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## 2 **1 Introduction**

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4 An economic model was developed to compare the cost-effectiveness of CABG and PCI for  
5 patients considered suitable for either revascularisation method (Chapter 12). In our economic  
6 literature review we found several studies (Chapter 12) but none of them met the quality and  
7 applicability criteria in full. Some{Abizaid, 2001 9151 /id;de Feyter, 2002 39 /id;Eefting,  
8 2003 1030 /id;Legrand, 2004 1001 /id;Weintraub, 1995 350 /id;Weintraub, 2000 9168  
9 /id} were not UK based and therefore only partially applicable. UK-based studies were  
10 either cost-consequences analyses{Henderson, 1998 263 /id;Sculpher, 1994 86 /id;Zhang,  
11 2006 532 /id} or cost-utility analysis based on cohort studies{Griffin, 2007 53 /id} with high  
12 risk of bias, or had a limited follow-up time{Weintraub, 2004 114 /id}.

13 The GDG considered it was necessary to build a model to formally evaluate the uncertain  
14 trade-offs between clinical outcomes and costs of the two revascularisation strategies.

15

## 16 **2 Methods**

### 17 **2.1 Model overview**

18 A cost-utility analysis was undertaken where costs and quality-adjusted life-years (QALYs)  
19 were considered from a UK NHS and personal social services perspective. Both costs and  
20 QALYs were discounted at a rate of 3.5% per annum in line with NICE methodological  
21 guidance{National Institute for Health and Clinical Excellence, 2009 15955 /id}.

22

23 The following general principles were adhered to:

- 24 • The GDG was consulted during the construction and interpretation of the model.
- 25 • When published data was not available we used expert opinion to populate the  
26 model.
- 27 • Model assumptions were reported fully and transparently.
- 28 • The results were subject to sensitivity analysis and limitations were discussed.
- 29 • The model employed a cost-effectiveness threshold of £20,000 per QALY  
30 gained.
- 31 • The model was peer-reviewed by another health economist at the NCGC.

#### 32 **2.1.1 Comparators**

33 The interventions compared are CABG and PCI (with either drug-eluting stents [DES] or bare-  
34 metal stents [BMS] or both). In the original meta-analysis (see review protocol in Appendix C)  
35 PCI included coronary balloon angioplasty but we decided to focus the economic analysis on  
36 PCI with stents as this is the widely used intervention and it is believed to be more effective

1 than coronary balloon angioplasty. Costs and effectiveness in the model are therefore  
2 applicable to CABG and PCI with stents.

### 3 **2.1.2 Population**

4 We looked for data on patients with single vessel disease and multi-vessel disease separately  
5 as interventions might yield different outcomes (e.g. different probability of repeating  
6 intervention). We found only scarce data on the single vessel group (small sample sizes) and  
7 therefore focused solely on patients with multi-vessel disease.

### 8 **2.1.3 Time horizon**

9 In the base case analysis we adopted a ten-year time horizon, which was the longest follow-  
10 up available from the RCTs. In a sensitivity analysis we extrapolated results up to a life-time  
11 horizon assuming the annual probabilities of clinical events are constant from year ten.

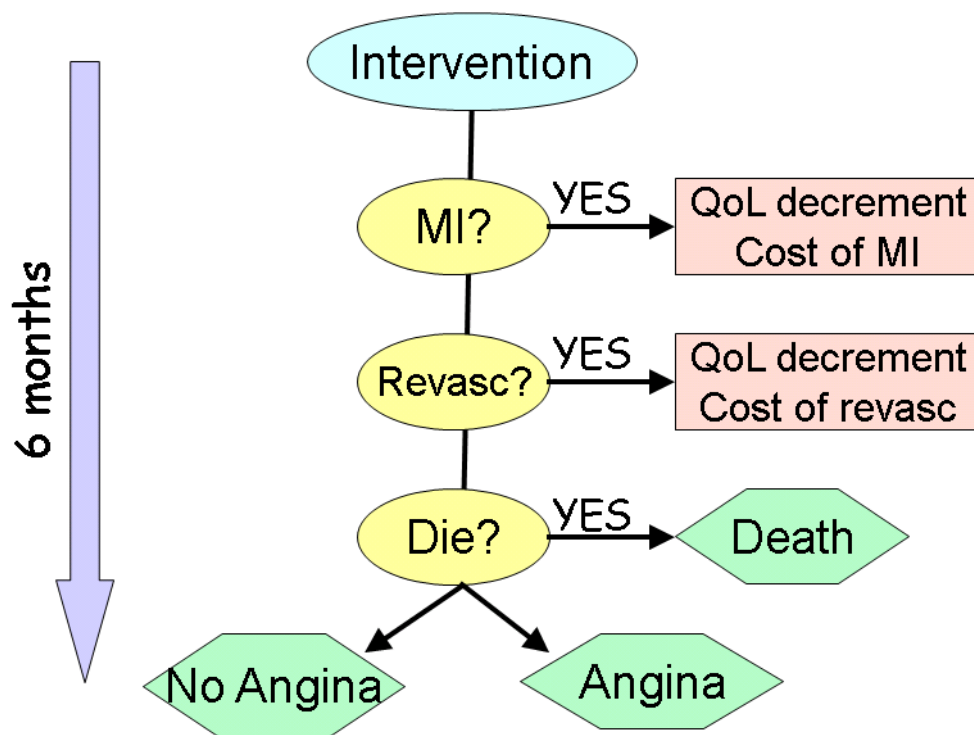
## 12 **2.2 Approach to modelling**

### 13 **2.2.1 Model structure**

14 Given the recurrences of events over time, we decided to build a Markov model with a six-  
15 month cycle length as this was deemed the minimum clinically meaningful time interval to  
16 detect differences between interventions. All the probabilities, costs and health utilities were  
17 converted to reflect the six-month cycle length.

18  
19 Clinical outcomes considered in the model were mortality, myocardial infarction (MI), further  
20 revascularisation procedures, and presence or absence of angina symptoms. Stroke was  
21 included in the clinical review; we did not include this outcome in the base case of the model as  
22 we observed only a non-significant trend for stroke to be more frequent in the CABG arm and  
23 the definition and severity of stroke was not reported in each study.

24  
25 Both arms of the model have the same structure. In the first cycle (   
26 Figure 1), patients undergo the intervention and in the following six months can experience one  
27 of the transitional events considered: MI, revascularisation, or death. In the first two events, a  
28 HRQoL decrement is applied to MI and the cost of treating MI or the cost of further  
29 revascularisation is added. In case of death, the patient ends up in the dead health state  
30 which is associated with no cost and a HRQoL equal to 0. If the patient is still alive at the end  
31 of the cycle, they can either still have or not have angina symptoms. The presence of angina  
32 symptoms defines the health state of the following cycle ('No angina' or 'Angina').  
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3 **Figure 1 - First cycle of the model**

4

5 In the following cycles patients re-enter the model and the same transitional events are  
6 evaluated with different time-dependent probabilities (see paragraph 2.3.2).

7 When a patient undergoes a further revascularisation in the base case we have assumed that  
8 this is a PCI. We have varied this assumption in a sensitivity analysis using different proportion  
9 of CABG and PCI for additional revascularisation.

10

11 For each strategy the expected healthcare costs and expected QALYs were calculated by  
12 estimating the costs and QALYs for each state and then multiplying them by the proportion of  
13 patients who would be in that state as determined by the strategy taken (see 2.4).

## 14 **2.2.2 Uncertainty**

15 In the **probabilistic analysis** a probability distribution is defined for each model input  
16 parameter. When the model is run a value for each input is randomly selected from its  
17 respective probability distribution and mean costs and mean QALYs are calculated using these  
18 values. The model is run repeatedly – in this case 10,000 times – and results are summarised.  
19 Probability distributions in the analysis were based on error estimates from data sources, for  
20 example confidence intervals around relative risk estimates.

21 The way in which distributions are defined reflects the nature of the data, so for example  
22 probabilities were given a beta distribution, which is bounded by zero and one – see Table 1.  
23 All of the variables that were probabilistic in the model and their distributional parameters  
24 are detailed in Table 2.

1 **Table 1: Description of the type and properties of distributions used in the probabilistic sensitivity analysis**

Parameter	Type of distribution	Properties of distribution	Parameters for the distribution
Probabilities	Beta	Bounded on 0 – 1 interval. Derived from sample size, number of patients experiencing events.	$\alpha$ = events $\beta$ = sample size – $\alpha$
Cost	Gamma	Bounded at 0. Derived from mean and standard error.	$\alpha$ = (mean/SEM) <sup>2</sup> $\lambda$ = mean/SEM <sup>2</sup>
Number of resources used (number of stents)	Triangular	Derived from expert opinion.	Min = minimum value Likeliest = mean Max = maximum value
Utility decrements	Gamma	Bounded at 0. Derived from mean and standard error.	$\alpha$ = (mean/SEM) <sup>2</sup> $\lambda$ = mean/SEM <sup>2</sup>
Relative risk	Lognormal	Bounded at 0. Derived from log (of the RR) and standard error.	$\mu$ = ln(RR) SD( $\mu$ ) = (ln[UpperCI] – ln[lowerCI])/1.96*2

2 SEM=standard error of the mean

3 For simplicity the following variables, were left deterministic (i.e. were not varied in the  
4 probabilistic analysis): discount rate and cost-effectiveness threshold (which were deemed to  
5 be fixed by NICE) and drug prices.

6 In addition, various **deterministic sensitivity analyses** were undertaken to test the robustness  
7 of model assumptions and data sources. In these one or more inputs were changed and the  
8 model rerun to see the impact on results.

9

## 10 **2.3 Model inputs**

### 11 **2.3.1 Summary table of model inputs (details in subsequent 12 sections)**

13  
14 **Table 2 - Summary of parameters used in the model**

Description of variable	Point estimate	Probability distribution	Parameters for the probability distribution	Source
<b><i>α) Probability of events (see 2.3.2)</i></b>				
Probability of death after CABG – 1 year	2.68%	Beta	$\alpha$ = 63 $\beta$ = 2288	Systematic review of clinical effectiveness (Appendix K)
Probability of death after CABG – from 1 to 2 years	0.37%	Beta	$\alpha$ = 0.4 $\beta$ = 1075	See 2.3.2
Probability of death after CABG – from 2 to 3 years	1.97%	Beta	$\alpha$ = 11.6 $\beta$ = 577	See 2.3.2

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<b>Probability of death after CABG – from 3 to 5 years</b>	4.49%	Beta	$\alpha = 34.6$ $\beta = 736$	See 2.3.2
<b>Probability of death after CABG – from 5 to 10 years</b>	17.79%	Beta	$\alpha = 32.9$ $\beta = 152$	See 2.3.2
<b>Probability of MI after CABG – 1 year</b>	4.44%	Beta	$\alpha = 102$ $\beta = 2197$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of MI after CABG – from 1 to 2 years</b>	0.72%	Beta	$\alpha = 4.2$ $\beta = 574$	See 2.3.2
<b>Probability of MI after CABG – from 2 to 3 years</b>	0.52%	Beta	$\alpha = 3$ $\beta = 571$	See 2.3.2
<b>Probability of MI after CABG – from 3 to 5 years</b>	3.49%	Beta	$\alpha = 26.6$ $\beta = 736$	See 2.3.2
<b>Probability of MI after CABG – from 5 to 10 years</b>	1.57%	Beta	$\alpha = 2.9$ $\beta = 182$	See 2.3.2
<b>Probability of repeating revascularisation after CABG – 1 year</b>	4.59%	Beta	$\alpha = 85$ $\beta = 1767$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of repeating revascularisation after CABG – from 1 to 2 years</b>	0.69%	Beta	$\alpha = 7.3$ $\beta = 1047$	See 2.3.2
<b>Probability of repeating revascularisation after CABG – from 2 to 3 years</b>	1.43%	Beta	$\alpha = 8.2$ $\beta = 565$	See 2.3.2
<b>Probability of repeating revascularisation after CABG – from 3 to 5 years</b>	0.87%	Beta	$\alpha = 6.6$ $\beta = 748$	See 2.3.2
<b>Probability of freedom from angina symptoms after CABG – 6 months</b>	85.20%	Beta	$\alpha = 121$ $\beta = 21$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of freedom from angina symptoms after CABG – 1 year</b>	80.94%	Beta	$\alpha = 1168$ $\beta = 275$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of freedom from angina symptoms after CABG – 2 years</b>	87.20%	Beta	$\alpha = 508$ $\beta = 75$	Systematic review of clinical effectiveness (Appendix K)

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<b>Probability of freedom from angina symptoms after CABG – 3 years</b>	87.20%	Beta	$\alpha = 503$ $\beta = 74$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of freedom from angina symptoms after CABG – 5 years</b>	78.84%	Beta	$\alpha = 637$ $\beta = 171$	Systematic review of clinical effectiveness (Appendix K)
<b>Probability of freedom from angina symptoms after CABG – 10 years</b>	64.04%	Beta	$\alpha = 130$ $\beta = 73$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of death at 1 year – PCI vs. CABG</b>	1.18	Log-normal	$\mu = 0.166$ $SD(\mu) = 0.168$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of death at 2 years – PCI vs. CABG</b>	1.32	Log-normal	$\mu = 0.278$ $SD(\mu) = 0.238$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of death at 3 years – PCI vs. CABG</b>	0.79	Log-normal	$\mu = -0.236$ $SD(\mu) = 0.278$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of death at 5 years – PCI vs. CABG</b>	1.11	Log-normal	$\mu = 0.104$ $SD(\mu) = 0.154$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of death at 10 years – PCI vs. CABG</b>	0.95	Log-normal	$\mu = -0.051$ $SD(\mu) = 0.173$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of MI at 1 year – PCI vs. CABG</b>	1.20	Log-normal	$\mu = 0.182$ $SD(\mu) = 0.130$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of MI at 2 years – PCI vs. CABG</b>	1.30	Log-normal	$\mu = 0.262$ $SD(\mu) = 0.231$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of MI at 3 years – PCI vs. CABG</b>	1.30	Log-normal	$\mu = 0.262$ $SD(\mu) = 0.220$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of MI at 5 years – PCI vs. CABG</b>	1.36	Log-normal	$\mu = 0.307$ $SD(\mu) = 0.146$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of MI at 10 years – PCI vs. CABG</b>	1.27	Log-normal	$\mu = 0.239$ $SD(\mu) = 0.276$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of repeating revascularisation at 1 year – PCI vs. CABG</b>	3.55	Log-normal	$\mu = 1.267$ $SD(\mu) = 0.117$	Systematic review of clinical effectiveness (Appendix K)

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<b>Relative risk of repeating revascularisation at 2 years – PCI vs. CABG</b>	4.42	Log-normal	$\mu = 1.486$ $SD(\mu) = 0.139$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of repeating revascularisation at 3 years – PCI vs. CABG</b>	4.03	Log-normal	$\mu = 1.393$ $SD(\mu) = 0.167$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of repeating revascularisation at 5 years – PCI vs. CABG</b>	4.15	Log-normal	$\mu = 1.423$ $SD(\mu) = 0.135$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of freedom from angina symptoms at 6 months – PCI vs. CABG</b>	1.01	Log-normal	$\mu = 0.010$ $SD(\mu) = 0.048$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of freedom from angina symptoms at 1 year – PCI vs. CABG</b>	0.87	Log-normal	$\mu = -0.139$ $SD(\mu) = 0.020$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of angina symptoms at 2 years – PCI vs. CABG</b>	0.92	Log-normal	$\mu = -0.083$ $SD(\mu) = 0.025$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of angina symptoms at 3 years – PCI vs. CABG</b>	0.94	Log-normal	$\mu = -0.062$ $SD(\mu) = 0.025$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of angina symptoms at 5 years – PCI vs. CABG</b>	0.92	Log-normal	$\mu = -0.083$ $SD(\mu) = 0.027$	Systematic review of clinical effectiveness (Appendix K)
<b>Relative risk of angina symptoms at 10 years – PCI vs. CABG</b>	0.91	Log-normal	$\mu = -0.094$ $SD(\mu) = 0.081$	Systematic review of clinical effectiveness (Appendix K)
<b>b) Quality of life values (see 2.3.3)</b>				
<b>Utility of No Angina</b>	0.87	Beta	$\alpha = 348$ $\beta = 52$	Melsop 2003{Melsop, 2003 8989 /id}
<b>Utility decrement of Angina vs. No angina</b>	-0.167	Gamma	$\alpha = 2.678$ $\lambda = 16.04$	See 2.3.3
<b>Utility decrement after MI</b>	-0.24	Gamma	$\alpha = 177.78$ $\lambda = 740.74$	See 2.3.3
<b>Utility decrement of CABG vs. PCI</b>	-0.06	Gamma	$\alpha = 39.81$ $\lambda = 663.46$	See 2.3.3
<b>c) Costs (see 2.3.4)</b>				

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<b>Cost of CABG procedure</b>	£7,959	Gamma	$\alpha = 13.04$ $\lambda = 0.0016$	NHS Reference Costs 2008-09, Elective Inpatient CABG 1st time{Department of Health, 10 A.D. 15958 /id}
<b>Cost of PCI procedure</b>	£2,610	Gamma	$\alpha = 2.64$ $\lambda = 0.0010$	NHS Reference Costs 2008-09, Elective Inpatient PCI 0 – 2 stents{Department of Health, 10 A.D. 15958 /id}
<b>Cost of each stent</b>	£300	Gamma	$\alpha = 15.19$ $\lambda = 0.0506$	Experts opinion
<b>Number of stents used</b>	4	Triangular	Min = 2 Likeliest = 4 Max = 6	Experts opinion
<b>Cost of Clopidogrel treatment over 12 months</b>	£436	None		BNF 59{Royal Pharmaceutical Society of Great Britain, 2010 15947 /id}
<b>Cost of Rehab</b>	£550	Gamma	$\alpha = 15.19$ $\lambda = 0.0276$	Bethell 2007{Bethell, 2009 162 /id}
<b>Cost of angiography</b>	£841	Gamma	$\alpha = 11.66$ $\lambda = 0.0139$	2008-09 NHS Ref costs: Day cases, HRG EA41Z - Other Non-Complex Cardiac Surgery + Catheterisation{Department of Health, 10 A.D. 15958 /id}
<b>Cost of MPS with SPECT</b>	£293	Gamma	$\alpha = 15.19$ $\lambda = 0.0518$	Chest Pain guideline{National Clinical Guideline Centre for Acute and Chronic Conditions, 2010 15959 /id}
<b>Cost of medications over 6 months</b>	£61.37	None		See 2.3.4.2
<b>Cost of treatment of MI</b>	£1,783	Gamma	$\alpha = 15.19$ $\lambda = 0.00852$	Acute Coronary Syndromes Guideline{National Clinical Guideline Centre for Acute and Chronic Conditions, 2010 15960 /id}



<b>Cost of referral</b>	£112	Gamma	$\alpha = 15.19$ $\lambda = 0.1356$	2008-09 NHS Reference Costs- Consultant Led: Follow up Attendance Non-Admitted Face to Face - Cardiology{Department of Health, 10 A.D. 15958 /id}
<b>d) Other parameters and assumption</b>				
<b>Discount rate (cost and QALYs)</b>	3.5%	none		NICE reference case

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### 3 2.3.2 Baseline event rates and relative treatment effects

4 CABG was used as the baseline arm of the model. Data on event rates in this arm were  
5 derived from the systematic review of clinical effectiveness (Appendix K). Events in the model  
6 were total MI (both fatal and non-fatal), repeat revascularisation, and death. Only studies of  
7 CABG versus PCI with stents were included and the probabilities of events for each available  
8 time point (1 year, 3 years, 5 years, and 10 years) were calculated as:

9 
$$P = r/n$$

10 Where r is the number of events in the CABG arm and n is the total number of patients  
11 randomised to CABG.

12 Probabilities of events at year 1 were taken directly from the meta-analysis for that time  
13 point. Probabilities at subsequent time points were calculated as follows:

14 
$$p_{t_2-t_1} = \frac{p_{t_2} - p_{t_1}}{1 - p_{t_1}}$$

15 Where

16  $p_{t_2-t_1}$  is the probability of an event between an initial time  $t_1$  and a subsequent time  $t_2$

17  $p_{t_1}$  is the total probability of events at the initial time  $t_1$

18 and  $p_{t_2}$  is the total probability of events at the subsequent time  $t_2$ .

19 Among the patients alive at follow-up, the proportions of those who had angina symptoms  
20 were obtained from those studies reporting the number or proportion of patients with angina  
21 or no angina. In some papers results were expressed as mean CCS score (e.g. Buszman et al.  
22 (2008){Buszman, 2008 9132 /id}) and were excluded. If papers reported the number of  
23 patients in each CCS scores we combined CCS 0 + I to represent the 'No Angina' state, and II  
24 + III + IV to represent the 'Angina' state. The overall proportion of patients with or without  
25 angina at a time-point is used in the model to determine the angina/no angina health state for  
26 the whole cohort reaching the end nodes. We assumed that the proportion in each cycle was  
27 the same as the proportion at the following available time point. For example, in cycles 6 to 9

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1 (corresponding to 3.5. up to 5 years) 78.84% of patients who are still alive have no angina in  
2 the CABG arm; this figure corresponds to the probability of being angina-free at 5 years.

3 Table 3 summarises the clinical effectiveness data used in the model.

4 Table 3 - Summary of estimates of effectiveness used in the base case model

Parameter	Time point	Probability at time x – CABG arm	Probability from time (x-n) to time x	RR PCI vs. CABG	Source
Death (all)	1 year	2.68%	-	1.18	Sigwart et al. 2002{Sigwart, 2002 3794 /id}, Eefting et al. (2003){Eefting, 2003 1030 /id}, Serruys et al. (2001){Serruys, 2001 3726 /id}, Buszman et al. (2008){Buszman, 2008 9132 /id}, Serruys et al. (2009){Serruys, 2009 3717 /id}, Hueb et al. (2004){Hueb, 2004 4637 /id}
	2 years	2.71%	0.37%	1.32	Unger et al. (2003){Unger, 2003 1120 /id}, Booth et al. (2008){Booth, 2008 267 /id}
	3 years	4.63%	1.97%	0.79	Serruys et al. (2005){Serruys, 2005 9140 /id}
	5 years	8.91%	4.49%	1.11	Serruys et al. (2005){Serruys, 2005 9140 /id}, Hueb et al. (2007){Hueb, 2007 2913 /id}
	10 years	25.12%	17.79%	0.95	Hueb et al. (2010){Hueb, 2010 15922 /id}
MI (all)	1 year	4.44%	-	1.20	Sigwart et al. 2002{Sigwart, 2002 3794 /id}, Eefting et al. (2003){Eefting, 2003 1030 /id}, Serruys et al. (2001){Serruys, 2001 3726 /id}, Serruys et al. (2009){Serruys, 2009 3717 /id}, Hueb et al. (2004){Hueb, 2004 4637 /id}

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	2 years	5.12%	0.73%	1.30	Unger et al. (2003){Unger, 2003 1120 /id}, Booth et al. (2008){Booth, 2008 267 /id}
	3 years	5.62%	0.52%	1.30	Serruys et al. (2005){Serruys, 2005 9140 /id}
	5 years	8.91%	3.49%	1.36	Serruys et al. (2005){Serruys, 2005 9140 /id}, Hueb et al. (2007){Hueb, 2007 2913 /id}
	10 years	10.34%	1.57%	1.27	Hueb et al. (2010){Hueb, 2010 15922 /id}
Repeat revascularisation	1 year	4.59%	-	3.55	Eefting et al. (2003){Eefting, 2003 1030 /id}, Serruys et al. (2001){Serruys, 2001 3726 /id}, Buszman et al. (2008){Buszman, 2008 9132 /id}, Serruys et al. (2009){Serruys, 2009 3717 /id}, Hueb et al. (2004){Hueb, 2004 4637 /id}
	2 years	5.70%	0.69%	4.42	Unger et al. (2003){Unger, 2003 1120 /id}, Booth et al. (2008){Booth, 2008 267 /id}
	3 years	6.61%	1.43%	4.03	Serruys et al. (2005){Serruys, 2005 9140 /id}
	5 years	7.43%	0.87%	4.15	Serruys et al. (2005){Serruys, 2005 9140 /id}, Hueb et al. (2007){Hueb, 2007 2913 /id}
Patients free of angina	6 months	85.20%	-	1.01	Eefting et al. (2003){Eefting, 2003 1030 /id}
	1 year	80.94%	-	0.87	Sigwart et al. 2002{Sigwart, 2002 3794 /id}, Eefting et al. (2003){Eefting, 2003 1030 /id}, Serruys et al. (2001){Serruys, 2001 3726 /id}, Hueb et al. (2004){Hueb, 2004 4637 /id}

	2 years	87.20%		0.92	Unger et al. (2003){Unger, 2003 1120 /id}
	3 years	87.20%	-	0.94	Legrand et al. (2004){Legrand, 2004 1001 /id}
	5 years	78.84%	-	0.92	Serruys et al. (2005){Serruys, 2005 9140 /id}, Hueb et al. (2007){Hueb, 2007 2913 /id}
	10 years	64.04%	-	0.91	Hueb et al. (2010){Hueb, 2010 15922 /id}

\* Data not used in the model as inconsistent with the trend.

Probability of death at 6 years was available from the study by Booth et al. (2008){Booth, 2008 267 /id}; however these data showed some inconsistencies when compared to the meta-analysis of all the studies at previous time points (i.e. lower mortality rate compared to previous year) and we decided not to use it in the model. The same decision was made for the repeat revascularisation at 10 years from Hueb et al. (2010){Hueb, 2010 15922 /id}, where the overall proportion of patients experiencing a repeat revascularisation was lower than that at 5 years as defined by the meta-analysis, which included the 5-year follow-up of the same study{Hueb, 2007 2913 /id}.

### 2.3.3 Utilities

For economic evaluation, a specific measure of HRQoL known as utility is required to calculate QALYs. Utilities indicate the preference for health states on a scale from 0 (death) to 1 (perfect health). The NICE reference case specifies that the preferred way for this to be assessed is by the EQ-5D instrument.

Utilities were attached to the health states in the model (angina, no angina, death) and decrements in HRQoL (disutilities) were calculated for the transitional events in the model (MI and initial revascularisation, in a sensitivity analysis also repeat revascularisation).

A systematic search identified few studies with de novo utility measures. We selected only those studies reporting utility values separately in patients with and without symptoms of angina. Serruys et al. (2001){Serruys, 2001 3726 /id} reported EQ-5D scores in a randomised trial of PCI versus CABG, but did not report EQ-5D scores separately for patients with or without angina. We therefore decided to use the utilities from another RCT{Melsop, 2003 8989 /id} on patients with multivessel coronary artery disease and angina or documented ischemia. In this study time trade-off scores in 400 patients with angina and in 58 patients without angina were obtained through telephone interviews in the USA. Scores in patients free of angina were significantly higher than scores in patients with angina ( $p < 0.01$ ). Disutility of CABG was calculated as a differential from the PCI intervention based on the study by Serruys et al. (2001){Serruys, 2001 3726 /id}. In this RCT, one month after the intervention patients in the surgery group had a EQ-5D score of 0.78 (SD  $\pm 0.17$ ) compared to 0.84 (SD  $\pm 0.16$ ) in patients one month after PCI. We assumed the difference in utility lasts only for one month as data up to this point was available. The total QALY loss is calculated as follows:

$$\text{QALY loss} = (u_{\text{PCI}} - u_{\text{CABG}}) / (12 \text{ months}) = (0.84 - 0.86) / 12 = 0.005$$

Where  
uPCI is the EQ-5D score in the PCI group one month after the intervention  
and uCABG is the EQ-5D score in the CABG group one month after the intervention.

However in a study by Scuffham et al. (2006){Scuffham, 2006 9238 /id}, the recovery time after CABG was considered to be 2.5 months. Compared to this study, we have underestimated the decrement in HRQoL after surgery.

To estimate the disutility after a MI, we used the value reported in the HTA by Ward et al. (2007){Ward, 2004 9021 /id}; this was obtained from personal communication with the author of a RCT{Goodacre, 2004 103 /id}. In this study{Goodacre, 2004 103 /id} EQ-5D questionnaires were administered to patients with chest pain for whom a record of diagnosis including MI was available. The EQ-5D scores for patients with MI was 0.760 (uMI); as 1 was the utility representing perfect health (uPH), the disutility due to MI (disMI) corresponds to:

$$\text{disMI} = -(\text{uPH} - \text{uMI}) = -(1 - 0.760) = -0.24$$

This figure was divided by 2 to reflect the six-month cycle length.

Utilities used in the base case analysis are reported in Table 4.

**Table 4 - Utility values used in the model**

Parameter	Base case value	Source
Utility no angina	0.87 (SE 0.0435)	Melsop 2003{Melsop, 2003 8989 /id}
Utility angina	0.703 (SE 0.0923)	Melsop 2003{Melsop, 2003 8989 /id}
Immediate disutility CABG (QALYs lost)	-0.005	Calculated from Serruys2001{Serruys, 2001 3726 /id}
Immediate disutility MI (QALYs lost)	-0.24	Calculated from Ward2007{Ward, 2004 9021 /id}

While in the base case the disutility from CABG was estimated as a differential from PCI and no disutility was attached to PCI, in a sensitivity analysis we have calculated the disutility from both PCI and CABG as differentials from the No Angina state. In this way we incorporated an estimate of the disutility associated with the repeat PCI during follow-up (see 3.2). In another study identified in our search{Shrive, 2007 9345 /id}, EQ-5D scores were calculated for patients in the procedure subgroups: event free, repeat PCI, repeat CABG. In a sensitivity analysis we used the differential utility between the event free group (0.85) and the repeat PCI group (0.77) to estimate the disutility associated with the repeat revascularisation, assuming it lasts for one month. Results are reported in 3.2.

### 2.3.4 Resource use and cost

Costs are associated either with initial strategy (CABG or PCI), health states ('angina' or 'no angina'), or transitional events (MI, revascularisation, and development of angina).

#### 2.3.4.1 Cost of initial strategy

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1 The cost of the initial strategy is used in the first cycle of the model (cycle 0). Cost components  
2 are described in Table 5 and comprise the cost of initial procedure, necessary medical  
3 therapy following PCI, cost of medical treatment as for the 'no angina' state (see 2.3.4.2) and  
4 rehabilitation. In a study by Bethell et al. (2007){Bethell, 2009 162 /id} a different  
5 proportion of patients have rehabilitation after CABG compared to PCI. However in the  
6 model we assume everyone undergoes rehabilitation regardless of their initial intervention.  
7

8 **Table 5 - Initial cost of intervention**

	CABG	PCI	Source
Cost of initial procedure - CABG	£7,959	-	NHS Reference Costs 2008-09, Elective Inpatient CABG 1st time{Department of Health, 10 A.D. 15958 /id}
Cost of initial procedure - PCI	-	£2,610	NHS Reference Costs 2008-09, Elective Inpatient PCI 0 – 2 stents Or PCI 3 or more stents (EA49Z){Department of Health, 10 A.D. 15958 /id}
Cost of additional stents	-	4 * £300	Experts opinion
Treatment with Clopidogrel for 12 months*	-	12*£36.35	BNF 59{Royal Pharmaceutical Society of Great Britain, 2010 15947 /id}
Medical treatment (no Angina)	£43	£42.55	BNF 59{Royal Pharmaceutical Society of Great Britain, 2010 15947 /id}
Rehabilitation	£550	£550	Bethell et al. (2007){Bethell, 2009 162 /id}
<b>TOTAL</b>	<b>£8,552</b>	<b>£4,839</b>	

9 \* the total 12 month cost of the treatment was added to the first 6-month cycle

10  
11 In the NHS reference costs{Department of Health, 10 A.D. 15958 /id}, the cost of PCI  
12 procedure includes the cost of 0 to 2 stents. In our model, patients had multi-vessel disease  
13 and would have more than two stents. We asked the experts of our GDG to estimate the  
14 average number of stents required in this intervention for the included population (4 stents).  
15 We could not find the cost of stents from publicly available sources therefore the GDG  
16 experts provided us with this estimate as well (£300 each).  
17

18 In the review of the economic literature we found a study{Weintraub, 2004 114 /id}  
19 comparing the one-year costs of PCI and CABG in patients enrolled in the SoS trial, which was  
20 included in our review of clinical effectiveness (see Appendix E and Appendix G). In this study  
21 the cost of the initial procedure including hospitalisation and ward costs was higher in the  
22 CABG group compared to the PCI group (£7,321 vs. £3,884; p<0.05). These figures are very  
23 similar to the initial cost calculated in our model.

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1 **2.3.4.2 Cost of health states**

2 The possible health states in which a patient could be in the model are 'angina', 'no angina'  
3 and 'death'. We collected information on the resources used while in these states from the  
4 GDG experts (data on medications use from a GP practice) which were supported by the  
5 estimates of medications used in patients randomised to optimal medical treatment in the  
6 COURAGE trial{Weintraub, 2008 9247 /id}. We estimated the 6-month costs of the defined  
7 medical treatment based on national sources of unit costs{Royal Pharmaceutical Society of  
8 Great Britain, 2010 15947 /id}.

9 Patients who still have angina symptoms after the intervention are treated medically  
10 according to the treatment profile reported in Table 6.

11 **Table 6 - Resources and cost of medical treatment in patients with angina**

Class of drug	Name of drug <sup>a</sup>	Proportion of patients treated <sup>b</sup>	Total cost for 6 months <sup>c</sup>
Statins	Simvastatin 40mg 1/day	100%	£9.15
Aspirin	Aspirin 75 mg, 1/day	100%	£6.40
BB and CCB	Bisoprolol 5mg 1/day Amlodipine 10mg 1/day	Total 100% (BB 85%, CCB 15%)	£7.85
Ivabradine	Ivabradine 5mg, 2/day	2%	£5.10
ACE inhibitors and ARB	Ramipril 5mg 1/day Losartan 50mg 1/day	Total 100% (ACE 75%, ARB 25%)	£27.00
Other drugs	Nicorandil 20mg, 2/day	5%	£4.75
Nitrates	Isosorbide mononitrate 20mg, 2/day	16%	£1.14
<b>Total</b>			<b>£61.39</b>

13 a) The most commonly used drug within the same class was identified by the GDG experts  
14 b) Data from a GP practice (personal communications).  
15 c) Source of cost BNF 59{Royal Pharmaceutical Society of Great Britain, 2010 15947 /id}. Cost of drugs was  
16 calculated using the lowest cost of non-proprietary medicines. E.g. if capsules were cheaper than tablets then the  
17 cost of capsules was used.

18  
19 In a sensitivity analysis we have increased the cost of medications in the angina state based on  
20 the annual cost reported in the study by Ward et al. (2007){Ward, 2004 9021 /id} which  
21 was £171; we added the cost of statins (reported in Table 6) to this figure.

22 In the model, patients with no angina would still be medically treated to prevent  
23 cardiovascular events. Drugs used and the computation of their cost are reported in Table 7.

24 **Table 7 - Resources and cost of medical treatment in patients with no angina symptoms**

Class of drug	Name of drug	Proportion of patients	Total cost for 6 months*
Statins	Simvastatin 40mg 1/day	100%	£9.15
Aspirin	Aspirin 75 mg, 1/day	100%	£6.40
ACE inhibitors and ARB	Ramipril 5mg 1/day Losartan 50mg 1/day	Total 100% (ACE 75%, ARB 25%)	£27.00
<b>Total</b>			<b>£42.55</b>

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\* Source of cost BNF 59{Royal Pharmaceutical Society of Great Britain, 2010 15947 /id}. Cost of drugs was calculated using the lowest cost of non-proprietary medicines. E.g. if capsules were cheaper than tablets then the cost of capsules was used.

No costs were associated with the death state.

**2.3.4.3 Cost of transitional events**

Transitional events in the model were MI, further revascularisation, and the appearance of angina symptoms (event preceding the ‘angina’ health state).

Each of these events is associated with some costs (Table 8).

The cost of MI was obtained from the Acute Coronary Syndromes Guideline{National Clinical Guideline Centre for Acute and Chronic Conditions, 2010 15960 /id}, and it incorporates the cost of hospital stay, ambulance and A&E.

When a further revascularisation was required according to the clinical probability (2.3.2), this was assumed to be a PCI and its cost as calculated in 2.3.4.1 was used. This assumption was varied in a one-way sensitivity analysis where we increased the proportion of CABG/PCI as revascularisation procedure up to 1. The cost of CABG was used for the selected proportion of patients undergoing this procedure.

Patients who transit from the ‘no angina’ state to the ‘angina’ state are all assumed to incur the costs of a cardiology outpatient consultation, myocardial perfusion scan with SPECT, and coronary angiography as reported in Table 8.

Table 8 - Cost of transitional events in the model

Event in the model	Resource	Cost	Source
MI	Hospital stay, ambulance and A&E	£1,783	Acute Coronary Syndromes Guideline{National Clinical Guideline Centre for Acute and Chronic Conditions, 2010 15960 /id}
	TOTAL £1,783		
Further revascularisation	PCI procedure	£2,610	NHS Reference Costs 2008-09, Elective Inpatient PCI 0 – 2 stents
	Stents	4*£300	Or PCI 3 or more stents (EA49Z){Department of Health, 10 A.D. 15958 /id}
	TOTAL £3,810		Experts opinion
Transition to ‘angina’ state	Referral to cardiologist	£112	NHS Reference Costs 2008-09 - Consultant Led: Follow up Attendance Non-Admitted Face to Face - Cardiology{Department of Health, 10 A.D. 15958 /id}
	Invasive coronary angiography	£841	NHS Reference Costs 2008-09, Day cases, HRG EA41Z - Other Non-Complex Cardiac Surgery + Catheterisation{Department of Health, 10 A.D. 15958 /id}
	Myocardial perfusion scan	£293	Chest Pain



	with SPECT		guideline{National Clinical Guideline Centre for Acute and Chronic Conditions, 2010 15959 /id}
TOTAL £1,246			

1  
2  
3

## 4 **2.4 Computations**

5 The mean cost and effectiveness of the two strategies were calculated using TreeAge Pro  
6 2008. The incremental cost-effectiveness ratio was calculated in Microsoft Office Excel 2007.

### 7 **2.4.1 Calculating QALYs gained**

8 For each strategy, the expected QALYs in each cycle are calculated as follows:

$$9 \quad \text{Expected QALYs} = \text{Dis}U_p + \sum_{j=1}^{19} \sum_{i=1}^3 U_i P_{ij} + \sum_{j=1}^{19} \sum_{x=1}^3 \text{Dis}U_x P_{xj}$$

10 where

11  $\text{Dis}U_p$  = the disutility for the initial intervention p

12  $U_i$  = the utility score for health state i

13  $P_i$  = the proportion of patients in health state i

14  $\text{Dis}U_x$  = the disutility for event x

15  $P_{xj}$  = the probability of event x in cycle j

16 and where intervention p could be either PCI or CABG, health state i could be any of  
17 health states represented by the green boxes in

18 Figure 1 (death, angina, no angina) and event x could be MI or further revascularisation.

19 The proportion of patients in each health state depends on the effectiveness of the treatment,  
20 in terms of mortality and improvement of symptoms.

21 QALYs were then discounted to reflect time preference. QALYs during cycle 0 were not  
22 discounted. The total discounted QALYs was the sum of the discounted QALYs per cycle.

23 The overall 10-year expected QALYs are given by the sum of the discounted QALYs  
24 calculated for each cycle. The *incremental QALYs gained* associated with a treatment strategy  
25 are calculated as the difference between the expected QALYs with that strategy and the  
26 expected QALYs with the comparator.

27

### 28 **2.4.2 Calculating costs**

29 For each strategy, the expected cost per cohort of patients is calculated as follows:

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1            
$$\text{Expected cost} = C_s + \sum_{j=1}^{19} \sum_{i=1}^3 C_i P_{ij} + \sum_{j=1}^{19} \sum_{x=1}^3 C_x P_{xj}$$

2    where

3             $C_s$  = cost of the initial strategy (PCI or CABG)

4             $C_i$  = cost of health state  $i$

5             $P_{ij}$  = proportion of patients in health state  $i$  in cycle  $j$

6             $C_x$  = cost of event  $x$

7             $P_{xj}$  = probability of event  $x$  in cycle  $j$

8            and where health state  $i$  could be any of the health states represented by the green  
9            boxes in

10          Figure 1 (death, angina, no angina), and event  $x$  could be any of the events described in  
11          Table 8.

12          The proportion of patients in each health state depends on the effectiveness of the treatment,  
13          in terms of mortality and improvement of symptoms.

14          Future costs (those occurring after cycle 1) were discounted to reflect time preference.

15          The overall 10-year expected costs are given by the sum of the discounted costs calculated  
16          for each cycle. The incremental cost associated with a treatment strategy is calculated as the  
17          difference between the expected cost with that strategy and the expected cost with the  
18          comparator.

19          **2.4.3 Calculating cost-effectiveness**

20          The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This  
21          is calculated by dividing the difference in costs associated with two alternatives by the  
22          difference in QALYs. The decision rule then applied is that if the ICER falls below a given cost  
23          per QALY threshold then the result is considered to be cost-effective. If both costs are lower  
24          and QALYs are higher the option is said to dominate and an ICER is not calculated.

25            
$$ICER = \frac{\text{Costs (B)} - \text{Costs (A)}}{\text{QALYs (B)} - \text{QALYs (A)}}$$

26          Where:

27             $\text{Costs/QALYs}(X)$  = total discounted costs/QALYs for option  $X$

28            Option B is cost-effective if:  $ICER < \text{Threshold}$

29          It is also possible, for a particular cost-effectiveness threshold, to re-express cost-effectiveness  
30          results in term of net benefit (NB). This is calculated by multiplying the total QALYs for a  
31          comparator by the threshold cost per QALY value (for example, £20,000) and then  
32          subtracting the total costs. The decision rule then applied is that the comparator with the  
33          highest NB is the most cost-effective option at the specified threshold. That is the option that

1 provides the highest number of QALYs at an acceptable cost. For ease of computation NB is  
2 used to identify the optimal strategy in the probabilistic analysis simulations.

3 
$$Net\ Benefit(X) = QALYs(X) \times D - Costs(X)$$

4 Where: Costs/QALYs(X) = total discounted costs/QALYs for option X; D = cost-effectiveness  
5 threshold

6 The probabilistic analysis was run for 10,000 simulations. For each simulation, total discounted  
7 costs and total discounted QALYs were calculated for each treatment option. The net benefit  
8 was also calculated and the most cost-effective option identified (that is, the one with the  
9 highest net benefit), at a threshold of £20,000 per QALY gained.

10 The results of the probabilistic analysis were summarised in terms of mean discounted costs  
11 and QALYs with confidence intervals, where means were the average of the 10,000 simulated  
12 estimates and the 95% confidence intervals are the 2.5 and 97.5 percentiles. A cost-  
13 effectiveness ratio was calculated from the mean costs and QALYs. The percentage of  
14 simulations where each strategy was the most cost-effective gives an indication of the strength  
15 of evidence in favour of that strategy being cost-effective.

#### 16 **2.4.4 Interpreting results**

17 Our analysis was built around clinical data and costs for patients with multi-vessel disease who  
18 are eligible for both procedures. Consideration will be given to the fact that in patients with  
19 single vessel disease PCI is likely to be less costly and have the same effectiveness. In many  
20 parameters of our model we have favoured CABG, e.g. we excluded stroke from the  
21 outcomes, and we have included RCTs where a mix of stent and non-stent PCI was used  
22 (MASS-II trial){Hueb, 2010 15922 /id}.

## 24 **3 Results**

### 25 **3.1 Base case results**

26 The base case results show that CABG generates more QALYs than PCI over a ten-year  
27 period but it generates more costs too (Table 9). The ICER is above what NICE considers to be  
28 cost-effective (£20,000/QALY). Therefore PCI is the most cost-effective choice among these  
29 two procedures for patients with characteristics similar to the ones enrolled in the trials  
30 included in the analysis.

31 **Table 9 - Results of base case analysis**

Strategy	Cost	Incr Cost	Eff	Incr Eff	ICER
PCI Stents	£10,638		6.1167		
CABG	£13,085	£2,447	6.1992	0.0825	£29,661

33  
34 Table 10 reports the costs associated with the different types of resources considered in the  
35 model.

36 **Table 10 – Cost breakdown – discounted cost per patient in the PCI and CABG strategy**

Cost category	PCI	CABG
Procedures (including	£4,816	£8,221

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repeats)		
Drugs	£1,165	£715
Further assessments	£3,895	£3,431
Treating MI	£212	£168
Rehabilitation	£500	£500
TOTAL	£10,638	£13,085

Overall CABG decreases those costs which occur later in the model (medication, further assessments, and treatment of MI) but in terms of cost of procedures CABG largely exceeds the cost in the PCI group even when the probability of repeating the procedure (higher in the PCI group) is accounted for.

## 3.2 Sensitivity analysis

### 3.2.1 Deterministic sensitivity analyses

The main driver of the results was the high initial cost of the CABG procedure.

Since PCI is associated with higher rates of repeat revascularisation, we have explored if results were sensitive to the future costs both by eliminating the discounting for costs and effectiveness (which in the base case favours interventions with low initial costs even if associated with higher future costs) and by changing the assumption around the type of procedure used as a repeat revascularisation (PCI in all the cases in the base case; CABG was possible in the sensitivity analysis).

In the base case the initial disutility associated with the CABG intervention was calculated incrementally compared to PCI; in a sensitivity analysis we have incorporated the disutility of repeating PCI by calculating the decrement in HRQoL as a differential from the 'no angina' state. We have also used alternative data on disutilities obtained from a separate study{Shrive, 2007 9345 /id}.

Our clinical data were limited to a 10-year period; however we could extrapolate data to a lifetime horizon assuming a constant rate of events except for death which was assumed to be equal to the general population after 10 years from the intervention and therefore did not vary according to the initial intervention.

The results of the sensitivity analyses conducted are reported in Table 11.

**Table 11 - Results of sensitivity analyses**

Type of sensitivity analysis	Result
No discount rate	ICER CABG vs. PCI = £24,016/QALY
Threshold analysis on proportion of CABG as repeat revascularisation procedure	PCI is the most cost-effective initial strategy if less than 85% of the repeat revascularisation procedures are CABG
Disutilities of PCI and CABG calculated as differential from 'no angina' state	ICER CABG vs. PCI = £28,850/QALY
Threshold analysis on proportion of CABG as repeat revascularisation procedure after disutilities of PCI and CABG were calculated as differential from 'no angina' state	PCI is the most cost-effective initial strategy if less than 83% of the repeat revascularisation procedures are CABG
Disutility of PCI calculated from Shrive et al. (2007){Shrive, 2007 9345 /id}	ICER CABG vs. PCI = £27,070/QALY

Cost of medication in the angina state = £171 per year excluding simvastatin{Ward, 2004 9021 /id}	ICER CABG vs. PCI = £29,354/QALY
Lifetime horizon (mean patient's age = 65)	ICER CABG vs. PCI = £20,050/QALY

1

2 **3.2.2 Probabilistic sensitivity analysis**

3 The results of the PSA show the uncertainty over the base case results (Table 12). In non-linear  
4 models, such as Markov models, there is often a difference between the deterministic and  
5 probabilistic results and in such cases the probabilistic results should take precedence.

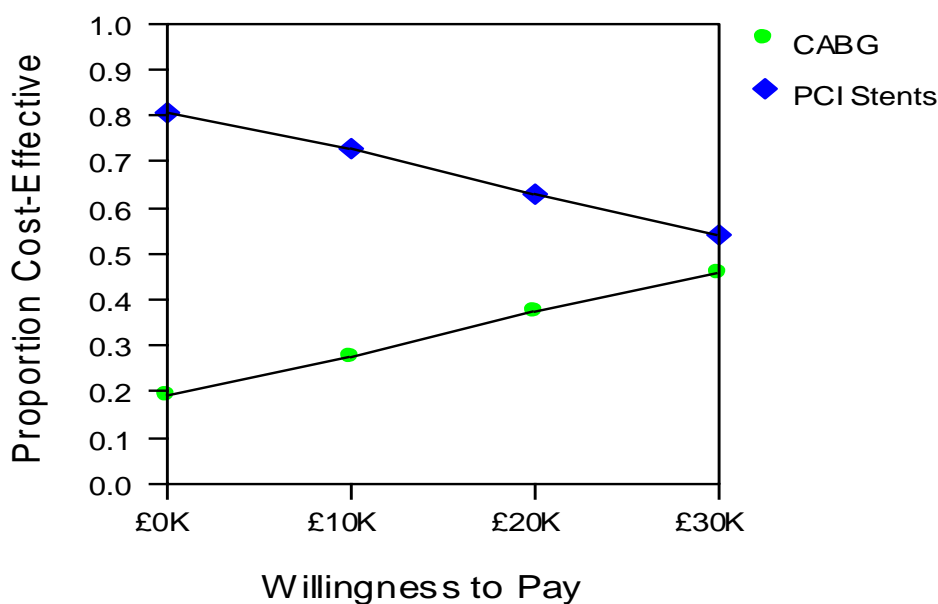
6 If we consider a 95% confidence interval the base case results did not reach statistical  
7 significance.

8 **Table 12 - Results of PSA - CABG vs. PCI**

Mean cost (£)	Mean QALYs	Mean ICER (£/QALY)	95% CI – lower limit (£/QALY)	95% CI – upper limit (£/QALY)	Probability of being cost-effective at £20,000/QALY
PCI 10,555	PCI 6.0857	34,971	CABG dominates	PCI dominates	PCI 63%
CABG 12,982	CABG 6.1551				CABG 37%

9

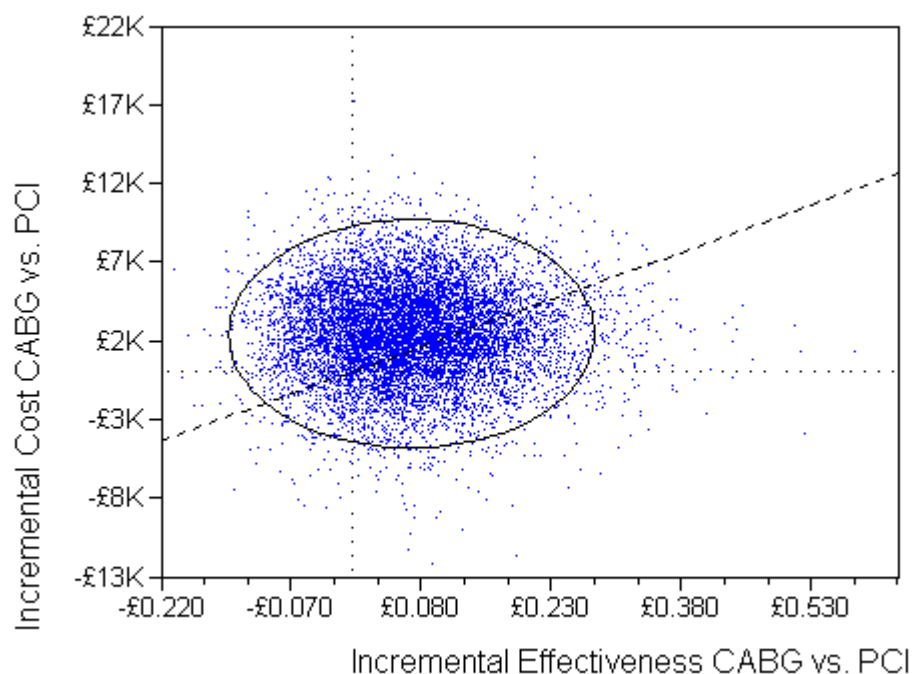
10 At a willingness to pay of £20,000/QALY PCI has only a 63% probability of being cost-  
11 effective; the two interventions have a similar probability (54% and 46% respectively for PCI  
12 and CABG) when a £30,000/QALY threshold is adopted (Figure 2).



13

14 **Figure 2 - Acceptability curve of PCI and CABG**

1 The uncertainty can also be graphically represented by plotting the results of the incremental  
2 analysis for all the 10,000 simulations into a cost-effectiveness plane (Figure 3). Each point  
3 represents the ICER of CABG vs. PCI for each simulation. The dotted line represents the  
4 £20,000/QALY threshold: the dots below the line indicate a simulation where CABG was cost-  
5 effective and those above the line where CABG was not cost-effective. The ellipse delimits the  
6 95% confidence area.



7

8 **Figure 3 - Incremental cost-effectiveness scatterplot - CABG vs. PCI**

9

## 10 **4 Discussion**

### 11 **4.1 Summary of results**

12 A new cost-utility analysis was developed which compared CABG and PCI as a  
13 revascularisation procedure for patients with angina who are eligible for both. This was based  
14 on the RCT data identified in the clinical review; the clinical outcomes incorporated in the  
15 model were mortality, myocardial infarction, repeat revascularisation, and presence of angina  
16 symptoms. Costs and QALYs were considered from a NHS and personal social services  
17 perspective.

18 We found that CABG was not cost effective when compared to PCI. This conclusion was robust  
19 to various deterministic sensitivity analyses; however, when parameters were varied  
20 simultaneously in a PSA the results were uncertain.

### 21 **4.2 Limitations & interpretation**

22 The analysis is based on clinical studies and therefore issues concerning the interpretation of  
23 the clinical studies also apply to the interpretation of the economic analysis. One of the main

1 limitations of the model is the possibility that the included population is not representative of  
2 the general population of patients with angina. Moreover, the trials in the analysis were  
3 conducted over a long time period and the use of different surgical and percutaneous  
4 techniques may have influenced the relative risks and benefits of the two revascularisation  
5 strategies.

6 The model structure was kept simple and did not incorporate the different mortality rate in  
7 patients with MI or angina. This was a pragmatic approach because the trials did not report  
8 different mortality rates in people with MI or angina in each arm.

9 We had to disregard some clinical data (i.e. mortality at 6 years from the SoS trial, and  
10 repeat revascularisation at 10 years from MASS-II trial) because they were inconsistent with  
11 the trend from the meta-analysis of all the studies at previous time points; in fact, the  
12 cumulative proportion of patients who were alive in the SoS trial or who had a repeat  
13 procedure in the MASS-II trial was smaller than the proportion at the previous time point  
14 calculated from the meta-analysis of clinical studies. In the latter example, the meta-analysis  
15 at a previous time point included the MASS-II trial as well.

16 HRQoL data were not available from most of the trials; some values were available from the  
17 ARTS study{Legrand, 2004 1001 /id}; however, had we used HRQoL outcomes from one trial  
18 we would have had to disregard the intermediate clinical outcomes (incidence of MI, angina  
19 symptoms) from other trials. In our model we used one estimate of utility attached to the  
20 'angina' health state, thus we did not capture the possible impact of differences in symptom  
21 severity.

22 We decided not to include stroke in the analysis because of concern about heterogeneity in  
23 the definition of stroke across the studies. Furthermore many assumptions on the severity and  
24 cost of treatment for stroke would have had to be made. Since the results of the model  
25 showed that PCI was more cost-effective and stroke was more frequent in the CABG group  
26 (see chapter 12) inclusion of stroke in the model would not have changed the overall result.

27 Furthermore, our analysis has been unfavourable to PCI as we added the cost of additional  
28 stents to the basic cost of the procedure, which already included the use of some stents. In  
29 addition, for every patient developing angina in any cycle after the initial intervention we  
30 included the costs of a referral, myocardial perfusion scan with SPECT, and coronary  
31 angiography, and this is likely to overestimate the true requirement for these additional  
32 procedures.

33

### 34 **4.3 Generalisability to other populations / settings**

35 Individuals participating in the trials included in the analysis were a highly selected  
36 population. The analysis was based on randomised trials of PCI versus CABG and the results  
37 only directly apply to patients considered eligible for either revascularisation procedure.

38 A validated risk score for patients with stable angina is not available and therefore a  
39 stratified analysis on different baseline risk was not performed as in practice the baseline risk  
40 cannot be precisely quantified.

41 Patients in the trials had multi-vessel disease; in single vessel disease the repeat  
42 revascularisation rate is generally lower compared to multi-vessel disease and PCI is likely to  
43 be an even more cost-effective option for this group of patients.

1

#### 2 **4.4 Comparisons with published studies**

3 All the studies identified in our review (see Chapter 12 and economic evidence tables in  
4 Appendix G) consistently reported higher cost of CABG compared to PCI. The difference in  
5 costs tends to decrease when a longer follow-up time was considered (e.g. in the ARTS  
6 study{Legrand, 2004 1001 /id}, RITA trial{Henderson, 1998 263 /id}). Of the other three  
7 cost-utility analyses{Eefting, 2003 1030 /id;Griffin, 2007 53 /id;Weintraub, 2004 114 /id},  
8 two{Eefting, 2003 1030 /id;Weintraub, 2004 114 /id} showed that CABG was not cost-  
9 effective but their analysis was limited to a one-year time horizon. The other analysis{Griffin,  
10 2007 53 /id} concluded that CABG was cost-effective in patients suitable for both  
11 procedures; however this study was based on non-randomised data and probably most of the  
12 PCI procedures were without stents.

13 Our analysis included the routine use of stent during PCI procedures, and combines short and  
14 long follow-up data from a systematic review of RCTs.

15

#### 16 **4.5 Conclusion= Evidence statement**

17 Our analysis suggests that CABG is effective but not cost-effective compared with PCI for  
18 patients eligible for both procedures but there is some uncertainty around this conclusion.

19

#### 20 **4.6 Implications for future research**

21 Had a validated score for risk stratification for stable angina been available at the time of  
22 our analysis we could have identified the most appropriate population for each of the  
23 interventions compared. This would mean the resources are distributed more cost-effectively  
24 (i.e. offering CABG or PCI only to those patients that would benefit more from the  
25 intervention).

26