of angina and minimal coronary heart disease	Statins (HMG CoA reductase inhibitors) atorvastatin, fluvastatin, pravastatin, rosuvastatin, simvastatin (+/- standard anti-anginal treatment)	Placebo or no treatment (+/- standard anti-anginal treatment)	Mortality @ longest available evaluation time point (preferred 5yr, 10 yr) Preferred outcomes : All cause mortality Cardiac mortality Other outcomes:
Preferred: Double blind RCTs Minimum number				Cardiovascular mortality Major cardiac events @ longest available evaluation time point (preferred 1yr, 5yr, 10yr)

of participants n=50 >60% patients		Preferred outcome: Nonfatal MI
with stable angina Minimum 1yr follow up		Hospitalisation @1yr
Adverse event data to be sourced from RCTs only		Revascularisation @ 1yr, 5yr, 10yr if available
		Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation timepoint (preferred 1y, 5y, 10y)
		Adverse events

		PCI (includes coronary	PCI vs. CABG	
Q 8) In adults with	Adults with a diagnosis	angioplasty and stents),		exercise tolerance @ 6 months and
angina, what is the	of stable angina			longer
clinical/cost		CABG		
effectiveness of	Subgroups:			Mortality @ longest available
revascularisation	diabetes, South			evaluation time point (preferred 5yr,
techniques to	Asians, women,			10 yr)
alleviate angina	Number of			Preferred outcomes:
symptoms and to	vessels – single,			All cause mortality
improve long term	double, or triple vessel			Cardiac mortality
outcomes?	coronary artery			
	disease, (with or with			Other outcomes:

BCTs	not involving proximal		Cardiovascular mortality
• Nors	left anterior		Caralovascalar monality
			Anging fraguenov/agyarity @ langagt
N=50			Angina frequency/sevenity @ longest
 >60% stable 	artery)		available evaluation time point
angina	Left main stem		(preferred 1yr, 5yr, 10yr, not below 3
 Adverse 	disease (LMS)		months)
event data	LV function		Preferred outcomes:
to be	Prior		Angina incidence reported in
sourced	revascularisation		diaries
from PCTs			GTN usage
only			CCS score
Only			
Conort			
studies N >			Major pardias aventa @ longast
2000			
			available evaluation time point
			(preferred 1yr, 5yr, 10yr)
			Preferred outcome:
			Nonfatal MI
			Hospitalisation @ 6m and longer
			Revascularisation @ 1vr. 5vr. 10vr if
			available
			Quality of Life e.g. EQ-5D SE-36
			\Box
			nad, etc e iongest available
			evaluation time point (preferred Ty,
			5y, 10y)

Q 9) What is the clinical/cost effectiveness of	Adults with a diagnosis of stable angina	PCI , CABG	PCI vs. Medical therapy	exercise tolerance @ 6 months and longer
revascularisation compared to pharmacotherapy	Subgroups: • diabetes, South Asians, women,		CABG vs. Medical therapy	Mortality @ longest available evaluation time point (preferred 5yr, 10 yr)
in stable angina?	• Number of vessels – single, double, or triple vessel		PCI +CABG vs. Medical therapy	Preferred outcomes:All cause mortalityCardiac mortality
RCTs Minimum N=50 >60% stable	disease, (with or with not involving proximal left anterior			Other outcomes: • Cardiovascular mortality
angina Adverse event data to be sourced from RCTs only	descending (LAD) artery) • Left main stem disease (LMS)			Angina frequency/severity @ longest available evaluation time point (preferred 1yr, 5yr, 10yr, not below 3 months)
2000	 LV function Prior revascularisation 			 Preferred outcomes: Angina incidence reported in diaries GTN usage CCS score
				Major cardiac events @ longest available evaluation time point

		(preferred 1yr, 5yr, 10yr)
		Preferred outcome:Nonfatal MI
		Hospitalisation @ 6m and longer
		Revascularisation @ 1yr, 5yr, 10yr if available
		Quality of Life eg EQ-5D, SF-36, HAD, etc @ longest available evaluation time point (preferred 1y, 5y, 10y)

Q10) What is the clinical/cost effectiveness of cardiac	Adults with stable angina - including people with	 Exercise based cardiac rehabilitation programmes 	Standard care/usual medical care as defined by the study	Improvement in Angina symptoms- Frequency of angina Consumption of nitroglycerin
rehabilitation programmes for patients with stable angina	diabetes, South Asians minimal coronary heart disease and women?	 Psychological interventions Behavioural interventions Cognitive interventions 		All cause mortality, cardiac mortality, cardiovascular mortality @ 5yr, 10yr Frequency of angina, improvement
Threshold of reporting for all = angina patients> 60% of population		 Health education interventions. Exercise training in 		in exercise tolerance e.g. 1m, 1yr, 5yr Major cardiac events – non fatal MI

addition to	e.g. 1yr, 5yr
behavioural and/or health education	Hospitalisation e.g. 1yr, 5yr, 10yr
interventions. (i.e.	Revascularisation rates e.g. 5yr,
Comprehensive rehab	10yr
programmes)	Quality of Life (including anyioty and
	depression) e.g. EQ-5D, SE-36
	HAD, etc @ 1yr, 5yr, 10 yr
• .	Adverse effects

Questions	Population (and subgroups)	Intervention	Comparison	Outcomes
11) Cardiac syndrome X	All adults with a diagnosis of syndrome X	BB, nitrates, CCB, ACEs , ARBs, Nicorandil, Ranolazine, Ivabradine, Aspirin	BB, nitrates, CCB, ACEs , ARBs, Nicorandil, Ranolazine, Ivabradine, Aspirin	Immediate improvement in exercise tolerance – within 30 mins of intervention Preferred outcome: • Change in total exercise time Other outcomes: • Change in time to ST depression • Change in time to onset of symptoms • Change in time to stopping exercise

		Change in workload
		 Frequency and/or severity of angina (and prophylaxic use) Preferred outcomes: Time to relief of pain Incidence of angina post- intervention Other outcomes: Pain severity Duration of pain
		Important adverse events (headache and syncope)

Questions	Population (and subgroups)	Intervention	Comparison	Outcomes
Questions 12) Which tables, equations, engines, models or scoring systems are most effective for prognostic -risk stratification in prediction of adverse cardiac outcomes in adults with stable angina?	Population (and subgroups) Adults with a diagnosis of stable angina – including people with diabetes, South Asians, women	Intervention Risk tables, equations, engines, models or scoring systems	Comparison Possible Clinical variables : Age Gender Hypertension Diabetes mellitus Previous MI Heart rate Smoking history Current drug therapy Body Mass Index Waist circumference ECG	Outcomes All cause mortality, cardiac mortality, cardiovascular mortality, Major cardiac events – fatal MI, non fatal MI Hospitalisation Look at Registry studies of people with Angina with prognosis purposes and risk scores. Cohort studies over 1000 Large randomised trials patients. Look at – ACTION Score trial

Q13) What is the INCREMENTAL	Adults with a diagnosis of stable angina	Anatomical/functional tests	Clinical assessment	All cause mortality, cardiac mortality, cardiovascular mortality.
value/effectiveness		-Exercise ECG / exercise		······································
of	– including people with	tolerance test / exercise		Major cardiac events –fatal MI, non-
anatomical/functi	diabetes, South	stress test / stress ECG.		fatal MI
onal tests for	Asians, women			
prognostic risk		-Stress		Hospitalisation
stratification in		echocardiography/exercise,		
prediction of		dobutamine, dipyridamole,		
adverse cardiac		adenosine- stress		
outcomes in adults		echocardiography.		
with stable				
angina?		-Stress myocardial perfusion		
		Imaging/ IVIPS/ myocardial		
		oversise thellium MPS		
		exercise mailum MFS.		
		-MPS using single photon		
		emission CT (SPECT).		
		-Stress magnetic resonance		
		imaging / stress perfusion		
		imaging / stress induced		
		motion wall abnormalities.		
		-Magnetic resonance		
		coronary angiography.		
		-Computed tomography CT /		
		CI coronary angiography /		

	multi slice CT / CT coronary angiography / CAT	
	-Ca scoring	
	-Electron beam CT (EBCT).	
	- Coronary angiography	

Q14) What is the	Adults with diagnosed	Pain management	Treatment vs. no	All cause mortality, cardiac mortality,
clinical/cost	stable angina		treatment	cardiovascular mortality, @ 5yr,
effectiveness of		TENS (Transcutaneous		10yr
(angina specific)	- including people with	electric nerve stimulation),	Treatment vs.	
specialised pain	diabetes, South	Spinal cord stimulation (NICE	placebo	Frequency of angina, improvement
interventions in	Asians, refractory	TA),		in exercise tolerance (immediate
patients with stable	angina, minimal	Cognitive Behavioural	Treatment A vs.	relief, symptoms over longer period
angina?	coronary heart disease	Therapy,	treatment B	e.g. 5yr, 10yr)
	and women	Temporary or destructive		
		sympathectomy,		Major cardiac events – non fatal MI
	(Comment only - not to	Analgesics (inc opioids – oral,		
	be reviewed) patients	transdermal, epidural,		Procedural morbidity e.g. @ 1m, 1yr
	who have recurrence	transthecal.),		
	of anginal symptoms	Myocardial laser		Hospitalisation e.g. 5yr, 10yr
	following	(percutaneous or		
	revascularisation	transmyocardial)		Revascularisation rates e.g. 5yr,
		(NICE TA),		10yr
		EECP (Enhanced external		

		counterpulsation) Acupuncture		Quality of Life e.g. EQ-5D, SF-36, HAD, etc @ 1yr, 5yr, 10yr
				Adverse events
Q15) What are the	Adults with a diagnosis	Patient education/information	No comparison	Information on -
education and information	of stable angina	interventions	group. This is a question best	Condition and the symptoms
needs of adults with stable angina to optimise their understanding of their diagnosis and of their participation in treatment decisions?	including people with diabetes, South Asians, women, refractory angina, minimal coronary heart disease	(including information on sexual activity, choice of drugs vs. revascularisation)	answered using qualitative methods or studies with good validated survey methodology.	 Treatment Side effects of Drugs Choice of drugs Choice of treatment (drugs or revascularization) Post treatment care Need for Rehab Type of rehab Diet Prevention Activities for daily living Quality of life Prognosis /complications-
				As reported in the papers

Q16) What is the	Adults with stable	Programmes specifically for	No life style changes	All cause mortality, cardiac mortality,
clinical /cost	angina	angina patients which modify		cardiovascular mortality @ 1yr, 5yr,
effectiveness of		lifestyle/CVD risk factors		10yr
angina specific	- including people with	including		
interventions to	diabetes, South			Frequency of angina, improvement in
modify	Asians, refractory	Diet (including folic acid,		exercise tolerance e.g. 1m, 1yr, 5yr
lifestyle/CVD risk	angina, minimal	vitamin E,C, beta carotene		
factors to reduce	coronary heart disease	supplements, Omega 3-acid		Major cardiac events – non fatal MI
symptoms,	and women?	ethyl esters, Mediterranean		e.g. 1yr, 5yr, 10yr
morbidity and		diet, low saturated diet, plant		
mortality and		sterols esters, low glycemic		Hospitalisation e.g. 1yr, 5yr, 10yr
improve quality		diet, fruit and vegetables, fish		
of life in angina		diet, high fibre diet)		Revascularisation rates e.g. 1yr, 5yr,
patients?				10yr
		Physical activity		
				Quality of Life (including anxiety and
		Alcohol consumption		depression) e.g. EQ-5D, SF-36, HAD,
		Smoking cessation		etc @ 1yr, 5yr, 10 yr
		Weight management		
				Adverse effects
		(*Any other life style factors		
		to be included??)		