## Appendix G. Evidence tables: Economic studies

## **Abbreviations**

CABG Coronary artery bypass graft
CCS Canadian cardiovascular society

CVD Confidence interval
CVD Cardiovascular disease

EVPI Enhanced external counterpulsation

EVPI Expected value of perfect information

**HRQoL** Health-related quality of life

ICER Incremental cost-effectiveness ratio

ICU Intensive care unit

ITT Intention to treat analysis

Int Intervention

LOS Length of stay

MACCE Major adverse cardiac and cerebrovascular event

M/F Male/female

MI Myocardial infarction

N Total number of patients randomised

NA Not applicable
NR Not reported

**PCI** Percutaneous coronary intervention

PTCA Percutaneous transluminal coronary angioplasty

QALY Quality-Adjusted Life Years

RCT Randomised controlled trial

SA Sensitivity analysis

**SAQ** Seattle Angina Questionnaire

SD Standard deviation
SE Standard error

Sig Statistically significant at 5%

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Abizaid 2001{Abizaid, 2001 9151 /id}	coronary artery disease from the ARTS trial.  ic All patients : N: 208 Sequences Age (mean): NR M/F: 149/59 Unstable angina: 82 Drop outs: 0  Group 1 N: 112	Group 1: PCI Stent	Number of patients dead at 1 year	Group 1: 7 (6.3%) Group 2: 3 (3.1%) p value: 0.294	Funding/conflict of interest:
USA Economic analysis:		Group 2: CABG	Number of patients experiencing cerebrovascular events at 1 year	Group 1: 2 (1.8%) Group 2: 6 (6.3%) p value: 0.096	Limitations: Short time-horizon. Cost of further
Cost consequences analysis  Study design		N/F: 149/59 Instable angina: 82	Number of patients experiencing myocardial infarction at 1 year	Group 1: 7 (6.3%) Group 2: 3 (3.1%) p value: 0.294	medications not included (only hospital costs). Costs of resources from one hospital only.
RCT*  Duration of follow-up:		Group 1		Number of patients having repeated vascularisation (CABG and PTCA) at 1 year	Group 1: 25 (22.3%) Group 2: 3 (3.1%) p value: <0.001
1 year Perspective:	M/F: 82/30 Unstable angina: 44 Drop outs: 0		Number of event-free patients alive at 1 year	Group 1: 71 (63.4%) Group 2: 81 (84.4%) p value: <0.001	Potentially serious limitations; partial applicability.  Data sources: Unit costs from Dijkzigt
Healthcare provider  Discount rates: Costs: NA	Group 2 N: 96		Mean cost per patient 1998 USD, cost of procedure and follow-up	Group 1: \$12,855 (£8,291) Group 2: \$16,585 (£10,052) p value: <0.001	
Effects: NA M/F: 67 Unstab	Age (mean): 62.6 M/F: 67/29 Unstable angina: 38 Drop outs: 0		Cost-effectiveness** Incremental cost per additional event-free patient	Group 2 vs Group 1: \$8,386 (£5,409)	Hospital.  Notes:  * based on a subgroup from the ARTS trial
			Sensitivity analysis	NR	**calculated by NCGC

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Borghi 2000{Borghi, 2000 78 /id} UK <b>Economic analysis:</b> Cost analysis	Patient group: New, switched and existing stable angina patients.  All patients	Group 1: Beta-blocker (Tenormin)  Group 2:	Mean cost per patient without comorbidities over one year a) new patient b) after switching c) existing patient 1997/98 GBP. Cost of anti-anginal	Group 1: a) £656 b) £871 c) £320 Group 2: a) £1,014 b) £774 c) £336 p value: NR	Funding/conflict of interest: NR  Limitations: Based on a cross-
Study design Cross-sectional study	N: 1825 N with comorbidities: 640 (35%) Group 1	Calcium-channel blocker (Tildiem)	drugs, additional medication, GP-initiated tests, GP and practice nurse visits, outpatient visits, elective and emergency admissions.		sectional study. No measure of effectiveness was assessed.
Duration of follow- up: One year	N: 1253 N with comorbidities: 473 (38%)		Cost-effectiveness	NR	Overall quality and applicability
Perspective: UK NHS	Group 2 N: 572		Sensitivity analysis One-way SA	The costs in patients with comorbidities had the same trend in the year after switching and for existing patients. Only for new patients with comorbidities treatment with beta-	Potentially serious limitations; partial applicability.
Discount rates: Costs: NA Effects: NA	N with comorbidities: 167 (29%)			blocker was associated with higher costs.  The overall results do not change when: - frequency of GP visits is varied - incidence of hospitalisation is varied (from 0 to double) - the cost of generic drugs is used.	Data sources: Resource use data obtained from the IMS Health Database, UK Mediplus ® Resource costs obtained from NHS databases and UK cost studies.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
De Feyter 2002{de Feyter, 2002 39 /id} Netherlands	Patient group: patients with stable angina from the ARTS trial	Group 1: Stented angioplasty	Number of patients dead at 1 year	Group 1: 9 (2.4%) Group 2: 12 (3.2%) p value: Not sig	Funding/conflict of interest: NR
Economic analysis:	All patients** N: 755	Group 2: CABG	Number of patients experiencing cerebrovascular accidents at 1 year	Group 1: 9 (2.1%) Group 2: 5 (1.3%) p value: Not sig	Limitations: No sensitivity analysis was performed. No HRQoL
Cost-effectiveness analysis  Study design	Age (mean): NR M/F: 574/181 Drop outs: 0		Number of patients experiencing myocardial infarction at 1 year	Group 1: 19 (5.1%) Group 2: 11 (2.9%) p value: Not sig	outcomes were considered. Some costs (e.g. GP visits) might have been missed.
RCT*  Duration of follow-	Group 1 N: 381 Mean age (range): 62 (32-81)		Number of patients having repeat revascularisation at 1 year	Group 1: 63 (16.8%) Group 2: 13 (3.5%) p value: <0.01	Overall quality and applicability Potentially serious limitations;
up: 12 months	M/F: 293/88 Drop outs: 0		Number of angina and medication free patients at 1 year	Group 1: 67 (18%) Group 2: 160 (42%) p value: <0.003	partial applicability.  Data sources:
Perspective: Healthcare provider	Mean age (range): 61 (35-83)		Number of MACCE-free patients at 1 year	Group 1: 275 (73.5%) Group 2: 340 (89.2%) p value: <0.0001	Unit cost from the Netherlands.
Discount rates: Costs: NA Effects: NA	ts: NA Drop outs: 0		Mean cost per patient 1998 USD, cost of procedure, hospitalisation, follow-up, rehospitalisation, medication.	Group 1: \$10,368 (£6,687) Group 2: \$12,960 (£8,359) p value: Not sig	<ul> <li>Notes:         *ARTS trial         **Only subset of stable angina patients is included in our review.</li> </ul>
			Cost-effectiveness Incremental cost per additional MACCE-free patient.	Group 2 vs Group 1: \$16,510 (£10,649)	
			Sensitivity analysis	NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Eefting 2003{Eefting, 2003 1030 /id}	Patient group: Patients with stable or unstable angina and/or documented	-	Number of patients dead at 1 year	Group 1: 0 (0.0%) Group 2: 4 (2.8%) p value: NR	Funding/conflict of interest: Netherlands National Health Insurance Council.
The Netherlands  Economic	ischemia.  All patients	of standard techniques.	Number of patients experiencing myocardial infarction at 1 year	Group 1: 6 (4.4%) Group 2: 7 (4.9%) p value: Not Sig	Limitations: Short follow-up. Lack of blinding.
analysis: Cost-utility analysis Study design	N: 280 Age (mean): NR Stable angina CCS I or II: 60 Stable angina CCS III or IV: 128	Group 2: Off-pump bypass surgery by use of the Octopus tissue	Number of patients with repeated revascularisation at 1 year	Group 1: 21 (15.2%) Group 2: 6 (4.2%) p value: Sig	At baseline patients in Group 1 had more severe angina symptoms.  Overall quality and applicability
RCT	M/F: 199/81 Drop outs: 0 a		Number of event-free patients still alive at 1 year	Group 1: 118 (85.5%) Group 2: 130 (91.5%) p value: Not Sig	Potentially serious limitations; partial applicability.
Duration of follow- up: 1 year	Group 1 N: 138 Age (mean): 60.3		QALYs	Group 1: 0.82 Group 2: 0.79 p value: 0.09	Notes:  a 7 in Group 1 and 6 in Group 2 did not undergo the assigned treatment
Perspective: NHS  Discount rates: Costs: NA Effects: NA	Stable angina CCS I or II: 22 <sup>b</sup> Stable angina CCS III or IV: 73 <sup>b</sup> Stable angina CCS III or IV: 73 <sup>b</sup> M/F: 97/41 Drop outs: 0 <sup>a</sup> Discount rates:  Costs: NA  Group 2		Mean cost per patient at 1 year 1999 USD c, direct cost of procedure, hospitalisation, follow-up including reoperation, rehabilitation, medications and tests d.	Group 1: \$7,043 (£4,599) Group 2: \$9,518 (£6,215) p value: <0.01	b significantly more patients in Group 1 were in CCS III or IV. c costs were estimated in Dutch florins and converted to US dollars (\$1 = 2.5 DFL). d The main cost drivers were operating room, intensive care, ward, additional investigations and outpatient rehab.
			Cost-effectiveness Incremental cost per QALY gained	Stenting is dominant	Tilvestigations and outpatient renab.
			Sensitivity analysis Bootstrap simulation	Stenting is dominant in 95% of the 500 simulations.	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments	
Griffin 2007{Griffin, 2007 53 /id} UK	were suitable for both CABG and PCI. Their suitability to have revascularisation was assessed using the RAND  Group 3:  Medical	PCI Group 2:	Number of patients who died at 6 years	Group 1: 28 (16%) Group 2: 18 (12%) Group 3: 34 (17%) p value: Adjusted HR sig for Group 2 vs Group 1	Funding/conflict of interest: British Heart Foundation. The authors declared no competing interests.	
Economic analysis: Cost-utility analysis		suitable for both CABG CI. Their suitability to revascularisation was  Group 3:	Number of patients with angina at 6 years	Group 1: 61/102 (60%) Group 2: 52/89 (58%) Group 3: 82/119 (69%) p value: Adjusted odd ratio not sig	Limitations:  Not a randomised study.  PCI procedure could have been without stents. EQ-5D data were not collected at	
Study design Cohort study  Duration of follow-		appropriateness method. manageme	management	non-fatal myocardial infarction at 6 years	Group 1: 19 (11%) Group 2: 15 (10%) Group 3: 16 (8%) p value: NR	baseline and at one year; scores were only predicted at these time points from other variables.
up: 6 years			Number of patients having further revascularisation at 6 years	Group 1: 47 (27%) Group 2: 9 (6%) Group 3: 83 (42%) p value: NR	Criteria for assessment of the suitability for revascularisation could have changed since time of study.	
Perspective: NHS	Group 1 N: 173 Age (mean): NR M/F:NR		Number of patients admitted for chest pain at 6 years	Group 1: 73 (42%) Group 2: 58 (39%) Group 3: 82 (41%) p value: NR	Overall quality and applicability Potentially serious limitations;	
Discount rates: Costs: 3.5% Effects: 3.5%	sts: 3.5%		Discounted mean QALYs (SD) over 6 years	Group 1: 2.93 (1.65) (n=127) Group 2: 3.13 (1.37) (n=114) Group 3: 2.83 (1.39) (n=164) p value: NR	partial applicability.  Data sources:  Occurrence of admissions and LOS from the NHS-wide	
	M/F: NR Drop outs: NR  Group 3 N: 198		Discounted mean cost per patient over 6 years 2004 GBP, cost of intervention, angiography, hospital stay, drugs, admissions for chest pain,	Group 1: 14,007 (SD 10,453) Group 2: 17,859 (SD 6,940) Group 3: 10,690 (SD 7,888) p value: Sig	clearing service; data on drugs from hospital case notes, GP and patients' questionnaires; unit costs from published studies and	
	Age (mean): NR		GP and outpatient visits, visits to the emergency department.		pricing lists for the UK	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	M/F: NR Drop outs: NR		Cost-effectiveness incremental cost per QALY gained	Group 1 vs 3: £22,900/QALY* Group 2 vs 1: £15,917/QALY* Group 2 vs 3: £18,603/QALY*	Notes: * based on the adjusted mean difference of QALYs (0.24 vs
			Sensitivity analysis	For patients deemed appropriate for CABG only, the ICERs become: Group 1 vs 3 £10,560/QALY Group 2 vs 1 £21,533/QALY Group 2 vs 3 £14,675/QALY  For patients deemed appropriate for PCI only, CABG is dominated and the ICER of Group 1 vs 3 is £47,450.  At a threshold of £20,000/QALY all the strategies have a similar probability of being cost-effective.	Group 1 and 0.39 vs Group 3) and costs (£3,820 vs Group 1 and £7,255 vs group 3).

Study details	Patients	Interventions	Outcome measures	Effect size	Comments				
Hambrecht 2004{Hambrecht, 2004 9023 /id}	Patient group: male patients aged 70 years or less with stable CAD and one native coronary	Group 1: Stent angioplasty	Number of deaths of cardiac causes	Group 1: 0 Group 2: 0 p value: NA	Funding/conflict of interest: Unconditional scientific				
Germany  Economic analysis:	artery stenosis of at least 75% by visual assessment amenable to PCI; class I to II of angina with documented myocardial	ast 75% by lenable to gina with fial buring the first two weeks patients exercised in the hospital 6 times per day for 10 minutes on a bicycle ergometer at 70% of the symptom-limited maximal heart rate. At discharge, patients were asked to exercise for 20 minutes per day and to participate in one 60 minute gray market.	Number of cerebrovascular accidents (%)	Group 1: 3 (6%) Group 2: 2 (3.9%) p value: Not sig	grant from Aventis, Germany.  Limitations:				
cost-consequences analysis	ischemia. Patients who had CABG or PCI within the last 12 months were excluded.		weeks patients exercised in the hospital 6 times per	weeks patients exercised in the hospital 6 times per	weeks patients exercised in the hospital 6 times per	Group 1: 10 (20%) Group 2: 3 (5.9%) p value: Not sig	A breakdown of costs was not provided. An overall summary of cost-		
Study design RCT	All patients N: 101 Age (mean):		Hospitalisation and coronary angiography	Group 1: 7 (14%) Group 2: 1 (2%) p value: Not sig	effectiveness was provided only in the text.  Overall quality and				
Duration of follow- up: 1 year	M/F: 101/0 Drop outs: 4  Group 1		At discharge, patients were asked to exercise for 20 minutes per day and to participate in one	Mean cost per patient (±SE) 2003 USD, cost of interventions including hospital charges, expenses for supervised training sessions,	Group 1: \$6,086 (±370) (£3,846) Group 2: \$3,708 (±156) (£2,344)	applicability Potentially serious limitations; partial applicability.			
Perspective: Health care provider	N: 50 Age (mean): 60±1 M/F: 50/0			to participate in one	to participate in one	to participate in one and	(mean): 60±1 to participate in one	bicycle ergometer, coronary angiographies, and rehospitalisation.	p value: <0.001
Discount rates: Costs: NA	Drop outs: 2		Cost-effectiveness	NR	To gain 1CCS class, the cost was \$6956 (£4,396) in the angioplasty group				
Effects: NA	week.    Group 2	Sensitivity analysis	NR	and \$3429 (£2,167) in the exercise group.					

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Henderson 1998{Henderson, 1998 263 /id}	Patient group: Patients with angina, with single- or multi-vessel disease,	atients with angina, with angle- or multi-vessel disease, whom equivalent vascularisation could be chieved by either CABG or TCA.    PTCA without stents. Stents were used in only 14 PTCAs.   Stents were used in only 14 PTCAs.   Number of patients experiencing non-fatal myocardial infarction   Number of patients having repeated revascularisation (either PTCA or CABG) at follow-up   Group 2: 45 (9.0% p value: 0.51	Group 1: 39 (7.6%) Group 2: 45 (9.0%) p value: 0.51	Funding/conflict of interest: UK Department of Health;	
UK Economic	revascularisation could be achieved by either CABG or		experiencing non-fatal	Group 1: 55 (10.8%) Group 2: 37 (7.4%) p value: 0.08	British Heart Foundation and the British Cardiac
analysis: Cost consequences analysis  Study design RCT*	All patients N: 1011 Age (mean): NR (the majority		having repeated revascularisation (either	Group 1: 226 (44.3%) Group 2: 54 (10.8%) p value: NR	Limitations: Not an incremental analysis. HRQoL was not assessed.
Duration of follow- up: 6.5 years (median)	was in the range 50-59)  Patients working the range 50-59 or no angi	Patients with improved or no angina between 1-year and 5-year follow-up visits	Group 1: 312/461 (67.8%) Group 2: 334/446 (74.9%) p value: NR	Overall quality and applicability Potentially serious	
Perspective: NHS	Group 1** N: 510 Age (mean): NR M/F: NR		Discounted mean cost per patient at 5 years 1997 GBP, cost of initial procedure, subsequent	Group 1: £8,842 (SD £7,516) Group 2: £9,268 (SD £5,384) p value: Not sig	limitations; partial applicability.  Data sources:
Discount rates: Costs: 6% Effects: NR	Group 2** N: 501		procedures, other inpatient care, medications.		Unit costs taken from one London centre and one centre from
	Age (mean): NR M/F: NR		Cost-effectiveness	NR	elsewhere.  Notes:
	Drop outs: 11		Sensitivity analysis One-way SA	When a 3% discount rate was used the costs of PTCA were 96% of the costs of CABG; if no discount rate is used the ratio is 98% (cost difference not statistically significant at any of these rates)	* based on the RITA-1 trial ** An intention-to-treat analysis was performed.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hlatky 2009{Hlatky, 2009 9244 /id} USA  Economic analysis: Cost-utility analysis  Study design Multi-centre RCT*	Patient group: patients with type 2 diabetes mellitus and stable, angiographically documented coronary disease.  All patients N: 2005	Group 1: Early revascularisation with a) CABG b) PCI as decided by the physician	Life years***	a) CABG stratum Group 1: 3.56 Group 2: 3.59 p value: NR  b) PCI stratum Group 1: 3.58 Group 2: 3.65 p value: NR	Funding/conflict of interest: National Heart, Lung and Blood Institute, GlaxoSmithKline, Lantheus Medical Imaging, Astellas Pharma, Merck & Co, Abbott Laboratories, Pfizer, MediSense Products, Bayer Diagnostics, Becton, Dickinson and Co, J.R. Carlson Labs,
Duration of follow- up: 4 years Perspective: Healthcare provider	Drop outs: 1323**  Group 1 N: 988  Group 2 N: 1017	Group 2: Medical therapy	QALY ***	a) CABG stratum Group 1: 3.267 Group 2: 3.274 p value: NR b) PCI stratum Group 1: 3.221 Group 2: 3.248 p value: NR	Centocor Inc, Eli Lilly, lipoScience, Merck Sante, Novartis, Novo Nordisk.  Limitations: Not clear how utilities were used to calculate results in the study. In the clinical paper the probability of cardiovascular events was lower
Discount rates: Costs: 3% Effects: NR			Mean 4 year cost per patient # 2007 USD, hospitalisation, outpatient visits, nursing home/rehab, medications, test and procedure. Hospital costs calculated using a ratio of cost to charges.	a) CABG stratum Group 1: \$124,400 (£69,115) Group 2: \$103,600 (£57,560) p value: NR b) PCI stratum Group 1: \$106,300 (£59,060) Group 2: \$96,400 (£53,560) p value: NR	
			Cost-effectiveness incremental cost per QALY gained	Medical therapy is dominant.	baseline factors that affected cumulative costs at 2 years (intervention assigned, use of
			Sensitivity analysis	Medical therapy was not dominant but still cost-effective when: - results were extrapolated to lifetime assuming costs after 4	insulin, baseline HbA level, gender, body mass index). None of these factors had a significant interaction with treatment

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				indefinitely medical treatment is reported to be less cost-effective (counterintuitive).	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Legrand 2004{Legrand, 2004 1001 /id}	Patient group: Patients with multivessel disease**	Group 1: Stent	Number of patients dead at 3 years	Group 1: 22 (3.7%) Group 2: 28 (4.6%) p value: Not Sig	Funding/conflict of interest: NR
The Netherlands  Economic	All patients N: 1205	Group 2: CABG	Number of patients experiencing cardiovascular accident at 3 years	Group 1: 20 (3.3%) Group 2: 20 (3.3%) p value: Not sig	Limitations: Baseline quality of life was not reported.
analysis: Cost-effectiveness analysis	Age (mean): 61 M/F: 922/283 Drop outs: 6***		Number of patients experiencing myocardial infarction at 3 years	Group 1: 44 (7.3%) Group 2: 34 (5.7%) p value: Not sig	Number of patients and percentages reported do not match. Unclear if discounting was
Study design RCT*	Group 1 N: 600 Age (mean): 61		Number of patients having repeated procedure (either PCI or CABG) at 3 years	Group 1: 175 (29.2%) Group 2: 44 (7.3%) p value: Sig	applied to costs and effects.  Overall quality and
Duration of follow- up: 3 years	M/F: 462/138 Drop outs: NR		Number of event-free patients still alive at 1 year	Group 1: 395 (65.8%) Group 2: 504 (83.3%) p value: <0.0001	applicability Potentially serious limitations; partial applicability.
Perspective: Healthcare provider	Group 2 N: 605 Age (mean): 61		Summary of EQ-5D score at 3 years (mean ± SD)	Group 1: 85 ± 17 Group 2: 86 ± 17 p value: 0.74	Additional outcomes: At 3 years patients in Group 2 had significantly less angina
Discount rates: Costs: NR Effects: NR	tts: NR	op outs: NR	1998 Euro, diagnostic tests, devices	Group 1: €14,302 (£10,183) Group 2: €16,100 (£11,463) p value: 0.0001	(12.8% vs 18.4%, P=0.011) and lower rate of use of antianginal medications (65.4% vs 78.4%, P<0.001).
			Cost-effectiveness Incremental cost for additional event- free patient	Group 2 vs Group 1: €10, 492 (£7,470) 95%CI €3,722 – €20,772 (£2,650– £14,790)	Notes: * based on the ARTS trial.
			Sensitivity analysis One-way SA	The ICER is less favourable to CAGB when repeated procedure is excluded as an efficacy end point or when a shorter follow-up (1 year) is considered.	** both stable and unstable angina patients ****1 lost to follow-up, 3 withdrew consent, 2 never treated by either modality.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McKenna 2009{McKenna, 2009 9392 /id}	Patient group: patients with angina with an average age of 64	Intervention 1: No treatment	QALY	Int 1: 7.237 Int 2: 7.492 p value: NR	Funding/conflict of interest: HTA programme
UK  Economic analysis: CUA  Study design	years.	Intervention 2: EECP	Mean cost per patient 2008 GBP, capital cost of EECP machine, equipment replacement costs, consumables, staffing costs, overheads, repeat operations.	Int 1: 0 Int 2: 4,750 p value: NR	Limitations: The analysis was based on limited data (one small RCT). Utilities were obtained from an algorithm converting SF-36 to EQ-5D. Durability of benefits obtained from expert opinion. The model does not consider: the effect
Decision analysis based on the MUST-EECP RCT.			Cost-effectiveness Cost per QALY gained	Int 2 vs Int 1: £18,643/QALY	of intervention on mortality or MI, the cost of escalating medical treatment over
Time horizon: lifetime  Perspective: UK NHS and Personal Social Services  Discount rates: Costs:3.5% Effects: 3.5%			Sensitivity analysis One-way SA:	Ranges of ICER calculated varying the following: Probability of sustaining QoL benefits over time from separate expert opinion: £10,664 - £28,158. Cost of EECP per patient increased/decreased by £1000: £14,353 - £22,932. Results not sensitive to the rate of repeat EECP within two years (varied from 10% to 30%), subgroup analysis of women/men and different ages; discount rates 6% for costs and 1.5% for outcomes.	cost of escalating medical treatment over time, costs associated with no intervention. Only 20% of the patients in the EUROPA trial had angina and they could have a different mortality compared to refractory angina patients.  Overall quality and applicability Potentially serious limitations; direct applicability.  Additional outcomes: At a threshold £20k/QALY individual patient EVPI is £971 and population EVPI is £107,556,668.
			Worst-case/best-case scenario	When QoL benefits from EECP are only sustained in the first year, the ICER =£63,000. When QoL benefits are sustained over a lifetime, the ICER = £5,830	Data sources: Based on the MUST-EECP (Arora 1999 and 2002). QoL improvement calculated as EQ-5D scores using an algorithm to convert the SF-36 scores into EQ-5D.
			Monte Carlo simulation	Probability of being cost-effective at £20k/QALY threshold: 44.4% EECP.	QoL after one year was estimated with expert elicitation techniques (frequency

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
					chart). Mortality data from CVD causes obtained from the EUROPA trial. General mortality based on standard UK rates adjusted to exclude CVD deaths. Cost data from personal communication and price list of supplier.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments			
O'Neill 1996{O'Neill, 1996 321 /id} UK	Patient group: patients in the Belfast area aged less than 75 years and known to have	Group 1: Three visits per year from a health visitor whose brief	Number of deaths	Group 1: 13 (3.8%) Group 2: 29 (8.4%) p value: Not sig	Funding/conflict of interest: Medical Research			
Economic analysis: cost-consequences analysis Study design RCT{O'Neill, 1996 9181 /id},{Cupples, 1994 9190 /id}	angina for at least 6 months  All patients N: 688 Drop outs: 29  Group 1 N: 342 Age (mean): 62.7 (SD 7.1) M/F: 203/139 Drop outs: 12	was discuss ways of living more easily with their disease and in which risks of further events might be reduced.  Group 2: control	more easily with their disease and in which risks of further events might be reduced.  Group 2: control	more easily with their disease and in which risks of further events might be reduced.  Group 2: control	more easily with their disease and in which risks of further events might be reduced.  Group 2: control	Mean cost per patient 1996 GBP, Cost of intervention (staff time and travel related costs), drugs, GP visits, hospital visits (inpatient and outpatient), tests and other treatments Community care costs were excluded.  Cost-effectiveness	Group 1: £1,851 Group 2: £1,812 p value: Not sig	Council.  Limitations: Unclear whether the costs are per patient over two years. Old study, medical treatment might have not been optimal at that time. Unclear what intervention the control
Duration of follow- up: 2 years	Group 2 N: 346 Age (mean): 63.6 (SD 6.8) M/F: 205/141		Sensitivity analysis	NR	group received. Not all the important outcomes were evaluated (e.g. angina symptoms, MI).			
Perspective: NHS  Discount rates: Costs: NR Effects: NR	Drop outs: 17				Overall quality and applicability Potentially serious limitations; partial applicability.			

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
86 /id}	Patient group: patients with arteriographically proven coronary artery disease	Group 1: Percutaneous transluminal	Number of patients dead at 2 years	Group 1: 13 (2.5%) Group 2: 9 (1.8%) p value: Not sig	Funding/conflict of interest: British Heart Foundation, British Cardiac Society, and Department
	requiring revascularisation. Patients with previous PTCA or CABG were excluded.	coronary angioplasty (PTCA)	Number of patients experiencing non-fatal myocardial infarction at 2 years	Group 1: 32 (6.3%) Group 2: 25 (4.9%) p value: Not sig	of Health; ACS UK (Basingstoke, Nats), Medtronic Ltd (Watford, Herts), Schneider (Staines, Middx).
cost consequences analysis  Study design	All patients N: 1011	Group 2: Coronary artery bypass grafting	Number of patients with no angina at 1 year	Group 1: 343 (69.1%) Group 2: 398 (82.9%) p value: <0.0001	Limitations: Not an incremental analysis. HRQoL was not assessed.
RCT <sup>a</sup> Duration of follow-	<b>Group 1 N:</b> 510 b, c	(CABG)	Number of patients with no angina at 2 years	Group 1: 328 (64.3%) Group 2: 373 (79.1%) p value: 0.0023	Overall quality and applicability Potentially serious limitations;
up: 2 years  Perspective:  Discount rates: Costs: 6% Effects: NA	N: 501 b, c	Mean cost per patient over 2 years d 1994 GBP, cost of procedures, admissions, reoperations, coronary arteriograms, hospital stay for reasons not related to revascularisation, antianginal medications.	Group 1: £5,448 (SE £173) Group 2: £6,498 (SE £134) p value: Sig	partial applicability.  Data sources: Hospital unit costs from two hospitals (one in London, one outside). Drugs cost from BNF.  Notes:	
			Cost-effectiveness	NR	a based on the RITA trial b cost data were missing for 6 patients. c ITT analysis: in the CABG group 5 patients had PCTA and 6 no intervention; in the PTCA group 7 patients had CABG, 29 PTCA and CABG in the same admission, and 10 no intervention. Data from non-London centre
			Sensitivity analysis	The difference in cost was £1823 (sig) when data from the London hospital were used; £1145 in the single vessel disease subgroup; £970 in the multiple vessel disease subgroup.	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Sculpher 2002{Sculpher, 2002 44 /id}	Patient group: patients with arteriographically	tients with reriographically bearing applicably oven coronary stery disease cruited from 20 intres in the UK d Ireland and itable for both intinued medical erapy and PTCA.  Medical management with possible discontinuation if a patient no longer had angina symptoms.  Medical management with possible discontinuation if a patient no longer had angina symptoms.  Number of deaths and MI at 3 years  Group 1: 21 (4.1%) Group 2: 37 (7.3%) p value: 0.025  Patients with grade 2 or worse angina at 1 year  Patients with grade 2 or worse angina at 3 years  Group 1: 139 (27.4%) Group 2: 83 (17.0%) p value: 0.001  Limitations Utility values No increment conducted. Seed and the properties of the propert	Funding/conflict of interest: British Heart Foundation; Medical Research Council; Advanced		
UK Economic	proven coronary artery disease recruited from 20		Number of deaths and MI at 3 years	<b>Group 2:</b> 37 (7.3%)	Cardiovascular Systems Inc. (USA), Interventions (UK), Cordis Ltd, Schneider (UK) and Nycomed
analysis: Cost consequences analysis.	and Ireland and suitable for both		· ·	<b>Group 2:</b> 83 (17.0%)	Limitations: Utility values were not estimated.
Study design RCT*	therapy and PTCA.  All patients			<b>Group 2:</b> 93 (19.5%)	No incremental analysis was conducted. Stents were not used in the primary intervention.
Duration of follow- up:	N: 1018 Age (mean): M/F:	interventional techniques were only used if initial	Number of subsequent revascularisation (CABG or PTCA) at 3 years	Group 1: 155 Group 2: 111 p value: NR	Overall quality and applicability Minor limitations; partial
3 years  Perspective: NHS  Discount rates:	Drop outs:  Group 1** N: 514 Age (mean): M/F:	revascularisation with balloon angioplasty was unsatisfactory.	Mean cost per patient 1999 GBP, cardiac procedures, in- hospital stay, subsequent procedures, GP and outpatient visits, antianginal and cardiac drugs	Group 1: £3,613 Group 2: £6,299 p value: Sig	Data sources: Unit costs from five UK hospitals in different locations and national
Costs: 6% Effects: NA	Drop outs:		Cost-effectiveness	NR	sources. Cost of drugs from the Prescription Pricing Authority.
Elicoto. IW	Group 2** N: 504 Age (mean): M/F: Drop outs:		Sensitivity analysis Subgroup analysis One-way SA	Similar results when patients were stratified by CCS score, breathlessness, exercise time, and overall score. Similar results when no discount	Notes:  * based on RITA-2{Chamberlain, 1997 3544 /id}  ** ITT analysis: 471 of group 2 underwent the randomised PTCA.
	.,			rate is applied, the cost of visits for non-cardiac reasons is excluded, or when unit costs from the 5 hospitals are used separately.	*** calculated by NCGC using a two-tailed Fisher's exact test

Study details	Patients	Interventions	Outcome measures	Effect size	Comments					
Walker 2006{Walker, 2006 8950 /id}	angina patients participating in the	<b>O</b> 1		Group 2 - Group 1: 2.4% p value: NR	Funding/conflict of interest: Merck KGaA					
UK Economic	IONA trial{Dargie, 2002 6190 /id}.	Group 2: Nicorandil + usual	Cases of definite acute coronary syndromes (coronary heart disease death, non-fatal myocardial infarction or unstable angina)*	Group 2 - Group 1: 1.5% p value: NR	Limitations: Effectiveness data were reported only in the					
analysis: Cost-effectiveness analysis  Study design RCT	All patients N: 5126  Group 1 N: 2561  Group 2	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87%	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87% pitrotes, 89% capirin	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87%	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87%	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87%	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87%	Usual care was 57% beta-blockers, 56% calcium channel blockers, 87% Number of people free from any major cardiovascular event (coronary heart disease death, non-fatal myocardial infarction, unstable angina, definite or probable angina, stroke or hospital admission for transient inchanging ettack)	Group 1: 2069 (80.8%) Group 2: 2136 (83.3%) p value: NR	incremental analysis. SA was made only on the primary analysis (cost of care after discharge excluded). HRQoL was not assessed.  Overall quality and
Duration of follow- up: 1.6 years	N: 2565	initiates, 00 % aspirii.	Mean cost per patient 2002 GBP, cost of nicorandil (including 10% dispensing fee and two additional physician visits), adverse events related to nicorandil, hospital admissions, surgical procedures	Group 1: 243.7 Group 2: 243.6 p value: NR	applicability Potentially serious limitations; partial applicability.					
Perspective: UK NHS  Discount rates:			Cost-effectiveness Cost per additional unit of effectiveness	Nicorandil+usual care was dominant for all the three outcomes considered	Data sources: Resources used from RCT{Dargie, 2002 6190 /id}. Cost of units from national					
Costs: 0% Effects: 0%			Sensitivity analysis One-way SA	Nicorandil is more costly than usual care when: - cost of care after discharge is included - either cost of cardiology, cardiac surgery or ICU is reduced by 20%	Notes: * calculated by NCGC from the incremental analysis					

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Weintraub 1995{Weintraub, 1995 350 /id}	Patient group: patients with multivessel coronary artery disease (60%	Group 1: PTCA	Number of in-hospital deaths	Group 1: 2 (1%) Group 2: 2 (1%) p value: Not sig	Funding/conflict of interest: Grant from the National Heart, Lung and Blood Institute.
USA Economic	two-vessel disease and 40% three-vessel disease)	Group 2: CABG	Number of in-hospital MI	Group 1: 6 (3%) Group 2: 20 (10.3%) p value: 0.005	Limitations: Other direct medical costs (e.g.
analysis: Cost consequences analysis	All patients** N: 392 M/F: 289/103 Diabetes: 90		Number of deaths during 3- year follow-up	Group 1: 14 (7.1%) Group 2: 12 (6.2%) p value: Not sig	medications) were not included. Costs were calculated based on charges. The authors note
Study design RCT*	Prior MI: 160 Drop outs: 8		Number of MI during 3-year follow-up	<b>Group 1</b> : 29/173 (14.6%) <b>Group 2</b> : 38/172 (19.6%) <b>p value</b> : Not sig	that costs and outcomes of procedures could vary over time. Costs from one US
Duration of follow- up: 3 years	Group 1 N: 198 Age (mean±Cl): 62±10		Patients requiring additional procedures during follow-up	Group 1: 89 (45%) Group 2: 25 (13%) p value: <0.0001	hospital only. HRQoL was not assessed.
Perspective: Health care provider	M/F: 148/50 Diabetes: 49 Prior MI: 81 Drop outs: 2		Proportion of patients in angina class 0 – 1 – 2 – 3 – 4 at 3 years.	<b>Group 1:</b> 76% - 4% - 7% - 5% - 7% <b>Group 2:</b> 86% - 2% - 5% - 1% - 6% <b>p value</b> : 0.056	Overall quality and applicability Potentially serious limitations;
Discount rates: Costs: NR Effects: NR	Group 2 N: 194		Proportion of patients on 0 – 1 – 2 – 3 antianginal medication	Group 1: 34% - 47% - 17% - 2% Group 2: 49% - 39% - 10% - 2% p value: 0.029	<ul> <li>partial applicability.</li> <li>Additional outcomes:</li> <li>Proportions of patients with overall good health, complete recovery, same economic status than before, returned to work, retired after procedure</li> </ul>
	Age (mean±Cl): 61±10 M/F: 141/53 Diabetes: 41 Prior MI: 79	1	Mean cost per 3-year procedure 1987 USD, hospital costs and physician charges.	Group 1: \$23,735 (£13,078) Group 2: \$25,310 (£13,946) p value: <0.0001	
	Drop outs: 6		Cost-effectiveness	NR	were not statistically different in the two groups.
			Sensitivity analysis	When costs were inflated to 1993 USD or when charges were used instead of costs, the overall results did not change. The two interventions had similar costs (difference not significant) in patients with triple vessel disease	Data sources: Costs were calculated from hospital charges applying the cost-to-charge ratios.  Notes:

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				with ≥50% diameter luminal narrowing in more than one site in at least one affected vessel.  Multiple regression analysis: the surgical group was strongly correlated with initial hospital costs but it was not correlated with 3-year cumulative costs.	* Based on the EAST trial ** Intention-to-treat analysis

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Weintraub 2000{Weintraub, 2000 9168 /id}	Patient group: patients with multivessel coronary artery disease (60%	Group 1: PTCA	Number of deaths during 8- year follow-up	Group 1: 41 (20.7%) Group 2: 34 (17.3%) p value: 0.40	Funding/conflict of interest: NR
USA  Economic analysis: Cost consequences analysis	two-vessel disease and 40%	three-vessel disease)  All patients** N: 392 M/F: 289/103	Group 2: 8-year procedure*** Group	Group 1: \$43,758 (£27,786) Group 2: \$46,225 (£29,353) p value: 0.29	Limitations: Other direct medical costs (e.g. medications) were not included. Costs were calculated based on charges. The authors note that costs and outcomes of
Study design RCT*	Diabetes: 90 Prior MI: 160 Drop outs: 8	Sensitivity analysis	NR	procedures could vary over time. Costs from one US hospital only. HRQoL was not assessed.	
Duration of follow- up: 8 years	Group 1 N: 198 Age (mean±Cl): 62±10 M/F: 148/50 Diabetes: 49				Overall quality and applicability Potentially serious limitations; partial applicability.
Perspective: Health care provider  Discount rates:	Prior MI: 81 Drop outs: 2				Data sources: Costs were calculated from hospital charges applying the cost-to-charge ratios.
Costs: 3% Effects: NR	N: 194 Age (mean±Cl): 61±10 M/F: 141/53 Diabetes: 41 Prior MI: 79 Drop outs: 6				Notes:  * Based on the EAST trial  ** Intention-to-treat analysis  *** cost data available for 197 patients in Group 1 and 189 in Group 2.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Weintraub 2004{Weintraub, 2004 114 /id}	Patient group: patients with multivessel disease	Group 1: Stent assisted PCI	Mortality rate	Group 1: 2.5% Group 2: 0.8% p value: 0.05	Funding/conflict of interest: consortium of stent manufacturers: Medtronic, Switzerland; Guidant, USA;
UK Economic	All patients N: 988	Group 2: CABG	Repeat revascularisation	Group 1: 17.2% Group 2: 4.2% p value: <0.001	Boston Scientific, Germany  Limitations:
analysis: Cost-utility analysis Study design	Group 1 N: 488 Group 2		QALY at one year**	Group 1: 0.6938 Group 2: 0.6954 p value: not sig	Very short follow-up. Utility data were missing at one or more time points for 30% of the overall sample.  No sensitivity analysis was conducted.
RCT**  Duration of follow-up: One year	N: 500			Mean cost per patient 2004 GBP, cost of hospitalisation, procedure, ward, complications, follow-up, readmission, rehabilitation, medications.	Group 1: 6,296 Group 2: 8,905 p value: sig
Perspective: UK NHS			Cost-effectiveness*** incremental cost per QALY gained	Group 2 vs Group 1: £1,630,525	Data sources: Resources used calculated for all the patients in the trial.
Discount rates: Costs: NA Effects: NA			Sensitivity analysis	NR	Costs per unit were obtained from BNF and NHS reference costs. Utilities were estimated from participants using EQ-5D scores.
					Notes:  * based on the SoS trial  **utility was imputed when missing at one or more of the three time points for 30% of the overall sample.  ***calculated by NCGC

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Weintraub 2008{Weintraub, 2008 9247 /id}	Patient group: patients with stable coronary artery disease with >70% stenosis in at least	Group 1: PCI – Stents and angioplasty	Utility estimated by Standard Gamble at 1 month – mean ± 95%CI	<b>Group 1:</b> 0.92±0.19 (n=665) <b>Group 2:</b> 0.91±0.20 (n=699) <b>p value:</b> 0.66	Funding/conflict of interest: Dept of Veterans Affairs, Canadian Institutes for Health
Economic	one major epicardial coronary artery with objective evidence of myocardial ischemia or at	Group 2:	Utility estimated by Standard Gamble at 3 months – mean ± 95%CI	<b>Group 1:</b> 0.93±0.17 (n=669) <b>Group 2:</b> 0.92±0.19 (n=678) <b>p value:</b> 0.008	research; Merck&Co Pfizer; Bristol-Myers Squibb Medical Imaging; Kos Pharmaceuticals;
analysis: Cost-utility analysis	least one coronary stenosis >80% and classic angina without provocative testing.	Medical therapy	Utility estimated by Standard Gamble at 6 months – mean ± 95%CI	<b>Group 1:</b> 0.93±0.17 (n=701) <b>Group 2:</b> 0.93±0.15 (n=665) <b>p value:</b> 0.20	Data Scope; Astra Zeneca; Key Pharmaceutical, Sanofi-Aventis; First Horizon; Nycomed Amersham.
Study design RCT*	All patients N: 2287 Age (mean): 62		Utility estimated by Standard Gamble at 1 year – mean ± 95%Cl	<b>Group 1:</b> 0.93±0.17 (n=648) <b>Group 2:</b> 0.93±0.15 (n=636) <b>p value:</b> 0.53	Limitations: Valuation of utilities not obtained
Duration of follow- up:	M/F: 1947/340 Previous MI: 876 Angina: 88%		Utility estimated by Standard Gamble at 2 years – mean ± 95%CI	<b>Group 1:</b> 0.93±0.17 (n=550) <b>Group 2:</b> 0.92±0.17 (n=532) <b>p value:</b> 0.59	from public but from patients. Patients in the study were low risk.
4.6 years 3 years for costs	Multivessel disease: 69% Drop outs: 0		Utility estimated by Standard Gamble at 3 years – mean ± 95%CI	Group 1: 0.92±0.20 (n=385) Group 2: 0.90±0.21 (n=379) p value: 0.004	Effectiveness was estimated for the total duration of the trial (4.6 years) while costs only for 3
Perspective: Healthcare provider	Group 1 N: 1149 Age (mean): 62 M/F: 979/170		Discounted in-trial life years – mean ± 95%Cl	Group 1: 4.15±1.50 Group 2: 4.12±1.51 p value: 0.03	years. These results were combined. PCI group included angioplasty too.
Discount rates: Costs: 3%	Previous MI: 437 Utility: 0.90 (95% CI ±0.20) (n=775)		Group 1: 3.56±1.34 Group 2: 3.51±1.36 p value: 0.05	Overall quality and applicability	
Effects: 3%	Drop outs: 0  Group 2 N: 1138 Age (mean): 62 M/F: 968/170 Previous MI: 439		Mean cost per patient over 3 years** 2004 USD, hospitalisation, PCI, medication, outpatient services.	Group 1: \$34,843 (£21,247) Group 2: \$24,718 (£15,073) p value: Sig (95% CI of difference is always positive)	Minor limitations; partial applicability.  Notes:  * based on the COURAGE
	Utility: 0.87 (95% CI ±0.22) (n=748)		Cost-effectiveness** Incremental cost per QALY gained	PCI vs Medical Treatment: \$206,229 (£125,759)	trial{Boden, 2007 483 /id}  ** 2008 GBP obtained by using the purchasing power parities

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Drop outs: 0		Sensitivity analysis Structural SA	Extrapolating beyond RCT follow-up: PCI is still significantly more costly and more effective (not sig); If drug-eluting stents are used, they assumed no revascularisation after PCI, added cost of \$600 in the initial PCI and clopidogrel for one year, PCI would not be costeffective (ICER=\$197,465).	and GDP deflator indexes (http://eppi.ioe.ac.uk/costconvers ion/default.aspx)
			One-way SA	Life-years gained with PCI was varied from -40% to +40% → PCI still not cost-effective.	
			Threshold analysis	To achieve an ICER<\$50,000/QALY, PCI would need to improve QALYs by 0.60.	
			PSA	Ranges of incremental QALY with PCI -0.5 to 0.5; incremental costs \$4,000 to \$16,000. At a \$50k/QALY threshold PCI has a 25% probability of being cost-effective.	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Zhang 2006{Zhang, 2006 532 /id} UK	Patient group: symptomatic patients with typical angina and multivessel disease eligible for	Group 1: Stent-assisted PCI	Number patients dead at 1 year (%)	Group 1: 4 (2.1%) Group 2: 1 (0.5%) p value: 0.168	Funding/conflict of interest: NR
Economic analysis:	both CABG and PCI.  All patients N: 395	Group 2: CABG	Number of patients experiencing Q-wave myocardial infarction at 1 year (%)	Group 1: 13 (6.8%) Group 2: 17 (8.3%) p value: 0.998	Limitations: Source of costs not clear. No incremental analysis was conducted. Short follow-up.
cost-consequences analysis  Study design	Age (range): NR M/F: 296/99 Drop outs: 0	CABG	Number of patients experiencing bleeding at 1 year (%)	Group 1: 3 (1.6%) Group 2: 5 (2.4%) p value: 0.219	Overall quality and applicability Potentially serious limitations; partial
RCT*	Group 1 N: 190		Number of patients experiencing cerebrovascular accidents at 1 year (%)	Group 1: 5 (2.6%) Group 2: 5 (2.4%) p value: 0.388	applicability.  Additional outcomes:
Duration of follow- up: 1 year	Age (mean): 70.4 M/F: 136/54 Drop outs: 0		Number of patients having a repeat revascularisation (%)	Group 1: 37 (19.5%) Group 2: 7 (3.4%) p value: <0.0001	In-hospital death, myocardial infarction, bleeding and cerebrovascular accident were not significantly different in the two
Perspective: Hospital	Group 2 N: 205 Age (mean): 70.6		Adjusted improvement in SAQ Quality of Life score at 6 months**	Group 1: 25.5 Group 2: 30.5 p value: 0.0335	groups. Average LOS was 13.2 days in group 2 vs 5.4 days in group 1 (Sig).  Data sources:
Discount rates: Costs: NA Effects: NA	M/F: 150/55 Drop outs: 0		Adjusted SAQ Quality of Life score at 1 year**	Group 1: 30.7 Group 2: 32.1 p value: 0.5601	UK unit costs were applied to resource use recorded in the trial
			Mean cost per patient 2000 GBP, cost of hospitalisation and follow-up	Group 1: £6,611 Group 2: £9,559 p value: Sig***	Notes:  * based on the SoS trial  ** scores of the Seattle Angina
			Cost-effectiveness	NR	Questionnaire (SAQ) range from 0 to 100. A clinically important change is
		Sensitivity analysis	Results were similar for younger patients (≤65 years).	between 5 and 8 points.  *** The difference was £2,948 (95% CI £1,432 – £4,198)	

 $All\ non-UK\ costs\ converted\ into\ GBP\ using\ the\ Purchasing\ Power\ Parities \{Organisation\ for\ Economic\ Cooperation\ and\ Development,\ 2010\ 15954\ /id\}.$