Drug-eluting stents:

a systematic review & economic evaluation

3’ Addendum

NICETAR 04/42

No commercial in confidence data have been included in the preparation of this report

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Addendum - additional evidence and analyses requested by Appraisal Committee

1. Introduction

1.1 Overview of scope of additional evidence and analyses

The first Appraisal Committee meeting for the drug-eluting stents (DES) appraisal was held on 1 February 2006. Clinical experts attending the meeting provided reference to additional available data on outcomes related to the use of DES. The conclusion reached by the committee was that they would appreciate additional economic analysis taking into consideration these data as well as further consideration of specific outcomes. An outline of the proposed additional analysis was developed by NICE and forwarded to the assessment group for response. The assessment group replied with a list of analysis that could be carried out and reported within the available timeframe (see Appendix 1).

This addendum provides information regarding expanded data sources utilised and additional analyses, as requested.

1.2 Overview of Data Sources

Several of the issues raised by the Appraisal Committee for further consideration involve careful examination of evidence from non-RCT studies of observational or audit data. Before discussing the uses to which we put such evidence it is important to provide a brief description of each source and aspects affecting its suitability for addressing the Appraisal Committee's questions.

Scottish Coronary Revascularisation Register 2003-2004 (UK) [1]

This is an annual review of information from all sites in Scotland carrying out interventional cardiology. Detailed data are provided of caseloads for 2003/4, particularly relating to percutaneous coronary interventions (PCIs) carried out as elective/stable or non-elective/unstable procedures. The coverage is good overall, but for some of the procedural information the coverage is only partial. Long-term

outcomes are provided for 30 days, 1 year and 5 years for mortality, acute myocardial infarction (AMI) and repeat revascularisation.

There are two important caveats relating to these outcome results:

- significant numbers of non-stented PCIs are included in the tabulations, which are likely to lead to overstating of some outcome results;

- the main long-term outcomes are calculated from patients treated over multiple years beginning at 1997, during which the take-up of stenting has increased rapidly. This inevitably means that the reported outcomes for repeat revascularisation will be overstated.

To clarify the problem of multiple years we have consulted a peer-reviewed publication reporting findings from the Scottish Coronary Revascularisation Register (SCRR) for the years 1997-9.[2]

BCIS Audit of Adult Interventional Procedures 2003 (UK) [3]

An annual audit of virtually all PCIs undertaken in the UK, including multiple outcomes and process measures, including procedural mortality and re-intervention rates. This is a comprehensive database of proven quality and credibility.

Cardiothoracic Treatment Centre Audit Database (UK) [4]

All stented PCI patients treated in two calendar years (2000-1 when drug-eluting stent use was minimal) were followed up for 12 months. Outcomes available include in-hospital mortality, and repeat revascularisation rates at 12 months. A multi-variate risk model was developed and is published, and described in the main Assessment Report.

Glenfield Hospital, Leicester Audit (UK) [5]

A review of clinical audit data on 1112 stented patients treated in 2003, available only in abstract. The authors report target lesion revascularisation (TLR) rates at 12 months.

APPROACH database (Canada) [6]

Outcomes from analysis of 7334 patients undergoing PCI with bare metal stents (BMS) between 1998 and 2000 are reported from the APPROACH database (which captures all patients undergoing cardiac catheterisation in Alberta, Canada). In a high proportion of cases (47%) the indication was AMI, and only 20% were for stable angina. Peri-procedural mortality, all-cause mortality at 6 months and repeat revascularisation at 12 months are reported. The APPROACH database is well known as a comprehensive and reliable source of evidence.

Agema (Netherlands) [7]

A multi-centre study at four academic hospitals involved a total of 3177 consecutive non-STEMI patients who underwent PCI in 1999-2001 were followed up and outcomes reported at 9 and 12 months for clinical restenosis and TVR. Only 77% of patients were stented. Various outcomes, and several multivariate models for risk indicators are reported.

BASKET (Switzerland) [8]

This is a randomised trial of almost all stented PCI patients in one Swiss hospital treated between 2003 and 2005, including 21% STEMI cases. Outcomes are reported at 6 months for cardiac death, AMI and TVR. This is the only 'real-life' independent RCT so far reported of drug-eluting stent (DES) versus BMS.

Medicare 5% sample (USA) [9]

A paper published recently in Circulation reports on a series of cross-sectional analyses of diagnostic and interventional procedures in a 5% sample of the national database for Medicare patients (i.e. the elderly) in the USA for the period 1993 to 2001. This covers a period of rapid changes and describes the expansion in cardiac diagnostic services (stress testing and cardiac catheterisation) and treatments (PCI and CABG). These trends are set against the annual rate of hospital admissions for AMI in the same population, as a proxy for the underlying prevalence of coronary artery disease.

The authors detail the proportion of PCIs involving stent deployment each year, as well as the proportion of patients receiving a further revascularisation within 6 months. No mention is made of mortality rates, life expectancy or sub-groups relevant to UK. The results include patients undergoing PCI as primary treatment for AMI (though probably a small proportion), and requires adjustment for the large shift during the period from balloon angioplasty to stented PCI. During the reported period the use of DES is likely to have been very limited.

Medicare in Ontario (Canada) [10]

This paper was published in the same issue of Circulation as the US Medicare paper, and follows a similar methodology, but uses record linkage of multiple databases across the whole adult population of Ontario. The authors concentrate on the financial impact of the changes in service levels over time and report no outcome measures. However, they do report the annual rate of hospital admissions for AMI. The treatment rates show much lower rates of testing and intervention than in the US, and these are broken down by age (<65 and 65+).

Toulouse (France) [11]

A prospective analysis of patients treated with stented PCI in a three year period (1996-9) in a French hospital was designed to compare the performance of the four most commonly used types of BMS. Only patients in whom types of stents were mixed were excluded. Follow-up was for 24 months. Three types of stents were of a similar era, but one used a silicon carbide coating and represented a newer phase of

development. Repeat revascularisation rates (TLR) were reported, and risk modelling undertaken.

Cleveland (USA) [12]

A retrospective analysis of any repeat revascularisation at 9 months follow-up for 5,239 consecutive BMS patients treated between 1994 and 2001 at a single US centre. Patients were excluded for coil stents use, technical failure, brachytherapy, staged procedure or stent thrombosis within 30 days.

Washington State (USA) [13]

This is a study of 3571 non-emergent first PCIs carried out in 26 locations in Washington state during 1999. Stent placement was recorded in 87.7% of patients. Figures are reported for all revascularisations within 12 months of the index procedure.

The following sections present the results of the additional analysis carried out by the Assessment Group and the order mirrors the list of analysis presented in Appendix 1.

2. Wastage Rates

In all Base Case analyses an assumption was made on clinical advice that 5% of stents purchased are not implanted for any reason and therefore wasted. This factor was incorporated as a simple on-cost to all stent prices in the model (BMS and DES) resulting in a corresponding 5% addition to the price premium. In order to test the sensitivity to this assumption, we have recalculated all Base Case results with both 1% and 10% wastage rates as shown in Tables A2.1-A2.6.

The differences from the main report results relate only to costs (not outcomes), and lead to minor variation in cost/utility ratios insufficient on their own to have any material impact on judgements of cost-effectiveness.

Table A2.1: Stent Wastage sensitivity analysis - All Elective patients

With 1% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£969	0.001932	**£501,300**	£879	0.001384	**£635,300**	£1,047	0.002084	**£502,500**	£1,193	0.004108	**£290,400**	£1,311	0.006096	**£215,100**
		Cypher	£1,041	0.001932	**£538,600**	£943	0.001384	**£681,600**	£1,125	0.002084	**£539,900**	£1,288	0.004108	**£313,500**	£1,422	0.006096	**£233,200**
	Broad	Taxus	£927	0.002572	**£360,300**	£849	0.001841	**£461,100**	£1,002	0.002773	**£361,300**	£1,103	0.005466	**£201,900**	£1,178	0.008111	**£145,300**
		Cypher	£998	0.002572	**£388,200**	£913	0.001841	**£495,700**	£1,079	0.002773	**£389,200**	£1,198	0.005466	**£219,100**	£1,287	0.008111	**£158,700**
Actual	Narrow	Taxus	£752	0.001932	**£389,200**	£687	0.001384	**£496,200**	£813	0.002084	**£390,200**	£907	0.004108	**£220,800**	£979	0.006096	**£160,600**
		Cypher	£947	0.001932	**£490,200**	£860	0.001384	**£621,600**	£1,024	0.002084	**£491,400**	£1,165	0.004108	**£283,500**	£1,278	0.006096	**£209,700**
	Broad	Taxus	£711	0.002572	**£276,600**	£657	0.001841	**£357,100**	£769	0.002773	**£277,400**	£820	0.005466	**£150,100**	£851	0.008111	**£104,900**
		Cypher	£905	0.002572	**£352,100**	£830	0.001841	**£450,800**	£979	0.002773	**£353,000**	£1,075	0.005466	**£196,800**	£1,146	0.008111	**£141,300**

With 5% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,011	0.001932	**£523,200**	£917	0.001384	**£662,500**	£1,093	0.002084	**£524,400**	£1,248	0.004108	**£303,900**	£1,375	0.006096	**£225,600**
		Cypher	£1,086	0.001932	**£561,900**	£983	0.001384	**£710,600**	£1,174	0.002084	**£563,300**	£1,347	0.004108	**£328,000**	£1,490	0.006096	**£244,500**
	Broad	Taxus	£969	0.002572	**£376,600**	£886	0.001841	**£481,400**	£1,047	0.002773	**£377,600**	£1,158	0.005466	**£211,900**	£1,241	0.008111	**£153,100**
		Cypher	£1,043	0.002572	**£405,600**	£952	0.001841	**£517,300**	£1,128	0.002773	**£406,600**	£1,256	0.005466	**£229,800**	£1,355	0.008111	**£167,000**
Actual	Narrow	Taxus	£786	0.001932	**£406,600**	£717	0.001384	**£517,900**	£850	0.002084	**£407,600**	£951	0.004108	**£231,500**	£1,030	0.006096	**£169,000**
		Cypher	£989	0.001932	**£511,700**	£897	0.001384	**£648,200**	£1,069	0.002084	**£512,900**	£1,219	0.004108	**£296,800**	£1,341	0.006096	**£220,000**
	Broad	Taxus	£745	0.002572	**£289,600**	£687	0.001841	**£373,200**	£805	0.002773	**£290,400**	£864	0.005466	**£158,000**	£901	0.008111	**£111,000**
		Cypher	£946	0.002572	**£368,000**	£867	0.001841	**£470,700**	£1,023	0.002773	**£369,000**	£1,129	0.005466	**£206,600**	£1,208	0.008111	**£148,900**

With 10% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,064	0.001932	**£550,500**	£964	0.001384	**£696,500**	£1,150	0.002084	**£551,900**	£1,318	0.004108	**£320,800**	£1,456	0.006096	**£238,800**
		Cypher	£1,142	0.001932	**£591,100**	£1,033	0.001384	**£746,900**	£1,235	0.002084	**£592,500**	£1,421	0.004108	**£346,000**	£1,576	0.006096	**£258,500**
	Broad	Taxus	£1,021	0.002572	**£397,000**	£933	0.001841	**£506,700**	£1,104	0.002773	**£398,000**	£1,227	0.005466	**£224,400**	£1,320	0.008111	**£162,800**
		Cypher	£1,099	0.002572	**£427,300**	£1,002	0.001841	**£544,400**	£1,188	0.002773	**£428,400**	£1,329	0.005466	**£243,200**	£1,439	0.008111	**£177,400**
Actual	Narrow	Taxus	£828	0.001932	**£428,400**	£754	0.001384	**£545,000**	£895	0.002084	**£429,500**	£1,006	0.004108	**£245,000**	£1,094	0.006096	**£179,500**
		Cypher	£1,041	0.001932	**£538,500**	£943	0.001384	**£681,500**	£1,125	0.002084	**£539,800**	£1,287	0.004108	**£313,300**	£1,420	0.006096	**£233,000**
	Broad	Taxus	£786	0.002572	**£305,800**	£724	0.001841	**£393,400**	£850	0.002773	**£306,600**	£918	0.005466	**£168,000**	£963	0.008111	**£118,800**
		Cypher	£998	0.002572	**£388,000**	£912	0.001841	**£495,500**	£1,079	0.002773	**£389,000**	£1,196	0.005466	**£218,800**	£1,285	0.008111	**£158,400**

Table A2.2: Stent Wastage sensitivity analysis - Elective patients if only 1 stent is required

With 1% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£585	0.001932	**£302,900**	£621	0.001384	**£449,100**	£575	0.002084	**£276,000**	£442	0.004108	**£107,600**	£311	0.006096	**£51,000**
		Cypher	£632	0.001932	**£326,900**	£668	0.001384	**£482,900**	£622	0.002084	**£298,200**	£487	0.004108	**£118,500**	£354	0.006096	**£58,100**
	Broad	Taxus	£543	0.002572	**£211,200**	£591	0.001841	**£321,200**	£530	0.002773	**£191,100**	£352	0.005466	**£64,500**	£178	0.008111	**£22,000**
		Cypher	£589	0.002572	**£229,100**	£638	0.001841	**£346,400**	£576	0.002773	**£207,600**	£396	0.005466	**£72,500**	£220	0.008111	**£27,100**
Actual	Narrow	Taxus	£446	0.001932	**£230,700**	£481	0.001384	**£347,500**	£436	0.002084	**£209,300**	£307	0.004108	**£74,800**	£180	0.006096	**£29,600**
		Cypher	£572	0.001932	**£295,700**	£608	0.001384	**£439,100**	£562	0.002084	**£269,400**	£429	0.004108	**£104,300**	£298	0.006096	**£48,900**
	Broad	Taxus	£405	0.002572	**£157,500**	£452	0.001841	**£245,300**	£392	0.002773	**£141,400**	£220	0.005466	**£40,300**	£52	0.008111	**£6,400**
		Cypher	£530	0.002572	**£205,900**	£578	0.001841	**£313,700**	£516	0.002773	**£186,200**	£339	0.005466	**£62,100**	£166	0.008111	**£20,400**

With 5% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£612	0.001932	**£316,900**	£649	0.001384	**£468,900**	£602	0.002084	**£289,000**	£468	0.004108	**£113,800**	£335	0.006096	**£55,000**
		Cypher	£661	0.001932	**£341,800**	£697	0.001384	**£504,100**	£650	0.002084	**£312,000**	£514	0.004108	**£125,200**	£381	0.006096	**£62,400**
	Broad	Taxus	£570	0.002572	**£221,600**	£618	0.001841	**£335,900**	£556	0.002773	**£200,700**	£377	0.005466	**£69,000**	£201	0.008111	**£24,800**
		Cypher	£618	0.002572	**£240,200**	£667	0.001841	**£362,100**	£604	0.002773	**£217,800**	£423	0.005466	**£77,400**	£245	0.008111	**£30,200**
Actual	Narrow	Taxus	£467	0.001932	**£241,900**	£503	0.001384	**£363,300**	£458	0.002084	**£219,600**	£328	0.004108	**£79,700**	£200	0.006096	**£32,800**
		Cypher	£598	0.001932	**£309,500**	£634	0.001384	**£458,500**	£588	0.002084	**£282,100**	£454	0.004108	**£110,500**	£322	0.006096	**£52,800**
	Broad	Taxus	£426	0.002572	**£165,800**	£473	0.001841	**£257,100**	£413	0.002773	**£149,100**	£240	0.005466	**£43,900**	£70	0.008111	**£8,700**
		Cypher	£556	0.002572	**£216,100**	£604	0.001841	**£328,100**	£542	0.002773	**£195,600**	£364	0.005466	**£66,600**	£189	0.008111	**£23,200**

With 10% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£646	0.001932	**£334,400**	£683	0.001384	**£493,700**	£636	0.002084	**£305,200**	£500	0.004108	**£121,700**	£366	0.006096	**£60,100**
		Cypher	£697	0.001932	**£360,500**	£734	0.001384	**£530,500**	£686	0.002084	**£329,300**	£549	0.004108	**£133,600**	£414	0.006096	**£67,800**
	Broad	Taxus	£603	0.002572	**£234,600**	£652	0.001841	**£354,300**	£590	0.002773	**£212,600**	£409	0.005466	**£74,800**	£231	0.008111	**£28,500**
		Cypher	£653	0.002572	**£254,000**	£703	0.001841	**£381,800**	£640	0.002773	**£230,600**	£456	0.005466	**£83,500**	£276	0.008111	**£34,100**
Actual	Narrow	Taxus	£494	0.001932	**£255,800**	£530	0.001384	**£383,000**	£485	0.002084	**£232,500**	£353	0.004108	**£86,000**	£224	0.006096	**£36,800**
		Cypher	£631	0.001932	**£326,600**	£668	0.001384	**£482,800**	£621	0.002084	**£298,000**	£485	0.004108	**£118,200**	£352	0.006096	**£57,800**
	Broad	Taxus	£453	0.002572	**£176,100**	£500	0.001841	**£271,700**	£440	0.002773	**£158,600**	£265	0.005466	**£48,500**	£93	0.008111	**£11,500**
		Cypher	£588	0.002572	**£228,800**	£637	0.001841	**£346,200**	£575	0.002773	**£207,300**	£394	0.005466	**£72,200**	£217	0.008111	**£26,800**

Table A2.3: Stent Wastage sensitivity analysis - Elective patients if only 2 stents are required

With 1% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,230	0.001932	**£636,500**	£1,266	0.001384	**£915,100**	£1,220	0.002084	**£585,400**	£1,087	0.004108	**£264,500**	£956	0.006096	**£156,800**
		Cypher	£1,320	0.001932	**£682,900**	£1,356	0.001384	**£980,100**	£1,309	0.002084	**£628,300**	£1,175	0.004108	**£285,900**	£1,042	0.006096	**£171,000**
	Broad	Taxus	£1,188	0.002572	**£461,900**	£1,236	0.001841	**£671,400**	£1,175	0.002773	**£423,600**	£997	0.005466	**£182,400**	£823	0.008111	**£101,500**
		Cypher	£1,277	0.002572	**£496,600**	£1,326	0.001841	**£720,000**	£1,264	0.002773	**£455,600**	£1,084	0.005466	**£198,300**	£908	0.008111	**£112,000**
Actual	Narrow	Taxus	£961	0.001932	**£497,200**	£996	0.001384	**£719,700**	£951	0.002084	**£456,300**	£822	0.004108	**£200,100**	£695	0.006096	**£114,100**
		Cypher	£1,203	0.001932	**£622,800**	£1,240	0.001384	**£895,800**	£1,194	0.002084	**£572,600**	£1,061	0.004108	**£258,200**	£930	0.006096	**£152,600**
	Broad	Taxus	£920	0.002572	**£357,800**	£967	0.001841	**£525,000**	£907	0.002773	**£327,100**	£735	0.005466	**£134,500**	£567	0.008111	**£69,900**
		Cypher	£1,161	0.002572	**£451,700**	£1,209	0.001841	**£656,900**	£1,148	0.002773	**£414,100**	£971	0.005466	**£177,700**	£798	0.008111	**£98,300**

With 5% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,283	0.001932	**£663,800**	£1,319	0.001384	**£953,400**	£1,273	0.002084	**£610,600**	£1,138	0.004108	**£277,000**	£1,006	0.006096	**£165,000**
		Cypher	£1,376	0.001932	**£711,900**	£1,413	0.001384	**£1,020,900**	£1,366	0.002084	**£655,200**	£1,229	0.004108	**£299,300**	£1,096	0.006096	**£179,800**
	Broad	Taxus	£1,240	0.002572	**£482,300**	£1,289	0.001841	**£700,000**	£1,227	0.002773	**£442,400**	£1,048	0.005466	**£191,700**	£872	0.008111	**£107,500**
		Cypher	£1,333	0.002572	**£518,300**	£1,382	0.001841	**£750,600**	£1,319	0.002773	**£475,700**	£1,138	0.005466	**£208,200**	£960	0.008111	**£118,400**
Actual	Narrow	Taxus	£1,003	0.001932	**£518,900**	£1,038	0.001384	**£750,200**	£993	0.002084	**£476,400**	£863	0.004108	**£210,000**	£735	0.006096	**£120,600**
		Cypher	£1,255	0.001932	**£649,500**	£1,291	0.001384	**£933,300**	£1,245	0.002084	**£597,300**	£1,111	0.004108	**£270,400**	£979	0.006096	**£160,600**
	Broad	Taxus	£962	0.002572	**£373,900**	£1,009	0.001841	**£547,800**	£949	0.002773	**£342,100**	£776	0.005466	**£141,900**	£606	0.008111	**£74,700**
		Cypher	£1,213	0.002572	**£471,600**	£1,261	0.001841	**£685,000**	£1,199	0.002773	**£432,500**	£1,021	0.005466	**£186,800**	£846	0.008111	**£104,200**

With 10% wastage rate

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,348	0.001932	**£697,800**	£1,385	0.001384	**£1,001,200**	£1,338	0.002084	**£642,100**	£1,202	0.004108	**£292,600**	£1,069	0.006096	**£175,300**
		Cypher	£1,446	0.001932	**£748,300**	£1,483	0.001384	**£1,072,000**	£1,436	0.002084	**£688,800**	£1,298	0.004108	**£316,000**	£1,163	0.006096	**£190,800**
	Broad	Taxus	£1,305	0.002572	**£507,700**	£1,355	0.001841	**£735,800**	£1,292	0.002773	**£465,900**	£1,111	0.005466	**£203,200**	£933	0.008111	**£115,000**
		Cypher	£1,402	0.002572	**£545,400**	£1,452	0.001841	**£788,800**	£1,389	0.002773	**£500,800**	£1,206	0.005466	**£220,600**	£1,026	0.008111	**£126,500**
Actual	Narrow	Taxus	£1,055	0.001932	**£546,000**	£1,091	0.001384	**£788,300**	£1,045	0.002084	**£501,500**	£914	0.004108	**£222,500**	£785	0.006096	**£128,800**
		Cypher	£1,319	0.001932	**£682,800**	£1,356	0.001384	**£980,200**	£1,309	0.002084	**£628,200**	£1,174	0.004108	**£285,700**	£1,040	0.006096	**£170,700**
	Broad	Taxus	£1,014	0.002572	**£394,200**	£1,061	0.001841	**£576,300**	£1,001	0.002773	**£360,800**	£826	0.005466	**£151,100**	£654	0.008111	**£80,600**
		Cypher	£1,277	0.002572	**£496,400**	£1,326	0.001841	**£720,000**	£1,263	0.002773	**£455,500**	£1,083	0.005466	**£198,100**	£905	0.008111	**£111,600**

Table A2.4: Stent Wastage sensitivity analysis - All Non-elective patients

With 1% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£814	0.002444	**£333,200**	£807	0.002155	**£374,500**	£899	0.005332	**£168,600**	£583	0.009716	**£60,000**
		Cypher	£879	0.002444	**£359,600**	£870	0.002155	**£403,700**	£981	0.005332	**£184,000**	£661	0.009716	**£68,000**
	Broad	Taxus	£757	0.003251	**£232,900**	£757	0.002867	**£263,900**	£775	0.007095	**£109,200**	£356	0.012928	**£27,500**
		Cypher	£821	0.003251	**£252,600**	£819	0.002867	**£285,700**	£855	0.007095	**£120,600**	£432	0.012928	**£33,400**
Actual	Narrow	Taxus	£620	0.002444	**£253,900**	£618	0.002155	**£286,900**	£653	0.005332	**£122,500**	£347	0.009716	**£35,700**
		Cypher	£795	0.002444	**£325,400**	£789	0.002155	**£365,900**	£875	0.005332	**£164,100**	£559	0.009716	**£57,600**
	Broad	Taxus	£565	0.003251	**£173,800**	£569	0.002867	**£198,600**	£532	0.007095	**£75,000**	£126	0.012928	**£9,800**
		Cypher	£738	0.003251	**£227,100**	£738	0.002867	**£257,500**	£751	0.007095	**£105,800**	£333	0.012928	**£25,800**

With 5% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£852	0.002444	**£348,700**	£844	0.002155	**£391,600**	£947	0.005332	**£177,500**	£627	0.009716	**£64,600**
		Cypher	£919	0.002444	**£376,100**	£909	0.002155	**£421,900**	£1,032	0.005332	**£193,500**	£709	0.009716	**£73,000**
	Broad	Taxus	£795	0.003251	**£244,400**	£793	0.002867	**£276,600**	£821	0.007095	**£115,700**	£399	0.012928	**£30,800**
		Cypher	£861	0.003251	**£264,800**	£858	0.002867	**£299,200**	£905	0.007095	**£127,600**	£478	0.012928	**£37,000**
Actual	Narrow	Taxus	£651	0.002444	**£266,200**	£648	0.002155	**£300,500**	£691	0.005332	**£129,500**	£382	0.009716	**£39,300**
		Cypher	£832	0.002444	**£340,500**	£825	0.002155	**£382,600**	£921	0.005332	**£172,800**	£603	0.009716	**£62,100**
	Broad	Taxus	£595	0.003251	**£182,900**	£598	0.002867	**£208,700**	£569	0.007095	**£80,200**	£160	0.012928	**£12,400**
		Cypher	£775	0.003251	**£238,300**	£774	0.002867	**£269,900**	£796	0.007095	**£112,200**	£375	0.012928	**£29,000**

With 10% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£899	0.002444	**£368,000**	£890	0.002155	**£412,900**	£1,006	0.005332	**£188,700**	£683	0.009716	**£70,300**
		Cypher	£969	0.002444	**£396,700**	£958	0.002155	**£444,700**	£1,095	0.005332	**£205,400**	£769	0.009716	**£79,100**
	Broad	Taxus	£841	0.003251	**£258,700**	£839	0.002867	**£292,500**	£879	0.007095	**£123,900**	£452	0.012928	**£35,000**
		Cypher	£911	0.003251	**£280,100**	£907	0.002867	**£316,200**	£967	0.007095	**£136,300**	£536	0.012928	**£41,400**
Actual	Narrow	Taxus	£688	0.002444	**£281,600**	£684	0.002155	**£317,500**	£738	0.005332	**£138,400**	£426	0.009716	**£43,900**
		Cypher	£878	0.002444	**£359,400**	£870	0.002155	**£403,500**	£980	0.005332	**£183,700**	£658	0.009716	**£67,700**
	Broad	Taxus	£632	0.003251	**£194,300**	£635	0.002867	**£221,300**	£615	0.007095	**£86,700**	£203	0.012928	**£15,700**
		Cypher	£820	0.003251	**£252,300**	£819	0.002867	**£285,500**	£853	0.007095	**£120,300**	£428	0.012928	**£33,100**

Table A2.5: Stent Wastage sensitivity analysis - Non-elective patients if only 1 stent is required

With 1% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£506	0.002444	**£207,100**	£560	0.002155	**£260,100**	£302	0.005332	**£56,700**	-£7	0.009716	**-£800**
		Cypher	£550	0.002444	**£225,100**	£607	0.002155	**£281,600**	£344	0.005332	**£64,500**	£32	0.009716	**£3,300**
	Broad	Taxus	£449	0.003251	**£138,100**	£510	0.002867	**£177,900**	£178	0.007095	**£25,100**	-£234	0.012928	**-£18,100**
		Cypher	£492	0.003251	**£151,400**	£556	0.002867	**£193,900**	£218	0.007095	**£30,800**	-£197	0.012928	**-£15,300**
Actual	Narrow	Taxus	£374	0.002444	**£153,200**	£421	0.002155	**£195,500**	£176	0.005332	**£33,100**	-£124	0.009716	**-£12,800**
		Cypher	£493	0.002444	**£201,800**	£547	0.002155	**£253,700**	£290	0.005332	**£54,300**	-£19	0.009716	**-£1,900**
	Broad	Taxus	£319	0.003251	**£98,100**	£372	0.002867	**£129,900**	£55	0.007095	**£7,800**	-£345	0.012928	**-£26,700**
		Cypher	£436	0.003251	**£134,200**	£497	0.002867	**£173,200**	£166	0.007095	**£23,300**	-£245	0.012928	**-£19,000**

With 5% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£532	0.002444	**£217,600**	£588	0.002155	**£272,600**	£326	0.005332	**£61,200**	£14	0.009716	**£1,500**
		Cypher	£577	0.002444	**£236,200**	£636	0.002155	**£294,900**	£370	0.005332	**£69,300**	£55	0.009716	**£5,600**
	Broad	Taxus	£474	0.003251	**£145,800**	£537	0.002867	**£187,200**	£201	0.007095	**£28,300**	-£214	0.012928	**-£16,600**
		Cypher	£519	0.003251	**£159,700**	£584	0.002867	**£203,800**	£243	0.007095	**£34,200**	-£176	0.012928	**-£13,600**
Actual	Narrow	Taxus	£395	0.002444	**£161,500**	£443	0.002155	**£205,500**	£195	0.005332	**£36,600**	-£108	0.009716	**-£11,100**
		Cypher	£518	0.002444	**£212,000**	£573	0.002155	**£266,000**	£313	0.005332	**£58,700**	£2	0.009716	**£200**
	Broad	Taxus	£339	0.003251	**£104,200**	£394	0.002867	**£137,300**	£73	0.007095	**£10,300**	-£329	0.012928	**-£25,500**
		Cypher	£461	0.003251	**£141,700**	£523	0.002867	**£182,300**	£188	0.007095	**£26,500**	-£226	0.012928	**-£17,500**

With 10% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£564	0.002444	**£230,600**	£621	0.002155	**£288,300**	£356	0.005332	**£66,800**	£41	0.009716	**£4,200**
		Cypher	£611	0.002444	**£250,200**	£672	0.002155	**£311,700**	£402	0.005332	**£75,300**	£83	0.009716	**£8,600**
	Broad	Taxus	£506	0.003251	**£155,500**	£570	0.002867	**£198,800**	£229	0.007095	**£32,300**	-£190	0.012928	**-£14,700**
		Cypher	£553	0.003251	**£170,000**	£620	0.002867	**£216,200**	£274	0.007095	**£38,600**	-£150	0.012928	**-£11,600**
Actual	Narrow	Taxus	£420	0.002444	**£171,900**	£470	0.002155	**£217,900**	£219	0.005332	**£41,000**	-£87	0.009716	**-£8,900**
		Cypher	£549	0.002444	**£224,800**	£606	0.002155	**£281,300**	£342	0.005332	**£64,200**	£28	0.009716	**£2,900**
	Broad	Taxus	£364	0.003251	**£111,900**	£420	0.002867	**£146,500**	£96	0.007095	**£13,500**	-£310	0.012928	**-£24,000**
		Cypher	£492	0.003251	**£151,200**	£555	0.002867	**£193,600**	£216	0.007095	**£30,500**	-£202	0.012928	**-£15,600**

Table A2.6: Stent Wastage sensitivity analysis - Non-elective patients if only 2 stent are required

With 1% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,185	0.002444	**£484,900**	£1,273	0.002155	**£590,800**	£981	0.005332	**£184,000**	£671	0.009716	**£69,100**
		Cypher	£1,274	0.002444	**£521,400**	£1,367	0.002155	**£634,400**	£1,068	0.005332	**£200,300**	£756	0.009716	**£77,800**
	Broad	Taxus	£1,128	0.003251	**£346,900**	£1,223	0.002867	**£426,400**	£856	0.007095	**£120,700**	£445	0.012928	**£34,400**
		Cypher	£1,217	0.003251	**£374,200**	£1,316	0.002867	**£459,100**	£943	0.007095	**£132,900**	£527	0.012928	**£40,800**
Actual	Narrow	Taxus	£916	0.002444	**£375,000**	£990	0.002155	**£459,600**	£718	0.005332	**£134,700**	£418	0.009716	**£43,000**
		Cypher	£1,158	0.002444	**£474,000**	£1,245	0.002155	**£577,800**	£955	0.005332	**£179,100**	£646	0.009716	**£66,500**
	Broad	Taxus	£861	0.003251	**£264,800**	£942	0.002867	**£328,400**	£597	0.007095	**£84,200**	£197	0.012928	**£15,300**
		Cypher	£1,102	0.003251	**£338,800**	£1,195	0.002867	**£416,800**	£831	0.007095	**£117,100**	£420	0.012928	**£32,500**

With 5% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,237	0.002444	**£506,300**	£1,328	0.002155	**£616,400**	£1,032	0.005332	**£193,500**	£720	0.009716	**£74,100**
		Cypher	£1,330	0.002444	**£544,300**	£1,426	0.002155	**£661,700**	£1,122	0.005332	**£210,500**	£807	0.009716	**£83,100**
	Broad	Taxus	£1,180	0.003251	**£362,800**	£1,278	0.002867	**£445,600**	£906	0.007095	**£127,700**	£491	0.012928	**£38,000**
		Cypher	£1,272	0.003251	**£391,200**	£1,375	0.002867	**£479,500**	£996	0.007095	**£140,400**	£577	0.012928	**£44,600**
Actual	Narrow	Taxus	£958	0.002444	**£392,100**	£1,034	0.002155	**£480,000**	£759	0.005332	**£142,300**	£456	0.009716	**£46,900**
		Cypher	£1,210	0.002444	**£495,000**	£1,299	0.002155	**£602,900**	£1,005	0.005332	**£188,400**	£694	0.009716	**£71,400**
	Broad	Taxus	£902	0.003251	**£277,500**	£985	0.002867	**£343,600**	£637	0.007095	**£89,800**	£234	0.012928	**£18,100**
		Cypher	£1,152	0.003251	**£354,400**	£1,249	0.002867	**£435,500**	£880	0.007095	**£124,000**	£466	0.012928	**£36,000**

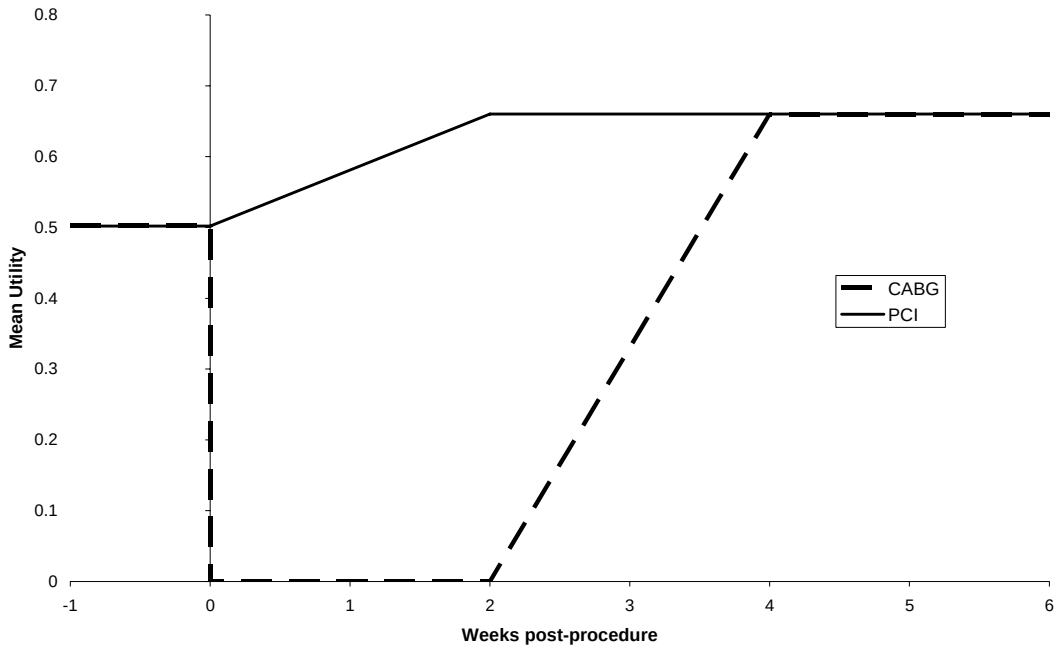
With 10% wastage rate

Non-Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,303	0.002444	**£533,100**	£1,397	0.002155	**£648,400**	£1,095	0.005332	**£205,400**	£780	0.009716	**£80,300**
		Cypher	£1,400	0.002444	**£572,900**	£1,500	0.002155	**£695,900**	£1,190	0.005332	**£223,200**	£872	0.009716	**£89,700**
	Broad	Taxus	£1,245	0.003251	**£382,800**	£1,346	0.002867	**£469,500**	£968	0.007095	**£136,500**	£549	0.012928	**£42,500**
		Cypher	£1,341	0.003251	**£412,500**	£1,448	0.002867	**£505,000**	£1,062	0.007095	**£149,700**	£639	0.012928	**£49,400**
Actual	Narrow	Taxus	£1,010	0.002444	**£413,500**	£1,090	0.002155	**£505,600**	£809	0.005332	**£151,700**	£504	0.009716	**£51,800**
		Cypher	£1,274	0.002444	**£521,300**	£1,367	0.002155	**£634,300**	£1,067	0.005332	**£200,100**	£753	0.009716	**£77,500**
	Broad	Taxus	£954	0.003251	**£293,400**	£1,040	0.002867	**£362,600**	£686	0.007095	**£96,700**	£280	0.012928	**£21,600**
		Cypher	£1,216	0.003251	**£374,000**	£1,316	0.002867	**£458,900**	£941	0.007095	**£132,600**	£523	0.012928	**£40,400**

3. Procedural Disutility

In all Base Case analyses it was assumed that patients undergoing a second revascularisation procedure would incur a common disutility, independent of the type of intervention (PCI or CABG) equivalent to recovery to symptom-free quality of life at a steady rate over a period of four weeks. It was suggested that this is unrealistic: that PCI patients feel benefit very quickly with little discomfort and few complications, but that CABG patients suffer a worse experience with severe pain and slower recovery. It is not possible to obtain observational data for the immediate period following intervention. Instead we consider a plausible alternative scenario to reflect the suggested effects illustrated in the Figure A.1.

Figure A.1: Alternate Disutility Assumptions



CABG: broken line, PCI: solid line

For CABG patients:

- we assume that for a 2 week post-operative period patients experience a severe loss of quality of life to a level considered equivalent to the health-related utility of death (0.0). For the next 2 weeks, the mean utility score recovers in a linear fashion achieving full benefit (0.660) by 4 weeks after the operation.

For PCI patients:

- we assume that patients recover full benefit linearly over a 2 week period following the intervention.

The effect of these assumptions is to substantially increase the disutility associated with CABG, but to decrease the procedural disutility of PCI. In addition, we can no longer assume in the model a common disutility effect for elective and non-elective patients since there is evidence that a higher proportion of repeat interventions require CABG among patients whose index procedure is non-elective (9.0% elective vs. 17.9% non-elective in CTC audit data). The Base-Case analyses have been recalculated on this new basis and are displayed in Tables A3.1 and A3.2.

Because of the reduced disutility for PCI and the lower proportion of CABG among elective patients, the mean disutility per patient is reduced leading to higher cost-effectiveness ratios for all elective patients. By contrast, for non-elective patients ICERs generally reduce slightly, but not sufficiently to alter determination of cost-effectiveness for any category of patients.

Table A3.1 Alternate Procedural Disutility Assumptions: Elective Patients

Average Use of Stents

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,011	0.001952	**£517,900**	£917	0.001398	**£655,700**	£1,093	0.002106	**£519,100**	£1,248	0.00415	**£300,800**	£1,375	0.006158	**£223,300**
		Cypher	£1,086	0.001952	**£556,200**	£983	0.001398	**£703,300**	£1,174	0.002106	**£557,500**	£1,347	0.00415	**£324,600**	£1,490	0.006158	**£242,000**
	Broad	Taxus	£969	0.002598	**£372,800**	£886	0.001860	**£476,500**	£1,047	0.002802	**£373,800**	£1,158	0.005522	**£209,700**	£1,241	0.008194	**£151,500**
		Cypher	£1,043	0.002598	**£401,400**	£952	0.001860	**£512,100**	£1,128	0.002802	**£402,500**	£1,256	0.005522	**£227,400**	£1,355	0.008194	**£165,300**
Actual	Narrow	Taxus	£786	0.001952	**£402,500**	£717	0.001398	**£512,600**	£850	0.002106	**£403,500**	£951	0.00415	**£229,200**	£1,030	0.006158	**£167,300**
		Cypher	£989	0.001952	**£506,500**	£897	0.001398	**£641,600**	£1,069	0.002106	**£507,700**	£1,219	0.00415	**£293,700**	£1,341	0.006158	**£217,800**
	Broad	Taxus	£745	0.002598	**£286,600**	£687	0.001860	**£369,400**	£805	0.002802	**£287,400**	£864	0.005522	**£156,400**	£901	0.008194	**£109,900**
		Cypher	£946	0.002598	**£364,300**	£867	0.001860	**£465,900**	£1,023	0.002802	**£365,200**	£1,129	0.005522	**£204,500**	£1,208	0.008194	**£147,400**

Where only 1 stent is required

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£612	0.001952	**£313,700**	£649	0.001398	**£464,100**	£602	0.002106	**£286,000**	£468	0.00415	**£112,700**	£335	0.006158	**£54,500**
		Cypher	£661	0.001952	**£338,300**	£697	0.001398	**£498,900**	£650	0.002106	**£308,900**	£514	0.00415	**£123,900**	£381	0.006158	**£61,800**
	Broad	Taxus	£570	0.002598	**£219,300**	£618	0.001860	**£332,500**	£556	0.002802	**£198,600**	£377	0.005522	**£68,300**	£201	0.008194	**£24,600**
		Cypher	£618	0.002598	**£237,700**	£667	0.001860	**£358,400**	£604	0.002802	**£215,600**	£423	0.005522	**£76,600**	£245	0.008194	**£29,900**
Actual	Narrow	Taxus	£467	0.001952	**£239,400**	£503	0.001398	**£359,600**	£458	0.002106	**£217,300**	£328	0.00415	**£78,900**	£200	0.006158	**£32,400**
		Cypher	£598	0.001952	**£306,300**	£634	0.001398	**£453,800**	£588	0.002106	**£279,200**	£454	0.00415	**£109,300**	£322	0.006158	**£52,300**
	Broad	Taxus	£426	0.002598	**£164,100**	£473	0.001860	**£254,400**	£413	0.002802	**£147,500**	£240	0.005522	**£43,500**	£70	0.008194	**£8,600**
		Cypher	£556	0.002598	**£213,900**	£604	0.001860	**£324,800**	£542	0.002802	**£193,600**	£364	0.005522	**£65,900**	£189	0.008194	**£23,000**

Where only 2 stents are required

Elective Index PCI			All patients			No risk factors			1 risk factor			2 risk factors			3/4 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,283	0.001952	**£657,000**	£1,319	0.001398	**£943,600**	£1,273	0.002106	**£604,400**	£1,138	0.00415	**£274,200**	£1,006	0.006158	**£163,300**
		Cypher	£1,376	0.001952	**£704,700**	£1,413	0.001398	**£1,010,500**	£1,366	0.002106	**£648,500**	£1,229	0.00415	**£296,200**	£1,096	0.006158	**£177,900**
	Broad	Taxus	£1,240	0.002598	**£477,300**	£1,289	0.001860	**£692,800**	£1,227	0.002802	**£437,900**	£1,048	0.005522	**£189,700**	£872	0.008194	**£106,400**
		Cypher	£1,333	0.002598	**£513,000**	£1,382	0.001860	**£742,900**	£1,319	0.002802	**£470,900**	£1,138	0.005522	**£206,100**	£960	0.008194	**£117,200**
Actual	Narrow	Taxus	£1,003	0.001952	**£513,600**	£1,038	0.001398	**£742,500**	£993	0.002106	**£471,600**	£863	0.00415	**£207,900**	£735	0.006158	**£119,400**
		Cypher	£1,255	0.001952	**£642,800**	£1,291	0.001398	**£923,800**	£1,245	0.002106	**£591,300**	£1,111	0.00415	**£267,600**	£979	0.006158	**£159,000**
	Broad	Taxus	£962	0.002598	**£370,100**	£1,009	0.001860	**£542,200**	£949	0.002802	**£338,600**	£776	0.005522	**£140,400**	£606	0.008194	**£73,900**
		Cypher	£1,213	0.002598	**£466,800**	£1,261	0.001860	**£678,000**	£1,199	0.002802	**£428,100**	£1,021	0.005522	**£184,800**	£846	0.008194	**£103,200**

Table A3.2 Alternate Procedural Disutility Assumptions: Non-Elective Patients

Average Use of Stents

Non-Elective Index PCI

			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£852	0.002549	**£334,300**	£844	0.002248	**£375,400**	£947	0.005562	**£170,200**	£627	0.010135	**£61,900**
		Cypher	£919	0.002549	**£360,600**	£909	0.002248	**£404,500**	£1,032	0.005562	**£185,500**	£709	0.010135	**£69,900**
	Broad	Taxus	£795	0.003392	**£234,300**	£793	0.002991	**£265,200**	£821	0.007401	**£111,000**	£399	0.013485	**£29,600**
		Cypher	£861	0.003392	**£253,900**	£858	0.002991	**£286,900**	£905	0.007401	**£122,300**	£478	0.013485	**£35,400**
Actual	Narrow	Taxus	£651	0.002549	**£255,200**	£648	0.002248	**£288,100**	£691	0.005562	**£124,200**	£382	0.010135	**£37,700**
		Cypher	£832	0.002549	**£326,500**	£825	0.002248	**£366,800**	£921	0.005562	**£165,700**	£603	0.010135	**£59,500**
	Broad	Taxus	£595	0.003392	**£175,400**	£598	0.002991	**£200,100**	£569	0.007401	**£76,900**	£160	0.013485	**£11,900**
		Cypher	£775	0.003392	**£228,500**	£774	0.002991	**£258,800**	£796	0.007401	**£107,600**	£375	0.013485	**£27,800**

Where only 1 stent is required

Non-Elective Index PCI

			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£532	0.002549	**£208,600**	£588	0.002248	**£261,400**	£326	0.005562	**£58,600**	£14	0.010135	**£1,400**
		Cypher	£577	0.002549	**£226,500**	£636	0.002248	**£282,800**	£370	0.005562	**£66,500**	£55	0.010135	**£5,400**
	Broad	Taxus	£474	0.003392	**£139,800**	£537	0.002991	**£179,500**	£201	0.007401	**£27,100**	-£214	0.013485	**-£15,900**
		Cypher	£519	0.003392	**£153,100**	£584	0.002991	**£195,400**	£243	0.007401	**£32,800**	-£176	0.013485	**-£13,100**
Actual	Narrow	Taxus	£395	0.002549	**£154,800**	£443	0.002248	**£197,000**	£195	0.005562	**£35,100**	-£108	0.010135	**-£10,600**
		Cypher	£518	0.002549	**£203,300**	£573	0.002248	**£255,000**	£313	0.005562	**£56,300**	£2	0.010135	**£200**
	Broad	Taxus	£339	0.003392	**£99,900**	£394	0.002991	**£131,600**	£73	0.007401	**£9,900**	-£330	0.013485	**-£24,400**
		Cypher	£461	0.003392	**£135,900**	£523	0.002991	**£174,700**	£188	0.007401	**£25,400**	-£226	0.013485	**-£16,700**

Where only 2 stents is required

Non-Elective Index PCI

			All patients			No risk factors			1 risk factor			2 risk factors		
Prices	Effectiveness	Brand	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER	Δ C	Δ Q	ICER
Effective list	Narrow	Taxus	£1,237	0.002549	**£485,400**	£1,328	0.002248	**£590,900**	£1,032	0.005562	**£185,500**	£720	0.010135	**£71,000**
		Cypher	£1,330	0.002549	**£521,800**	£1,426	0.002248	**£634,400**	£1,122	0.005562	**£201,800**	£807	0.010135	**£79,700**
	Broad	Taxus	£1,180	0.003392	**£347,900**	£1,278	0.002991	**£427,200**	£906	0.007401	**£122,500**	£491	0.013485	**£36,400**
		Cypher	£1,272	0.003392	**£375,100**	£1,375	0.002991	**£459,700**	£996	0.007401	**£134,600**	£577	0.013485	**£42,800**
Actual	Narrow	Taxus	£958	0.002549	**£375,900**	£1,034	0.002248	**£460,200**	£759	0.005562	**£136,400**	£456	0.010135	**£45,000**
		Cypher	£1,210	0.002549	**£474,600**	£1,299	0.002248	**£578,000**	£1,005	0.005562	**£180,600**	£694	0.010135	**£68,400**
	Broad	Taxus	£902	0.003392	**£266,100**	£985	0.002991	**£329,400**	£637	0.007401	**£86,100**	£234	0.013485	**£17,400**
		Cypher	£1,152	0.003392	**£339,800**	£1,249	0.002991	**£417,500**	£880	0.007401	**£118,900**	£466	0.013485	**£34,500**

4. AMI and Mortality - is there a case for a DES effect?

Understanding the Issues

The extreme sensitivity of the economic analysis to any supposed survival gain has led some to question assumptions made in the Assesment Group economic model. In particular, we have assumed that there is no benefit to patients from DES arising from mortality risks associated with AMIs and peri-procedural fatalities. These assumptions were justified directly from the RCT evidence and meta-analyses presented in the main report, and which failed to find any significant differences between BMS and DES in AMIs and deaths in all follow-up periods to three years.

The suggestion has been made that these findings appear to be at variance with well documented important mortality risks associated with additional interventional procedures, and with widely held clinical beliefs that avoidance of stenosis should result in reduced frequency of AMIs, and AMI-related fatalities. Unless we take the radical step of discounting the combined RCT evidence as unreliable, these beliefs would need to be justified on the grounds that either the RCT evidence has no bearing on normal clinical practice, or that the combined patient numbers from the trials and/or the available follow-up time is insufficient to yield statistically significant results. In either case it has been suggested that non-significant 'trend' benefits should nonetheless be used for economic analysis.

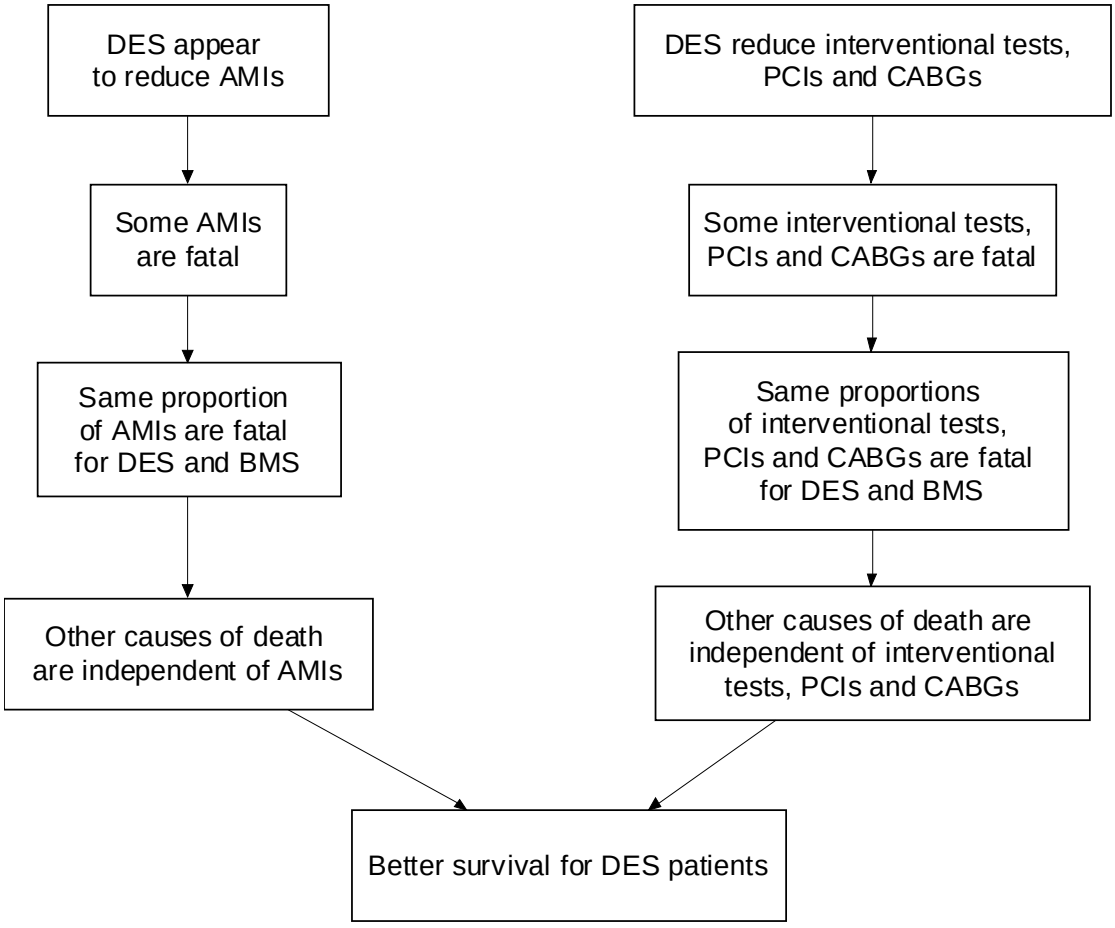
However, there is a conflict between the meta-analyses which renders this approach problematic. Although it appears that there are 'trends' in favour of DES for AMI events across all follow-up periods (6-9, 12, 24 and 36 months), this is not the case for overall mortality where odds ratios of 0.87, 1.31, 0.96 and 1.64 respectively arise from meta-analysis. Thus even if we allow a non-significant reduction in AMI events due to DES usage, it does not follow that overall mortality reduces in line with AMIs - indeed, the balance of evidence might support the suspicion that DES could lead to loss of life expectancy.

It is instructive to analyse the train of logic on which the suggestion of survival benefits is based (Figure A.2 below). All the steps shown must be established, and credible evidence-based values assigned, before any reliable estimates of survival gain (if any) can be deduced. Of particular concern are the assumptions of independence between the various process measures. To furnish realistic values for

these it would be necessary to draw on a variety of sources involving unrelated patients, and this presupposes mutual independence of effects. However, there are several known mechanisms by which important interactions can arise when values for several parameters are estimated from the same patients - not least that death acts as a censoring event for all other events. Thus in logical terms it is perfectly feasible for the initial propositions to be true, but the final assertion false.

The primary objection to the 'belief-based' line of reasoning for survival gains is that the trials have reported evidence of overall survival which encompasses both of the proposed mechanisms to deliver such gains. The failure of meta-analysis to identify a significant difference between DES and BMS, or even a consistent trend in either direction suggests strongly that in this instance the strongly-held beliefs may be founded on false perceptions.

Figure A.2: Implicit reasoning in support of survival gain for DES vs. BMS



Are AMI and Mortality rates reduced by PCI/Stents?

It is interesting to note that neither submissions nor expert evidence for the previous appraisal (which informed Guidance 71), nor for this assessment claimed that AMI reductions were among the benefits to be expected from stented PCI. Indeed it was clearly stated that the primary objective of PCI (with or without stenting) was to provide symptomatic relief and quality of life improvement. The reason for this is that the earlier research carried out compared the efficacy of different modes of revascularisation (PTCA and CABG) with conservative medical therapy.[14-17] Table A4.1 shows that despite considerable differences in the patient groups studied, there was a uniformly poorer outlook for patients undergoing PTCA in respect of AMI and overall mortality across all studies. This was partly explained by early procedural adverse events for PTCA, many of which are no longer applicable, but even when these are excluded, there is no evidence for AMI/mortality improvements with PTCA.

Table A4.1: Pooled outcomes of trials comparing PTCA to medical therapy

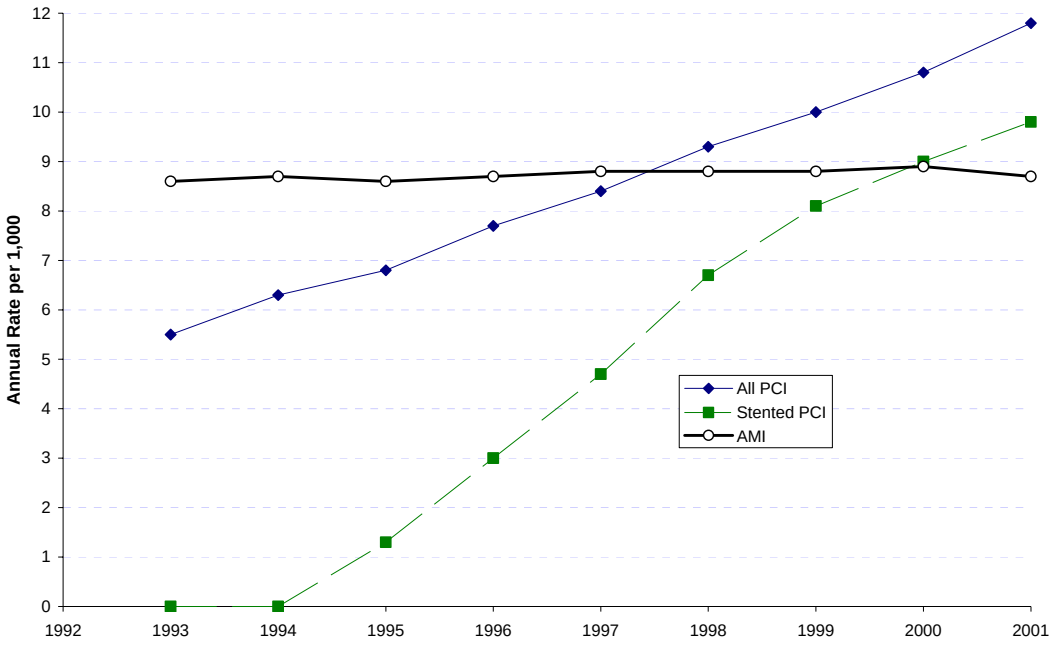
				AMI				Death			
	Patients		Follow-up	Rate		Annual risk		Rate		Annual risk	
Trial	PTCA	Medical	(years)	PTCA	Medical	PTCA	Medical	PTCA	Medical	PTCA	Medical
RITA-2	504	514	2.7	4.8%	2.9%	1.8%	1.1%	2.2%	1.4%	0.8%	0.5%
ACME	165	167	3	12.1%	8.4%	4.0%	2.8%	15.2%	15.0%	5.1%	5.0%
MASS	72	72	3	2.8%	2.8%	0.9%	0.9%	1.4%	0.0%	0.5%	0.0%
MASS-II	205	203	1	7.8%	4.9%	7.8%	4.9%	4.4%	1.5%	4.4%	1.5%
Pooled	**946**	**956**	**2.4**	**6.6%**	**4.3%**	**2.7%**	**1.8%**	**4.9%**	**3.7%**	**2.0%**	**1.5%**

The advent of coronary artery stenting has greatly reduced the problems of restenosis and reduced the unacceptably high rates on repeat interventions necessary following balloon angioplasty. However, the risks of AMI and death have not improved noticeably since the pre-stent era. For example, the long-term outcomes for PCI in Scotland show that AMI occurs in 3.0% of PCI patients in the first year, and at 1.0% per annum thereafter. For mortality, the Scottish rates are 2.6% and 1.7% respectively. Thus it is far from clear that any real improvement has taken place in these outcomes despite advances in both technology and clinical practice.

Longitudinal Evidence

Further light has been cast on this issue by the recent publication in *Circulation* of the results of large population longitudinal studies of the development of cardiology services in Canada and the USA.[9, 10] In particular, these allow direct comparison of time trends in revascularisation volumes and hospital admissions for AMI. If we believe that use of PCI leads to clinically meaningful reductions in AMI risk, then we should expect to see evidence over the last 10 years of a declining trend in AMIs corresponding to the exponential growth in PCI treatment, and particularly of stenting. However, the results are equally disappointing in both North American studies, showing no evidence of declines in AMI volumes, not even of any deflection from historic trends. (Figure A.3 shows the US results; Ontario results are very similar).

Figure A.3: Trends in the treatment rates for PCI and AMI in 5% sample of US Medicare patients 1992-2001



These findings confirm an earlier study[18] of all PCIs carried out in British Columbia between April 1994 and June 1997 (9594 procedures in 7880 patients), in which the authors state:

> ".. there was a significant stepwise reduction in the rates of adverse cardiac events at one year (from 28.8 percent in the period from April to June 1994 to 22.8 percent in the period from January to June 1997. P<0.001), due exclusively to declining rates of target-vessel revascularization (from 24.4 percent to 17.0 percent, P<0.001). Overall, the one-year rates of myocardial infarction (5.4 percent, P=0.28) and death from any cause (3.9 percent, P=0.65) remained stable."

Evidence from DES vs. BMS clinical trials

In order to understand the implications for cost-effectiveness of the non-significant trend towards additional MIs for patients undergoing BMS stenting (compared to DES), it is helpful to breakdown the total figures for each trial. Table A4.2 shows the outcomes after 12 months in the six trials featured in the meta-analysis plus the recent BASKET trial, disaggregated to show the fatal and non-fatal AMIs. It is clear that fatality is very low amongst AMI patients in this period, and that the rates are identical for DES and BMS patients. This establishes that no survival difference can be imputed in favour of DES due to fewer follow-up AMIs, as no such difference exists in the RCT evidence.

It follows that any benefit in favour of DES arises from a lower incidence of non-fatal AMIs (mainly non-Q wave MIs). These may have two important effects: to increase costs, due to extra hospital admissions, and to incur disutility from the MI event. Table A4.2 also shows the proportion of non-fatal MIs occurring whilst the patient is already in-hospital undergoing a PCI procedure. These constitute the majority of such events, and would not incur a separate Reference Cost payment. The remainder of events, which occur in the community will attract a hospitalisation cost if patients are admitted for treatment. It is not clear whether this will always be the case, since examination of IPD from one trial suggests that many such events may have been detected retrospectively from protocol testing after 6-8 months, and not because of a specific clinical event. Nonetheless, if we assume that all community-based AMIs are hospitalised at an average cost of £1,200, then the additional 1.1% of events in the BMS arm would result in a cost reduction for DES of approximately £13 per patient initially treated with DES.

Reliable information on the disutility associated with surviving an acute myocardial infarct is limited. The best source found is based on evidence from type 2 diabetes patients in the UKPDS trial[19] but was nonetheless hampered by small numbers of events recorded. Based on a Tobit model, the additional loss of utility during the first year post-infarct appears to be about 0.05. Combined with the additional 1.1% non-fatal MI events in the BMS arm, leads to an average utility gain per patient of 0.00055 when DES are used.

Summary

If the results of the review of clinical trial evidence for DES versus BMS were taken in isolation from all preceding and parallel studies then there might be some justification for exploring the possibility of unaccounted survival gains through either of the routes suggested, since any unmitigated loss of life expectancy (typically estimated at about 10 years) due to procedural complications (about 2% of CABG patients and 0.5% of PCI patients), or from fatal AMIs (about 18% of all AMIs) would certainly lead to very different cost-effectiveness ratios (though still unlikely to bring more than a small proportion of high-risk patients into the area considered acceptable on economic grounds). **However, the weight of prior evidence is sufficiently strong that a very compelling body of new information would be necessary to alter the current consensus that PCIs provide symptomatic relief but do not alter life expectancy by changing the incidence of AMI or by other means.**

This conclusion is consistent with the meta-analysis of clinical trial evidence when data are disaggregated by type of event. **However, it is clear that there is a trend towards increased numbers of non-fatal AMIs when BMS are used. The maximum likely effect of this on costs is equivalent to a cost saving of about £13 per patient, and a utility gain of about 0.00055 per patient when DES are used.**

Table A4.2 Analysis of incidence of myocardial infarction during 12 month follow-up after PCI

Trial	All M.I.s				Fatal M.I.s		Non-Fatal M.I.s		In-hospital M.I.s		In community M.I.s	
	DES		BMS		DES	BMS	DES	BMS	DES	BMS	DES	BMS
	M.I.s	Cases	M.I.s	Cases	M.I.s	M.I.s	M.I.s	M.I.s	M.I.s	M.I.s	M.I.s	M.I.s
TAXUS I	0	30	0	30	0	0	0	0	0	0	0	0
TAXUS II (SR)	3	129	7	132	0	0.5 [a]	3	6.5	2	5	1	2
TAXUS IV	23	662	30	652	4 [a]	4 [a]	19	26	16	14	7	16
RAVEL	4	120	5	118	0	1	4	4	3	3	1	2
SIRIUS	16	533	18	525	0	0	16	18	12	8	4	10
ENDEAVOR II (9 months)	16	594	23	585	1	0	15	23	15	16	1	7
BASKET (6 months)	12	430	12	220	3	1	9	11	6	6	6	6
Pooled	74	2498	95	2262	8	6.5	66	88.5	54	52	20	43
Rate	**2.96%**		**4.20%**		**0.32%**	**0.29%**	**2.64%**	**3.91%**	**2.16%**	**2.30%**	**0.80%**	**1.90%**

Notes: **a** - mid range of feasible values used where paper does not give full detail

5. Realistic Repeat Revascularization Rates

In Table 5.1 we have assembled the statistics presented in the various sources relevant to estimating the repeat revascularisation rate measured 12 months post-PCI. Where possible we have selected figures to match what would be expected in current UK practice if BMS were to be used generally. The first five entries relate to UK sources, and the remaining seven to international papers.

There is no standard method of reporting outcomes, and therefore it is necessary to attempt to adjust authors' chosen measures into a comparable standard, compatible with our economic model. This has involved employing additional evidence and assumptions, which in some cases are not as rigorously derived as we would have liked.

The main adjustments are as follows:

1. Because of the recent rapid pace of development in interventional cardiology the sources include widely varying use of stenting. For the purpose of this assessment, we have adjusted values (where possible) to 100% BMS use. In the case of the UK sources and the Netherlands, we have used a simple regression relationship involving British Cardiovascular Intervention Society (BCIS) historic data on stent usage and the proportion of PCIs required because of restenosis. However, this may not be appropriate in North America, so instead we calibrated a corresponding regression model from the historic Medicare sample for adjusting the US results.

2. In the case of the CTC audit data, we noted that a number of AMI patients had been inadvertently included in the non-elective group. These were removed and the revascularisation rates re-estimated - the changes from this modification are minor.

3. Where results are given in terms of TLR or target vessel revascularisation (TVR) rates, these have been increased to estimated total revascularisations rates, based on the composition of repeat interventions observed at Liverpool and shown in Tables 8-1 and 8-2 of the main report.

4. The BCIS report indicates that 17% of cases involved use of DES. We have increased the rate to remove the beneficial effect of DES, based on the effectiveness achieved in the BASKET trial.

5. The BCIS reported value may also be understated, due to a combination of the rapid rate of growth in PCIs in UK and the time lag between the index procedure and any consequent repeat interventions. By applying an uplift linked to the historic growth rate, this potential effect is fully compensated (and even possibly overstated).

6. It is also necessary to make adjustments where the reporting time differs from our standard (12 months). For converting from 9 to 12 months follow-up we have applied a multiplier derived from the CTC revascularisation time profile. However, we found that adopting a similar approach to move from 6 to 12 months suggested unrealistically large adjusted rates. This situation arises only in respect of two international sources (US and Switzerland), and we reasoned that differing clinical practices may not be compatible with using an adjustor based on UK experience. We have therefore adopted a more modest multiplier without specific evidence to support it.

7. In the Toulouse study, the ratio of overall revascularisation rates at 12 and 24 months was applied to estimate 12 months rates for types of stent. Also it is not clear whether any STEMI patients are included.

8. It is clear that there are significant case-mix differences between the populations studied by each of the sources. Ideally these should also be the subject of careful adjustment, but without a comprehensive multi-variate model and data on all relevant variables from every source, this was not possible.

Discussion

The five sources from UK show remarkable consistency after adjustment, four of the five giving overall repeat revascularisation rates between 7.5% and 8.5%. The exception in the 2003/4 report from SCRR, which seems to be out of line with the published paper from the same source. A particular problem arose when attempting to adjust the 2003/4 outcomes statistics for levels of stent use, since the report only gives stent usage for the latest year, though the outcomes appear to be calculated over several years when stent use was somewhat lower. A sensitivity analysis shows that the 2003/4 figures match the earlier SCRR values if we assume average stent usage of 60-63% over the period for which the outcomes were estimated, and this may be a reasonable explanation for the apparent discrepancy.

The international studies yield a wider range of estimated revascularisation rates, which may reflect the differing circumstances in each country, but is also heavily dependent on some of the assumptions made in standardising the estimates, as indicated above.

On the basis of the combined evidence it seems reasonable to assume that the overall repeat revascularisation rate in the UK 12 months post-PCI with BMS is in the range 7% to 9%, and the equivalent rates for elective and non-elective patients are 7% to 8% and 9% to 10% respectively.

Table 5.1: Derivation of Total Revascularisation Rates at 12 months post-PCI from Multiple Sources

Source	*Period*	*n*	*Reported Repeat Revascularisation Rate*	*Issues*	*Adjustments*	*Corrected Rate*	*Basis of adjustments*
Pell - SCRR (Scotland)	1997-99	4,775	At 12 months: Elective(1st) 14.1% Others 18.8% Overall 17.1%	Includes unstented patients.	Adjust for POBAs.	Elective(1st) 7.0% Others 9.3% Overall **8.4%**	BCIS: (51% -> 100% BMS) x 0.493
SCRR 2003/4 (Scotland)	1997-2003	12,446	At 12 months: Elective/stable 12.9% Non-elective/unstable 16.6% Overall 14.7%	Includes unstented patients.	Adjust for POBAs.	Elective/stable 9.7% Non-elective/unstable 13.5% Overall **11.5%**	BCIS: (Elective 84% -> 100% BMS) x 0.752 (Non-elective 89% -> 100% BMS) x 0.815
CTC Audit (England)	2000-1	2,884	At 12 months: Elective 7.4% Non-elective 10.2% Overall 8.3%	Non-electives include some STEMIs.	Recalculate Non-elective rate excluding STEMIs	Elective 7.8% Non-elective 10.0% Overall **8.5%**	-
BCIS 2003 (UK)	2003	53,261	4.3% of PCIs for restenosis	Excludes non-TLR procedures. May be understated due to rapid expansion of PCI volumes. Includes 17% DES use	Adjust to Total rate. Adjust for trend. Adjust for DES use.	**8.0%**	CTC: (TLR to Total) x 1.478 BASKET DES risk reduction of 41% x 1.075 BCIS: increase 2003 vs 2002 x 1.178
Glenfield Hospital Audit (England)	2003	1,112	5.1% TLR at 12 months	Not known if STEMI included. TLR understates total revascularisations.	Adjust to Total rate.	**7.5%**	CTC: (TLR to Total) x 1.478
Toulouse (France)	1996-9	1,340	At 12 months: TLR 9.6% At 24 months: Old stents TLR 11.4% New stents TLR 5.9% Overall TLR 10.7%	TLR understates total revascularisations.	Adjust to Total rate at 12 months.	Older stents 16.9% Newer stents 7.8% Overall **14.2%**	CTC: (TLR to Total) x 1.478 12month:24 month rates adjusted pro-rata
Medicare sample (USA)	1993-2001	~180,000 revascs. over 8 years	Declined from 25% in 1993 to 13% in 2001(at 6 months)	Stents introduced during period. STEMIs included in rates but numbers not reported. Not clear if post-CABG reinterventions included in rate.	Adjust for variable stent use. Adjust to 12 months.	**14.5%**	Use 2001 rate. Regression on study data: (83% -> 100%BMS) x 0.858 (6 to 12 months) x 1.3
Cleveland (USA)	1994-2001	5,239	13.4% at 9 months	Includes 7.1% AMI, and 58.8% unstable angina.	Estimate elective / non-elective from multivariate model. Adjust to 12 months	Elective 13.7% Non-elective 18.7% Overall **16.6%**	Stable/elective x 0.823 Unstable/nonelective x 1.124 CTC: (9 to 12 months) x 1.239
APPROACH (Canada)	1998-2000	7,334	8.2% at 12 months	Includes 47% STEMI.	Adjust for STEMIs.	**6.1%**	STEMI adjustment based on pooled analysis of 10 trials (5 papers)
Washington (USA)	1999	3,571	16.2% at 12 months	Included 12.3% unstented patients	Adjust for POBAs.	**14.8%**	Medicare regression (87.7% -> 100% BMS) x 0.915
Agema (Netherlands)	1999-2001	3,177	10.3% TVR minimum 9 months f/up	Only 74% stented. TVR understates total revascularisations.	Adjust for POBAs. Adjust to Total rate. Adjust to 12 months.	**10.4%**	BCIS: (74% -> 100% BMS) x 0.647 CTC: (TVR to Total) x 1.259 CTC: (9 to 12 months) x 1.239
BASKET (Switzerland)	2003-5	264	8.2% TVR at 6 months (excl. STEMIs)	Severe case-mix. TVR understates total revascularisations.	Adjust to Total rate. Adjust to 12 months.	**13.4%**	CTC: (TVR to Total) x 1.259 (6 to 12 months) x 1.3

6. Risk Factor Models and Sub-Groups

The choice of a suitable risk factor model is important in identifying sub-groups of the population most likely to benefit from the use of DES. The factors which are included in such a model depend on the nature of the data set available (patient and procedural characteristics), clinical practice, and design decisions in specifying the candidate risk factors for inclusion. The Appraisal Committee have expressed interest in understanding the range of models for the risk of the need for repeat revascularisation which have been published, with particular regard to the possible role of diabetes alongside the factors identified in the previous guidance. Firstly, we examine these issues using the CTC audit database patient-level data. Then, we look more widely at other models found in the literature, and consider the quality and applicability to the UK situation.

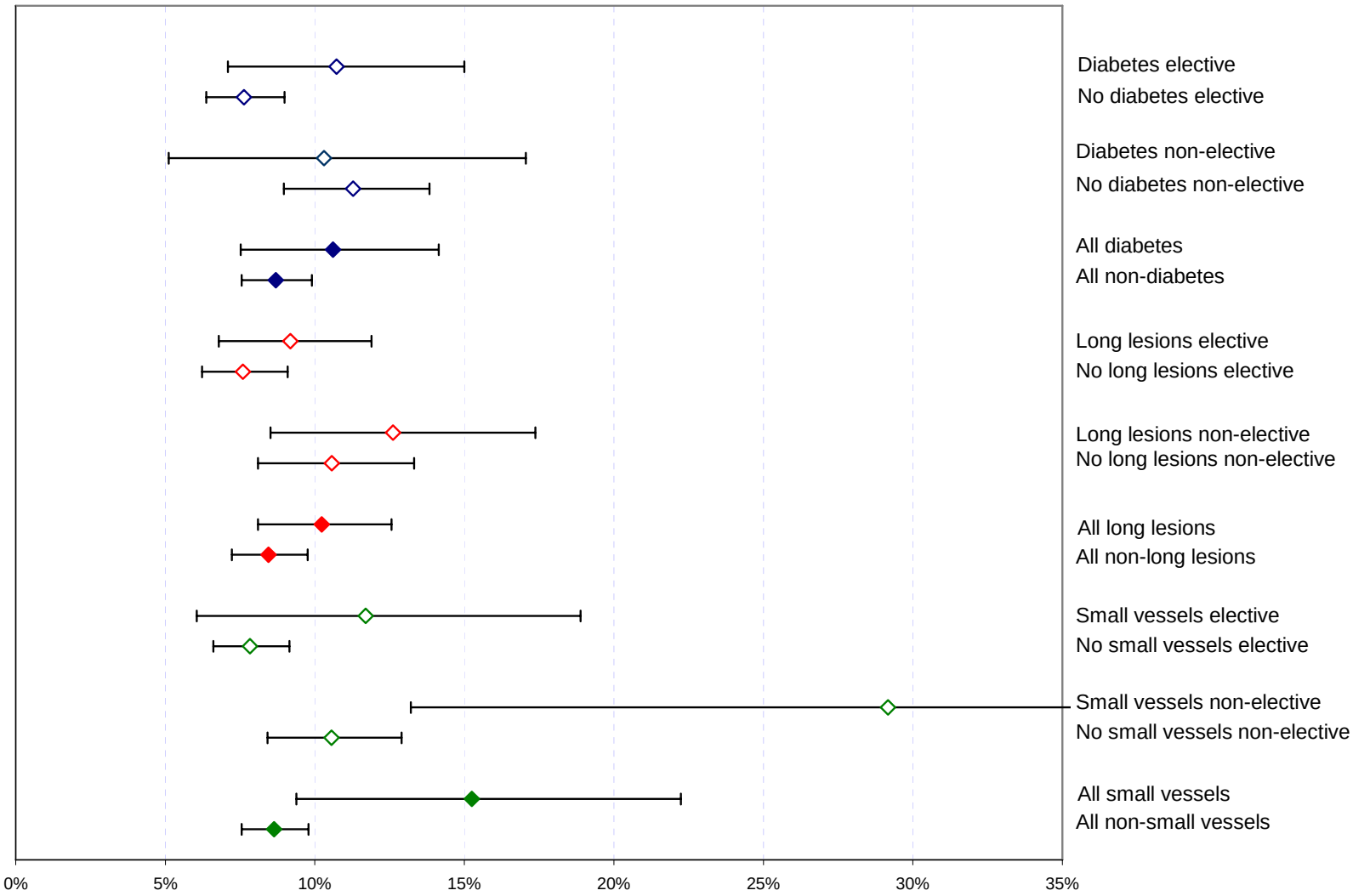
LRiG / CTC, Liverpool Audit Data

The current NICE guidance on DES identifies two risk factors for identifying groups of patients more likely to benefit from use of DES rather than BMS: where small vessels and/or where long lesions are to be stented. These were the only two factors for which evidence was available at the time suggestive of an increased risk of repeat intervention. Only one other potential factor had been proposed by the manufacturers for which any trial evidence was available, and examination of a very limited set of individual patient data led to the conclusion that diabetes did not appear to be an independent risk factor.

In the intervening period more peer-reviewed information has appeared, and access has been obtained to a prospective audit database of patients treated by stented PCI in Liverpool. This has facilitated derivation of new risk models using factors drawn more widely and including patient characteristics, co-morbidities and vessel/lesion characteristics.

In Figure A3, we display the repeat revascularisation rates (with 95% confidence intervals), for the influence of diabetes, small vessels (<2mm) and long lesions (>20mm). Only in the case of small vessels in non-elective patients does there appear to be an obvious strong effect - albeit with a very wide confidence interval. Of particular note is that diabetes has only a modest overall effect (about 2% greater risk overall), and this is not uniform between elective and non-elective patients.

Figure A3: Univariate analysis of 12-month repeat revascularisation rates in CTC audit data by conventional risk factors



In Table A6.1 we present results obtained by Cox proportional hazards regression analysis using several different risk model formulations.

The first elective model (LRiG) is that employed in cost-effectiveness analysis in the main report. This is compared with a model which features only the three factors in the current guidance or proposed by manufacturers. The final elective model includes all seven factors. The LRiG model was arrived at by a forward stepwise algorithm among a much wider panel of possible explanatory variables and represents the best formulation for these data. By contrast, the 'conventional factors' model not only has less explanatory power, but all three factors fail to achieve the conventional significance level required to indicate an independent predictor. The inclusion of all seven factors in the model causes only minor changes to the LRiG variable, but results in a serious worsening of the performance of the 'conventional factors'. All models were tested for interaction effects and none were found to be significant.

The published LRiG non-elective model inadvertently included data from some STEMI patients, not covered by this review. Therefore the LRiG model has been recalibrated on the reduced data set (n=827), and the results are presented in column 2 - both factors remain significant though the balance of influence has shifted slightly. When just 'conventional factors' are used, only small vessels appears to make a significant explanatory contribution, and when all four factors are used only the LRiG model factors are significant. In the non-elective models diabetes shows a trend to being inversely related to repeat revascularisation risk. All non-elective models were tested for interaction effects and none were found to be significant.

The success of the LRiG formulations to outperform other possibilities is not surprising since they were developed to provide 'best fit' to these data. However, it is notable that none of the additional variables widely believed to be most influential by the clinical community (and therefore factored into trial designs) showed any indication of independent effect, or acted to modify the LRiG factors to any serious extent. This suggests that common perceptions about the genesis of restenosis may be misconceived.

Table A6.1: Alternative risk models derived from CTC audit data

Elective patients (n=1951)	LRiG published model		Conventional factors		All factors	
Risk factor	*Hazard ratio*	*p*	*Hazard ratio*	*p*	*Hazard ratio*	*p*
Calcification	**1.89**	**0.002**	-	-	**1.92**	**0.001**
Angulation >45º	**1.51**	**0.019**	-	-	**1.48**	**0.027**
Restenotic lesion	**2.19**	**0.032**	-	-	**2.10**	**0.043**
Triple vessel disease	**1.56**	**0.042**	-	-	1.53	0.054
Diabetes	-	-	1.38	0.147	1.35	0.170
Small vessel <2.0mm	-	-	1.52	0.181	1.36	0.329
Long lesion >20mm	-	-	1.20	0.303	1.05	0.812
-2 log likelihood	2158.4		2179.2		2155.6	

Non-elective patients	LRiG published model (n=933)		LRiG model excl. STEMI (n=827)		Conventional factors (n=827)		All factors (n=827)	
Risk factor	*Hazard ratio*	*p*	*Hazard ratio*	*p*	*Hazard ratio*	*p*	*Hazard ratio*	*p*
Previous CABG	**2.27**	**0.015**	**2.59**	**0.005**	-	-	**2.63**	**0.004**
Diabetes	-	-	-	-	0.90	0.765	0.86	0.646
Small vessel <2.0mm	**2.91**	**0.004**	**2.78**	**0.010**	**2.62**	**0.015**	**2.81**	**0.009**
Long lesion >20mm	-	-	-	-	1.19	0.469	1.19	0.451
-2 log likelihood	1275.3		1093.8		1099.4		1093.0	

Other Published Risk Models

SCRR - Pell [1]

A multivariate Cox proportional hazards model from SCRR data from elective first revascularisation procedures for the period 1997-9. This combined patients undergoing PTCA (n=1732) with those receiving CABG (n=1168); only about 51% of percutaneous transluminal coronary angioplasty (PTCA) involved use of stents.

The model for repeat revascularisation was dominated by the much lower risk associated with CABG compared to PTCA. Only **three-vessel disease** achieved statistical significance (RR 1.69, 1.23-2.27).

The unsuccessful risk factors considered were:

- severe left ventricular impairment (RR 0.39, 0.06-1.93)

- hypertension (RR 1.18, 0.93-1.49)

- diabetes (RR 1.10, 0.78-1.54)

- cerebrovascular disease (RR 1.25, 0.47-2.62)

It is not clear to what extent restricting the model to PCI with stenting would have led to different results.

Toulouse[11]

Risk of TLR at 24 months was subject to Cox multivariate regression modelling including a full range of patient, angiographic and procedural variables. When the different types of stent employed was taken into account (later types showing a 53% reduction in hazard rate compared to the earlier generation), only one variate was found to be an independent risk predictor:

Post-procedural minimum luminal diameter <3mm (RR 2.09, 1.42-3.07)

Since this factor cannot be known when the choice of stent is made it is of no immediate value in assessing sub-groups with the highest risk of subsequent revascularisation. However, since small vessels with reference diameter <2mm must be included within this group, it does imply that patients with small vessels stented will be at higher risk of repeat intervention. This is confirmed by the univariate analysis which showed a significant relationship of TLR with **stent diameter <3mm** (RR 1.42, 1.02-1.99, p=0.04). Stent length, diabetes and other commonly cited risk factors did not show significant relationships in either analysis.

Netherlands[7]

A multivariate model of TVR among 2340 stented patients identified five risk factors associated with repeat revascularisation (diabetes, previous MI, total stent length, minimal stent diameter and multi-vessel disease). However, the removal criterion adopted for backwards stepwise regression was p>0.1, allowing variables in the final model which would have failed the conventional standard for significance (p=0.05). Adjusting the published results to permit direct comparison with other models suggests that only 3 variables are independently associated with risk of repeat revascularisation:

- previous MI (RR 0.68, 0.50-0.92)

- total stent length (RR 1.01 per unit, CIs difficult to estimate with precision)

- larger minimal stent diameter (RR 0.50, 0.34-0.73)

Cleveland, USA [12]

Total revascularisation risk at 9 months in 5,239 BMS patients was modelled by Cox multiple hazards regression. After standardization by age, procedure date and smoking status, eight additional risk factors were identified as independently associated with repeat revascularisation:

- reference diameter <2.75mm (RR 1.43 *estimated*)

- lesion length >20mm (RR 1.50 *estimated*)

- ostial location (RR 1.46, 1.24-1.73)

- unstable angina (RR 1.37, 1.18-1.60)

- restenotic lesion (RR 1.52, 1.16-1.97)

- multi-vessel disease (RR 1.20, 1.06-1.39 *estimated*)

- saphenous vein graft (RR 1.53, 1.10-1.73)

- LAD location (RR 1.19, 1.03-1.37)

The authors report that non-significant variables included ACE inhibitors, diabetes, high-sensitivity CRP, number of treated sites, renal insufficiency and statin use.

Washington State, USA [13]

A multivariate Cox regression model of all repeat revascularisations in 2,340 stented patients within 12 months identified five independent predictors:

- multivessel disease (RR 1.36, 1.12-1.66)

- stable angina (vs. no angina) (RR 1.27, 1.03-1.57)

- maximum stent length (RR 1.01 per 1mm, 1.002-1.020)

- prior MI (RR 0.77, 0.62-0.96)

- creatinine >1.2 mg/dl (RR 0.74, 0.56-0.98)

A sub-analysis for repeat PCIs only yielded similar results (excluding the angina variable). By contrast three risk factors were found for CABG as a repeat intervention - diabetes, prior MI and prior CABG.

Risk Factor Summary

In total seven published multivariate risk models of repeat revascularisation have been reviewed on a common basis from six sources. Although there is an inevitable variety of analytical structures leading to different collections of included variables in each model, some commonality can be identified:

- In none of the main analyses was diabetes shown to be an independent predictor;

- Very few individual factors achieved the level of significance generally considered as unequivocal evidence of a clear effect (RR of 2 or greater);

- Treating a small vessel was consistently found to be important either for all patients, or just for non-elective patients;

- Triple vessel disease, and longer lesions (or total lesion length) may show less pronounced effects;

- Other factors may have more importance to particular sub-populations (e.g. elective or non-elective);

- Surviving a previous MI appears to reduce the risk of a poor long-term outcome of PCI.

Potential Impact of Alternate Risk Models on Cost-Effectiveness

Using the CTC Audit data at the level of individual patient, it is possible to explore the implications of employing a different set of risk factors, when compared with those used in the Base Case. For this purpose we compare the LRiG models (Non-elective modified to exclude STEMIs) with the Conventional factors models as shown in Table A6.1.

Table A6.3 shows how these alternative models affect the cost-effectiveness ratios for the various risk-based sub-groups. The lower explanatory power of conventional risk factors is illustrated in Figure A6.1 in the case of elective patients. Greater discrimination between risk subgroups in the LRiG models is shown by the wider spread of cost-effectiveness results, with a higher proportion of caseload falling into

the cost-effectiveness range. With poorer discrimination, the conventional risk models aggregate patients closer to the average performance, losing the opportunity to distinguish very high and low risk sub-groups.

Figure A6.1 Comparison of Conventional Risks and LRiG models for elective patients

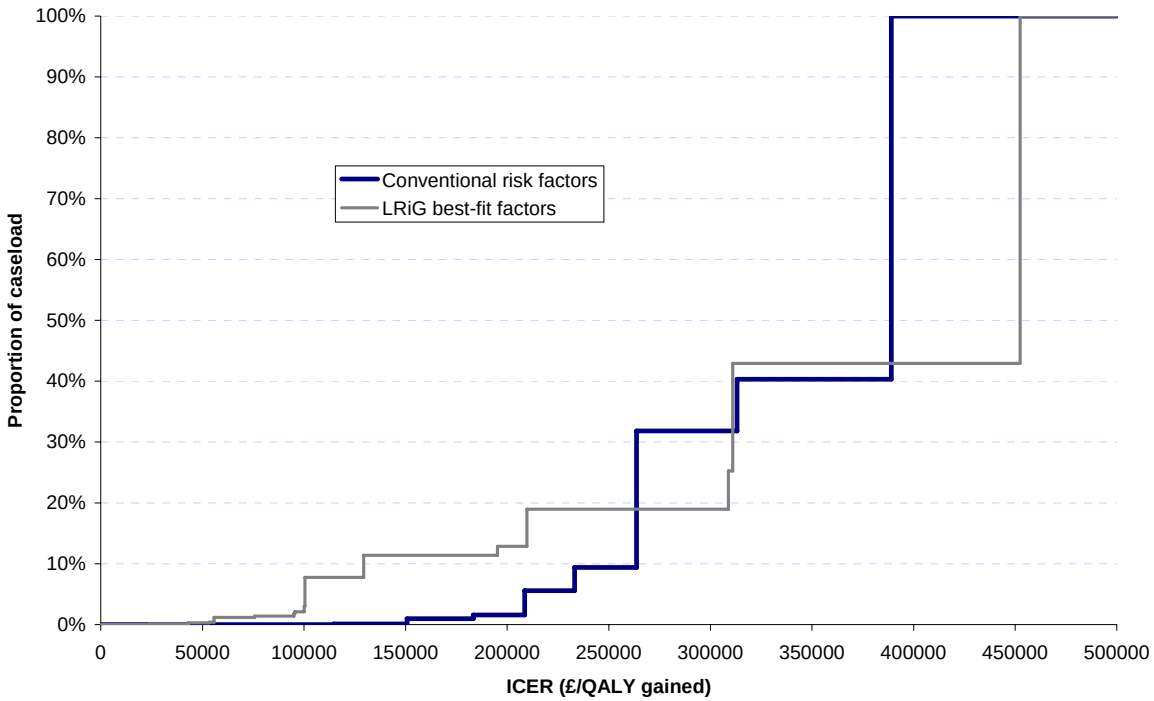


Table A6.2: Summary of risk model factors in reviewed papers

Risk factor	SCRR	Toulouse	Netherlands	Cleveland	Washington	LRiG elective	LRiG non-elective	Comment
3 vessel disease	√			√	√	√		Common, but not strong
Previous MI			√		√			MI has lower risk
Ostial location				√				
Unstable angina				√			(√)	Implied in LRiG formulation
Restenotic				√		√√		
Saphenous graft				√				
LAD				√				
Stable angina (vs. none)					√			
Creatinine					√			
Lesion length			√	√	√			Common, but not strong
Small vessel		√√	√√	√			√√	Strongest factor
Diabetes								Not included in any main analysis
Previous CABG							√√	
Calcification						√√		
Angulation						√		

√ = $p < 0.05$ & $RR < 1.6$, √√ = $RR >= 1.9$

Table A6.3: Exemplification of effects of using Conventional Risk Factors models on cost-effectiveness by sub-groups

Elective patients

Risk factors in sub-group			Caseload proportion		Relative	Absolute Risk by average AR for Elective cases					ICER by average AR for Elective cases				
Long	Small	Diabetes	Sub-group	Cumulative	Risk	7%	**7.79%**	8%	9%	10%	7%	**7.79%**	8%	9%	10%
No	No	No	59.7%	100.0%	1.00	6.0%	**6.7%**	6.9%	7.7%	8.6%	£ 415,000	**£ 367,500**	£ 354,800	£ 308,000	£ 270,600
No	No	Yes	8.5%	40.3%	1.20	7.2%	**9.2%**	8.2%	9.3%	10.3%	£ 334,800	**£ 295,200**	£ 284,600	£ 245,600	£ 214,400
Yes	No	No	22.5%	31.8%	1.38	8.3%	**8.0%**	9.5%	10.7%	11.9%	£ 282,400	**£ 248,100**	£ 238,900	£ 204,900	£ 177,800
No	Yes	No	3.8%	9.4%	1.52	9.1%	**11.1%**	10.4%	11.7%	13.1%	£ 250,300	**£ 219,000**	£ 210,700	£ 180,000	£ 155,300
Yes	No	Yes	4.0%	5.6%	1.66	10.0%	**10.2%**	11.4%	12.8%	14.2%	£ 224,300	**£ 195,700**	£ 188,000	£ 159,700	£ 137,100
No	Yes	Yes	0.6%	1.6%	1.82	11.0%	**14.0%**	12.5%	14.1%	15.7%	£ 197,600	**£ 171,600**	£ 164,600	£ 138,900	£ 118,400
Yes	Yes	No	0.9%	1.0%	2.10	12.6%	**12.2%**	14.4%	16.2%	18.0%	£ 163,100	**£ 140,500**	£ 134,500	£ 112,200	£ 94,300
Yes	Yes	Yes	0.1%	0.1%	2.52	15.1%	**16.8%**	17.3%	19.5%	21.6%	£ 124,900	**£ 106,000**	£ 101,000	£ 82,400	£ 67,500
27.4%	5.4%	13.2%													

Non-elective patients

Risk factors in sub-group			Caseload proportion		Relative	Absolute Risk by average for Non-elective cases					ICER by average for Non-elective cases				
Long	Small	Diabetes	Sub-group	Cumulative	Risk	9%	**10.00%**	11%	12%	13%	9%	**10.00%**	11%	12%	13%
No	No	Yes	8.0%	100.0%	0.90	7.3%	**8.1%**	9.0%	9.8%	10.6%	£ 295,100	**£ 258,500**	£ 228,500	£ 203,600	£ 182,500
No	No	No	60.1%	92.0%	1.00	8.1%	**9.1%**	10.0%	10.9%	11.8%	£ 258,500	**£ 225,600**	£ 198,600	£ 176,100	£ 157,100
Yes	No	Yes	4.5%	31.9%	1.07	8.7%	**9.7%**	10.7%	11.6%	12.6%	£ 236,700	**£ 205,900**	£ 180,700	£ 159,800	£ 142,000
Yes	No	No	23.7%	27.4%	1.19	9.7%	**10.8%**	11.9%	12.9%	14.0%	£ 205,900	**£ 178,200**	£ 155,600	£ 136,700	£ 120,700
No	Yes	Yes	0.2%	3.7%	2.36	19.2%	**21.4%**	23.5%	25.6%	27.8%	£ 68,800	**£ 54,800**	£ 43,400	£ 33,800	£ 25,800
No	Yes	No	2.5%	3.5%	2.62	21.4%	**23.7%**	26.1%	28.5%	30.8%	£ 54,800	**£ 42,200**	£ 31,900	£ 23,300	£ 16,100
Yes	Yes	Yes	0.2%	1.0%	2.81	22.9%	**25.4%**	27.9%	30.5%	33.0%	£ 46,400	**£ 34,700**	£ 25,100	£ 17,100	£ 10,300
Yes	Yes	No	0.7%	0.7%	3.12	25.4%	**28.2%**	31.1%	33.9%	36.7%	£ 34,700	**£ 24,100**	£ 15,500	£ 8,300	£ 2,200
29.1%	3.7%	12.9%													

Bold = CTC Audit point estimates of absolute risk

Assumptions: average number of stents per patient, 41% relative risk reduction due to DES (BASKET), actual price premium Cypher DES, 5% wastage

7. Sensitivity Analyses

The following tables contain a set of sensitivity analyses for both elective and non-elective patients. Each table allows 2-way exploration of variation in the absolute risk of repeat revascularisation when BMS are used versus. a range of price premium values. In addition to combined ("All Patients") tables, additional tables are included for each of the risk strata employed in the main report from the LRiG risk models - these are preferred on pragmatic grounds (shortage of time) and also because they are more discriminating than models based on 'conventional' factors, as described in section 6 above. The final row of each table includes the maximum (threshold) price premium value compatible with an ICER of £30,000 per QALY or below, which should be compared with the NHS Purchasing and Supply Agency survey based values (£672 or £717 for effective list price, and £537 or £659 for actual prices).

Several assumptions have been made in constructing these tables, which differ from the Base case in the main report:

- stent wastage rates have been set at 1% instead of 5%;

- the alternative procedural disutility calculations in section 3 have been adopted;

- no assumption of additional mortality is made in respect of either procedural fatalities or as a result of AMIs (as explained in section 4). However, each table includes a final column illustrating the magnitude of effect to be expected if procedural-related mortality were counted as a separate additional effect - this is not recommended as it should already be included in the all cause mortality estimates;

- modest additional utility gains and cost savings are attributed to DES as described in section 4;

- the risk of repeat revascularisation is shown for values encompassing the range of estimates presented in Table 5.1 for the UK sources, centred on the LRiG estimates (Base case);

- LRiG repeat revascularisation rates have been amended to exclude all AMI indicated patients from the non-elective group, and the risk model parameters re-estimated accordingly

- results are not presented for specific numbers of implanted stents, but the assumed average number of stents used in each analysis is shown, so that if required adjusted figures can be readily calculated by the reader.

Table 7.1

Elective Index PCI Average Use of Stents 1.615

	All patients	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	6%	7%	**7.8%**	8%	9%	10%	11%	12%	**7.8%**
	Utility per patient	0.00215	0.00242	**0.00263**	0.00268	0.00295	0.00322	0.00348	0.00375	**0.00397**
£100	Cost per patient	£58	£43	**£31**	£28	£12	-£3	-£18	-£34	**£31**
	Cost per QALY	£27,069	£17,744	£11,721	£10,272	£4,152	-£955	-£5,279	-£8,988	£7,765
£200	Cost per patient	£219	£203	**£191**	£187	£172	£156	£140	£124	**£191**
	Cost per QALY	£101,755	£84,014	**£72,555**	£69,799	£58,154	£48,440	£40,213	£33,157	**£48,068**
£300	Cost per patient	£379	£363	**£350**	£347	£331	£315	£299	£282	**£350**
	Cost per QALY	£176,440	£150,283	**£133,390**	£129,326	£112,157	£97,835	£85,706	£75,301	**£88,371**
£400	Cost per patient	£540	£523	**£510**	£507	£490	£474	£457	£440	**£510**
	Cost per QALY	£251,126	£216,553	**£194,224**	£188,852	£166,159	£147,229	£131,198	£117,446	**£128,674**
£500	Cost per patient	£701	£684	**£670**	£667	£650	£633	£616	£599	**£670**
	Cost per QALY	£325,811	£282,823	**£255,058**	£248,379	£220,162	£196,624	£176,690	£159,591	**£168,977**
£600	Cost per patient	£861	£844	**£830**	£826	£809	£791	£774	£757	**£830**
	Cost per QALY	£400,496	£349,092	**£315,892**	£307,905	£274,165	£246,019	£222,182	£201,735	**£209,280**
£700	Cost per patient	£1,022	£1,004	**£990**	£986	£968	£950	£932	£915	**£990**
	Cost per QALY	£475,182	£415,362	**£376,726**	£367,432	£328,167	£295,413	£267,674	£243,880	**£249,583**
£800	Cost per patient	£1,182	£1,164	**£1,150**	£1,146	£1,127	£1,109	£1,091	£1,073	**£1,150**
	Cost per QALY	£549,867	£481,631	**£437,560**	£426,958	£382,170	£344,808	£313,166	£286,025	**£289,885**
Threshold premium (£30000)		**£105**	**£120**	**£131**	**£134**	**£149**	**£164**	**£179**	**£194**	**£207**

Table 7.2

Elective Index PCI Average Use of Stents 1.430

	0 risk factors	Absolute risk of repeat revascularisation at 12 months							+ Procedural mortality
Price Premium	Incremental	4%	5%	**5.6%**	6%	7%	8%	9%	10%	**5.6%**
	Utility per patient	0.00162	0.00188	**0.00204**	0.00215	0.00242	0.00268	0.00295	0.00322	**0.00300**
£100	Cost per patient	£70	£55	**£46**	£39	£24	£9	-£6	-£22	**£46**
	Cost per QALY	£43,367	£29,093	£22,554	£18,360	£9,996	£3,294	-£2,196	-£6,776	£15,339
£200	Cost per patient	£213	£197	**£188**	£181	£166	£150	£134	£118	**£188**
	Cost per QALY	£131,631	£104,636	**£92,267**	£84,337	£68,518	£55,843	£45,460	£36,798	**£62,751**
£300	Cost per patient	£356	£339	**£330**	£323	£307	£291	£275	£259	**£330**
	Cost per QALY	£219,895	£180,178	**£161,981**	£150,313	£127,039	£108,392	£93,115	£80,372	**£110,163**
£400	Cost per patient	£498	£482	**£472**	£465	£448	£432	£415	£399	**£472**
	Cost per QALY	£308,159	£255,720	**£231,694**	£216,290	£185,561	£160,940	£140,771	£123,945	**£157,575**
£500	Cost per patient	£641	£624	**£614**	£607	£590	£573	£556	£539	**£614**
	Cost per QALY	£396,423	£331,262	**£301,408**	£282,266	£244,083	£213,489	£188,426	£167,519	**£204,987**
£600	Cost per patient	£784	£766	**£756**	£749	£731	£714	£696	£679	**£756**
	Cost per QALY	£484,687	£406,805	**£371,121**	£348,242	£302,604	£266,037	£236,082	£211,093	**£252,399**
£700	Cost per patient	£926	£908	**£898**	£891	£873	£855	£837	£819	**£898**
	Cost per QALY	£572,951	£482,347	**£440,835**	£414,219	£361,126	£318,586	£283,737	£254,666	**£299,811**
£800	Cost per patient	£1,069	£1,051	**£1,040**	£1,032	£1,014	£996	£978	£959	**£1,040**
	Cost per QALY	£661,215	£557,889	**£510,548**	£480,195	£419,647	£371,134	£331,392	£298,240	**£347,223**
Threshold premium (£30000)		**£86**	**£102**	**£112**	**£119**	**£136**	**£152**	**£169**	**£186**	**£176**

Table 7.3

Elective Index PCI Average Use of Stents 1.746

	1 risk factor	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	7%	8%	**8.4%**	9%	10%	11%	12%	13%	**8.4%**
	Utility per patient	0.00242	0.00268	**0.00279**	0.00295	0.00322	0.00348	0.00375	0.00402	**0.00423**
£100	Cost per patient	£56	£41	**£35**	£25	£10	-£5	-£21	-£36	**£35**
	Cost per QALY	£23,200	£15,186	£12,403	£8,621	£3,144	-£1,494	-£5,472	-£8,922	£8,174
£200	Cost per patient	£229	£214	**£207**	£198	£182	£166	£151	£135	**£207**
	Cost per QALY	£94,925	£79,625	**£74,313**	£67,092	£56,637	£47,783	£40,188	£33,602	**£48,977**
£300	Cost per patient	£403	£387	**£380**	£370	£354	£338	£322	£306	**£380**
	Cost per QALY	£166,649	£144,065	**£136,223**	£125,564	£110,130	£97,060	£85,848	£76,125	**£89,779**
£400	Cost per patient	£576	£560	**£553**	£543	£526	£510	£493	£477	**£553**
	Cost per QALY	£238,374	£208,505	**£198,133**	£184,036	£163,624	£146,337	£131,509	£118,649	**£130,582**
£500	Cost per patient	£749	£732	**£726**	£715	£698	£681	£664	£647	**£726**
	Cost per QALY	£310,099	£272,945	**£260,043**	£242,507	£217,117	£195,614	£177,169	£161,173	**£171,385**
£600	Cost per patient	£923	£905	**£898**	£888	£871	£853	£836	£818	**£898**
	Cost per QALY	£381,824	£337,385	**£321,954**	£300,979	£270,610	£244,891	£222,829	£203,697	**£212,187**
£700	Cost per patient	£1,096	£1,078	**£1,071**	£1,060	£1,043	£1,025	£1,007	£989	**£1,071**
	Cost per QALY	£453,549	£401,824	**£383,864**	£359,451	£324,103	£294,168	£268,490	£246,221	**£252,990**
£800	Cost per patient	£1,270	£1,251	**£1,244**	£1,233	£1,215	£1,196	£1,178	£1,160	**£1,244**
	Cost per QALY	£525,274	£466,264	**£445,774**	£417,923	£377,596	£343,445	£314,150	£288,745	**£293,792**
Threshold premium (£30000)		**£111**	**£124**	**£130**	**£138**	**£152**	**£166**	**£179**	**£193**	**£204**

Table 7.4

Elective Index PCI Average Use of Stents 2.157

	2 risk factors	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	15%	16%	**16.6%**	17%	18%	19%	20%	21%	**16.6%**
	Utility per patient	0.00455	0.00482	**0.00497**	0.00508	0.00535	0.00562	0.00588	0.00615	**0.00781**
£100	Cost per patient	-£25	-£40	**-£49**	-£56	-£71	-£86	-£102	-£117	**-£49**
	Cost per QALY	-£5,486	-£8,363	-£9,835	-£10,937	-£13,255	-£15,353	-£17,260	-£19,003	-£6,253
£200	Cost per patient	£187	£171	**£162**	£155	£139	£124	£108	£92	**£162**
	Cost per QALY	£40,991	£35,454	**£32,619**	£30,498	£26,036	£21,997	£18,325	£14,972	£20,738
£300	Cost per patient	£398	£382	**£373**	£366	£350	£333	£317	£301	**£373**
	Cost per QALY	£87,468	£79,270	**£75,074**	£71,933	£65,327	£59,348	£53,911	£48,946	**£47,728**
£400	Cost per patient	£610	£593	**£584**	£576	£560	£543	£527	£510	**£584**
	Cost per QALY	£133,945	£123,087	**£117,528**	£113,368	£104,617	£96,698	£89,497	£82,920	**£74,719**
£500	Cost per patient	£821	£804	**£794**	£787	£770	£753	£736	£719	**£794**
	Cost per QALY	£180,422	£166,903	**£159,983**	£154,802	£143,908	£134,048	£125,082	£116,894	**£101,709**
£600	Cost per patient	£1,032	£1,015	**£1,005**	£998	£980	£963	£945	£928	**£1,005**
	Cost per QALY	£226,899	£210,719	**£202,437**	£196,237	£183,199	£171,399	£160,668	£150,868	**£128,699**
£700	Cost per patient	£1,244	£1,226	**£1,216**	£1,208	£1,190	£1,173	£1,155	£1,137	**£1,216**
	Cost per QALY	£273,376	£254,536	**£244,892**	£237,672	£222,490	£208,749	£196,254	£184,842	**£155,690**
£800	Cost per patient	£1,455	£1,437	**£1,427**	£1,419	£1,401	£1,382	£1,364	£1,346	**£1,427**
	Cost per QALY	£319,853	£298,352	**£287,346**	£279,107	£261,781	£246,099	£231,839	£218,816	**£182,680**
Threshold premium (£30000)		**£178**	**£189**	**£196**	**£201**	**£212**	**£224**	**£235**	**£247**	**£308**

Table 7.5

Elective Index PCI Average Use of Stents 2.524

	3/4 risk factors	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	23%	24%	**24.6%**	25%	26%	27%	28%	29%	**24.6%**
	Utility per patient	0.00668	0.00695	**0.00710**	0.00722	0.00748	0.00775	0.00802	0.00828	**0.01132**
£100	Cost per patient	-£110	-£126	**-£134**	-£141	-£156	-£172	-£187	-£202	**-£134**
	Cost per QALY	-£16,520	-£18,091	-£18,933	-£19,544	-£20,895	-£22,152	-£23,326	-£24,424	-£11,874
£200	Cost per patient	£135	£119	**£110**	£103	£88	£72	£56	£40	**£110**
	Cost per QALY	£20,166	£17,127	£15,497	£14,314	£11,700	£9,267	£6,995	£4,870	£9,720
£300	Cost per patient	£380	£364	**£355**	£348	£332	£315	£299	£283	**£355**
	Cost per QALY	£56,852	£52,345	**£49,928**	£48,172	£44,296	£40,686	£37,317	£34,165	**£31,314**
£400	Cost per patient	£625	£609	**£599**	£592	£575	£559	£542	£526	**£599**
	Cost per QALY	£93,538	£87,563	**£84,358**	£82,030	£76,891	£72,106	£67,639	£63,459	**£52,909**
£500	Cost per patient	£870	£853	**£844**	£836	£819	£802	£785	£768	**£844**
	Cost per QALY	£130,224	£122,781	**£118,788**	£115,888	£109,486	£103,525	£97,960	£92,754	**£74,503**
£600	Cost per patient	£1,116	£1,098	**£1,088**	£1,081	£1,063	£1,046	£1,028	£1,011	**£1,088**
	Cost per QALY	£166,910	£157,999	**£153,218**	£149,746	£142,081	£134,944	£128,282	£122,048	**£96,097**
£700	Cost per patient	£1,361	£1,343	**£1,333**	£1,325	£1,307	£1,289	£1,272	£1,254	**£1,333**
	Cost per QALY	£203,596	£193,217	**£187,649**	£183,604	£174,677	£166,363	£158,603	£151,343	**£117,692**
£800	Cost per patient	£1,606	£1,588	**£1,577**	£1,569	£1,551	£1,533	£1,515	£1,496	**£1,577**
	Cost per QALY	£240,283	£228,435	**£222,079**	£217,462	£207,272	£197,783	£188,925	£180,637	**£139,286**
Threshold premium (£30000)		**£229**	**£239**	**£245**	**£249**	**£259**	**£269**	**£279**	**£289**	**£385**

Table 7.6

Non-Elective Index PCI Average Use of Stents 1.454

	All patients	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	8%	9%	**10.0%**	11%	12%	13%	14%	15%	**10.0%**
	Utility per patient	0.00262	0.00288	**0.00314**	0.00340	0.00365	0.00391	0.00417	0.00443	**0.00522**
£100	Cost per patient	£4	-£12	**-£28**	-£44	-£61	-£77	-£93	-£109	**-£28**
	Cost per QALY	£1,621	-£4,154	-£9,028	-£13,063	-£16,572	-£19,616	-£22,283	-£24,639	-£5,429
£200	Cost per patient	£148	£131	**£115**	£98	£82	£65	£48	£32	**£115**
	Cost per QALY	£56,498	£45,656	**£36,504**	£28,929	£22,342	£16,625	£11,618	£7,195	£21,950
£300	Cost per patient	£292	£275	**£258**	£241	£224	£207	£190	£173	**£258**
	Cost per QALY	£111,375	£95,466	**£82,036**	£70,921	£61,255	£52,867	£45,519	£39,029	**£49,328**
£400	Cost per patient	£436	£418	**£401**	£383	£366	£349	£331	£314	**£401**
	Cost per QALY	£166,251	£145,276	**£127,568**	£112,913	£100,168	£89,108	£79,420	£70,863	**£76,707**
£500	Cost per patient	£579	£562	**£544**	£526	£508	£490	£473	£455	**£544**
	Cost per QALY	£221,128	£195,086	**£173,101**	£154,905	£139,081	£125,350	£113,321	£102,697	**£104,085**
£600	Cost per patient	£723	£705	**£687**	£669	£650	£632	£614	£596	**£687**
	Cost per QALY	£276,005	£244,896	**£218,633**	£196,897	£177,994	£161,591	£147,222	£134,531	**£131,463**
£700	Cost per patient	£867	£848	**£829**	£811	£793	£774	£756	£737	**£829**
	Cost per QALY	£330,882	£294,705	**£264,165**	£238,889	£216,907	£197,833	£181,123	£166,366	**£158,842**
£800	Cost per patient	£1,011	£992	**£972**	£954	£935	£916	£897	£878	**£972**
	Cost per QALY	£385,759	£344,515	**£309,697**	£280,881	£255,821	£234,074	£215,025	£198,200	**£186,220**
Threshold premium (£30000)		**£153**	**£170**	**£188**	**£205**	**£222**	**£239**	**£257**	**£274**	**£299**

Table 7.7

Non-Elective Index PCI Average Use of Stents 1.413

	0 risk factors	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	7%	8%	**8.7%**	9%	10%	11%	12%	13%	**8.7%**
	Utility per patient	0.00236	0.00262	**0.00279**	0.00288	0.00314	0.00340	0.00365	0.00391	**0.00460**
£100	Cost per patient	£16	£0	**-£11**	-£16	-£32	-£48	-£65	-£81	**-£11**
	Cost per QALY	£6,925	£57	-£3,849	-£5,577	-£10,282	-£14,270	-£17,693	-£20,664	-£2,339
£200	Cost per patient	£156	£140	**£129**	£123	£107	£90	£73	£57	**£129**
	Cost per QALY	£66,244	£53,369	**£46,048**	£42,809	£33,990	£26,515	£20,099	£14,531	£27,982
£300	Cost per patient	£296	£279	**£268**	£262	£246	£229	£212	£195	**£268**
	Cost per QALY	£125,562	£106,682	**£95,945**	£91,195	£78,262	£67,301	£57,891	£49,725	**£58,303**
£400	Cost per patient	£436	£419	**£407**	£402	£384	£367	£350	£332	**£407**
	Cost per QALY	£184,881	£159,994	**£145,842**	£139,581	£122,535	£108,086	£95,682	£84,919	**£88,625**
£500	Cost per patient	£577	£559	**£547**	£541	£523	£506	£488	£470	**£547**
	Cost per QALY	£244,199	£213,307	**£195,739**	£187,967	£166,807	£148,871	£133,474	£120,113	**£118,946**
£600	Cost per patient	£717	£698	**£686**	£680	£662	£644	£626	£608	**£686**
	Cost per QALY	£303,518	£266,619	**£245,636**	£236,353	£211,079	£189,656	£171,266	£155,308	**£149,267**
£700	Cost per patient	£857	£838	**£826**	£820	£801	£782	£764	£745	**£826**
	Cost per QALY	£362,836	£319,931	**£295,533**	£284,739	£255,351	£230,441	£209,058	£190,502	**£179,588**
£800	Cost per patient	£997	£978	**£965**	£959	£940	£921	£902	£883	**£965**
	Cost per QALY	£422,155	£373,244	**£345,430**	£333,125	£299,624	£271,226	£246,850	£225,696	**£209,910**
Threshold premium (£30000)		**£140**	**£158**	**£170**	**£175**	**£193**	**£211**	**£228**	**£246**	**£270**

Table 7.8

Non-Elective Index PCI Average Use of Stents 1.880

	1 risk factor	Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	21%	22%	**22.8%**	23%	24%	25%	26%	27%	**22.8%**
	Utility per patient	0.00598	0.00624	**0.00645**	0.00650	0.00676	0.00702	0.00728	0.00753	**0.01120**
£100	Cost per patient	-£163	-£180	**-£193**	-£196	-£212	-£228	-£244	-£261	**-£193**
	Cost per QALY	-£27,311	-£28,775	-£29,891	-£30,122	-£31,366	-£32,519	-£33,589	-£34,586	-£17,224
£200	Cost per patient	£18	£2	**-£12**	-£15	-£31	-£48	-£65	-£81	**-£12**
	Cost per QALY	£3,059	£274	-£1,849	-£2,289	-£4,656	-£6,848	-£8,885	-£10,781	-£1,065
£300	Cost per patient	£200	£183	**£169**	£166	£149	£132	£115	£98	**£169**
	Cost per QALY	£33,428	£29,323	£26,193	£25,544	£22,054	£18,822	£15,820	£13,023	£15,094
£400	Cost per patient	£382	£364	**£350**	£347	£330	£312	£295	£277	**£350**
	Cost per QALY	£63,798	£58,372	**£54,235**	£53,377	£48,765	£44,492	£40,524	£36,828	**£31,253**
£500	Cost per patient	£563	£546	**£531**	£528	£510	£492	£475	£457	**£531**
	Cost per QALY	£94,168	£87,420	**£82,277**	£81,210	£75,475	£70,163	£65,228	£60,633	**£47,412**
£600	Cost per patient	£745	£727	**£712**	£709	£691	£672	£654	£636	**£712**
	Cost per QALY	£124,538	£116,469	**£110,319**	£109,043	£102,185	£95,833	£89,933	£84,438	**£63,571**
£700	Cost per patient	£927	£908	**£893**	£890	£871	£853	£834	£816	**£893**
	Cost per QALY	£154,907	£145,518	**£138,361**	£136,876	£128,896	£121,504	£114,637	£108,242	**£79,730**
£800	Cost per patient	£1,108	£1,090	**£1,074**	£1,071	£1,052	£1,033	£1,014	£995	**£1,074**
	Cost per QALY	£185,277	£174,567	**£166,403**	£164,709	£155,606	£147,174	£139,342	£132,047	**£95,889**
Threshold premium (£30000)		**£292**	**£305**	**£317**	**£319**	**£333**	**£347**	**£361**	**£375**	**£506**

Table 7.9

Non-Elective Index PCI Average Use of Stents 1.869

2 risk factors		Absolute risk of repeat revascularisation at 12 months								+ Procedural mortality
Price Premium	Incremental	39%	40%	**40.7%**	41%	42%	43%	44%	45%	**40.7%**
	Utility per patient	0.01064	0.01090	**0.01107**	0.01116	0.01142	0.01167	0.01193	0.01219	**0.01954**
£100	Cost per patient	-£456	-£472	**-£483**	-£488	-£505	-£521	-£537	-£553	**-£483**
	Cost per QALY	-£42,867	-£43,336	-£43,645	-£43,784	-£44,211	-£44,619	-£45,009	-£45,383	-£24,742
£200	Cost per patient	-£282	-£299	**-£310**	-£316	-£332	-£349	-£365	-£382	**-£310**
	Cost per QALY	-£26,545	-£27,437	-£28,023	-£28,288	-£29,100	-£29,876	-£30,619	-£31,330	-£15,887
£300	Cost per patient	-£109	-£126	**-£137**	-£143	-£160	-£177	-£194	-£211	**-£137**
	Cost per QALY	-£10,223	-£11,538	-£12,402	-£12,792	-£13,990	-£15,134	-£16,229	-£17,277	-£7,031
£400	Cost per patient	£65	£48	**£36**	£30	£13	-£5	-£22	-£39	**£36**
	Cost per QALY	£6,099	£4,361	£3,219	£2,703	£1,121	-£392	-£1,838	-£3,224	£1,825
£500	Cost per patient	£239	£221	**£209**	£203	£185	£168	£150	£132	**£209**
	Cost per QALY	£22,421	£20,260	£18,840	£18,199	£16,231	£14,351	£12,552	£10,829	£10,680
£600	Cost per patient	£412	£394	**£382**	£376	£358	£340	£321	£303	**£382**
	Cost per QALY	£38,743	£36,159	**£34,461**	£33,694	£31,342	£29,093	£26,942	£24,883	£19,536
£700	Cost per patient	£586	£567	**£555**	£549	£530	£512	£493	£475	**£555**
	Cost per QALY	£55,065	£52,058	**£50,082**	£49,190	£46,452	£43,836	£41,332	£38,936	£28,392
£800	Cost per patient	£759	£741	**£728**	£722	£703	£684	£665	£646	**£728**
	Cost per QALY	£71,387	£67,957	**£65,703**	£64,685	£61,562	£58,578	£55,723	£52,989	**£37,248**
Threshold premium (£30000)		**£552**	**£567**	**£577**	**£582**	**£597**	**£612**	**£627**	**£643**	**£926**

8. Summary

The principal findings of the additional research and analysis undertaken at the request of the Appraisal Committee are as follows:

- economic results are very insensitive to changes in stent wastage rates;
- introducing a more sophisticated (albeit conjectural) representation of the disutility due to PCI and CABG worsens the cost-effectiveness of DES for elective patients, but improves it for non-elective patients. This is due to the different proportions of repeat revascularisations requiring CABG;
- there is a strong body of evidence from both RCTs and observational studies to indicate that survival is not affected by stenting or the type of stent used, either directly or as a consequence of subsequent AMIs or re-interventions;
- there is some evidence from RCTs that BMS may be associated with a larger risk of non-fatal AMI than are DES, resulting in a small additional cost per patient treated, and a related utility effect;
- when adjusted to a common basis, UK data sources provide remarkably consistent estimates of the risks of repeat revascularisation close to those assumed in the main report. Estimates for non-UK sources are more variable possibly reflecting different environmental influences and clinical practices;
- 'conventional' risk factors are not efficient independent estimators for repeat revascularisation risks. In particular, diabetes does not feature in any of the published models reviewed, when assessed on a common basis. Stenting of a small vessel in the strongest predictor among the 'conventional' factors.

Appendix 1: Directory of NICE Addendum project specification and assessment group response

Assessment group response (including statement of limitations) to original NICE project proposal

Task	Proposed work and limitations	Location of further analyses within Addendum (Page)
To consider the implications for the cost-effectiveness of DES of varying stent wastage rates.	A simple sensitivity analysis from 0% to 10% (around baseline value of 5%).	2. Wastage Rates (7)
To consider the implications for the cost-effectiveness of DES of uncertainty in the post-procedural disutility associated with PCI/CABG.	Best/worst case scenarios for PCI and DES, and 2-way combinations of these.	3. Procedural Disutility (14)
To consider the implications for the cost-effectiveness of DES of incorporating into the analysis the peri-procedural mortality risks associated with PCI/CABG when undertaken as repeat interventions following primary PCI.	Minor modification of model and/or analysis to allow alternate estimates to be generated. *Limitations:* availability of suitable and relevant data on mortality risks and life expectancy following repeat intervention.	4. AMI and Mortality - is there a case for a DES effect? (18)
To reassess evidence for and against differential AMI rates following DES and BMS, and consider the possible implications of such a difference for estimated costs, outcomes and the cost-effectiveness of DES.	Review of evidence that might support the use of differential AMI rates and exploration of the implications of such a difference for estimates of cost-effectiveness. *Limitations:* though efforts will be made to identify evidence, it will not be possible to carry out a systematic search for all potentially relevant sources for parameter values.	4. AMI and Mortality - is there a case for a DES effect? (18)
To reassess evidence relevant to estimating	Identify any additional sources of evidence, assess their quality and	5. Realistic Repeat

Task	Proposed work and limitations	Location of further analyses within Addendum (Page)
realistic repeat revascularization rates from unselected patient populations, and assess its suitability for estimating rates appropriate to current clinical practice in England and Wales.	relevance, adjusting where possible for identifiable case-mix differences. Explore the results of using alternate estimates of repeat revascularization rates in the model. *Limitations:* though efforts will be made to identify evidence, it will not be possible to carry out a systematic search for all potentially relevant sources. In addition, the scope for obtaining additional information from authors/custodians to ensure comparability will be severely limited. In particular, account can only be taken on Scottish Audit data if rapid access to this is obtained by NICE.	Revascularization Rates (25)
To consider whether alternative published risk factor models could be employed in the analysis, and the implications of doing so for the cost-effectiveness of DES	Identify any additional sources of evidence, assess their quality and relevance, adjusting where possible for identifiable case-mix differences. Make minor modifications to the model and/or analysis to explore the implications alternate rates. *Limitations:* though efforts will be made to identify evidence, it will not be possible to carry out a systematic search for all potentially relevant sources, nor to obtain additional details from authors.	6. Risk Factor Models and Sub-Groups (29)
To carry out 2 or 3 way sensitivity analyses of major potential sources of uncertainty identified from the above tasks, including the influence of different values of the DES price premium.	Carry out sensitivity analyses with the current model (involving no more than minor amendments). *Limitations:* only selected sensitivity analyses can be undertaken in the time available.	7. Sensitivity Analyses (39)

NICE project specification with location of assessment group further analyses

Specification summary	Details of specification (with reference to location of further analyses within this Addendum)
Synopsis of the technical issue	At the Appraisal Committee meeting to discuss the development of the Appraisal Consultation Document a number of issues with the economic evaluation were raised. Most notably: • The Appraisal Committee was aware that no statistically significant differences for mortality or morbidity were found in the trials for DES versus BMS, however the Committee was mindful that although the trial data showed no statistical significance, there was a difference in AMI in favour of DES and that this should be taken account of in the economic evaluation. The Committee was also mindful of data in the literature regarding mortality and morbidity of CABG and repeat angiography. See: Section 4. (18) • After reviewing the utility values in the Assessment Group's model the Committee was mindful of the possibility that there could be an additional disutility associated with CABG during the initial six weeks following the procedure compared with PCI. See: Section 3 (14) • The Committee was persuaded that neither the Liverpool (CTC) and the Leicester registry data or the randomised controlled trial data were representative of repeat revascularisation rates in patients and as the BASKET trial and the Scottish Registry data had used methods that were likely to collect follow-up data from all patients, these data would therefore be more representative. See: Section 1 (3) • The Committee heard that there was no consensus in the trials or registries regarding which risk factors would put an individual at a high risk of revascularisation. They were persuaded that the Assessment Group's risk factors used in the current assessment report, based on the CTC registry data were one possibility, however risk factors which had been used in the previous appraisal should also be included in the current model. The Committee also heard that diabetes should be considered as an independent risk factor for restenosis too. See: Sections 1 (3) and 6 (29) • The Committee discussed the significance of the price premium (difference between DES and BMS price) and were mindful of the possibility that the price premium used in the Assessment Group's model was possibly too high (£560), given the procurement deals that took place in certain areas that brought the price premium down to less than £300. See:

Specification summary	Details of specification (with reference to location of further analyses within this Addendum)
	Section 7 (39) As a result of these points, further work was requested to be undertaken.
Question(s) to be answered by the Assessment Group	What is the cost effectiveness of DES in the treatment of ischaemic heart disease? The base-case scenario should be updated and if data allows should include: • the risk of AMI See: Section 4 (18) • the mortality risk associated with CABG See: Section 4 (18) • the mortality risk associated with angiography See: Section 4 (18) • the disutilities associated with CABG versus PCI immediately (in the 6 week period) following the procedure See: Section 3 (14) • the absolute risk of revascularisation of BMS taken from the Scottish registry data See: Section 1 (3) • the relative risks of the independent risk factors (small vessel and long lesion) taken from the trials See: Sections 1 (3), 5 (25) and 6 (29) • if it is identified from the clinical evidence to be an independent risk factor, diabetes as another risk factor See: Section 6 (29) Sensitivity analysis should be carried out on the above estimates if appropriate and around: • the price premium ranging from £255 (based on a cost used in Scotland) to £1000 (list price) for stents See: Section 7 (39) • the stent wastage rates at 1% and 5% See: Section 2 (7)
How will these questions be addressed in an addendum?	The Assessment Group will be asked to: • identify data in the literature regarding mortality and morbidity of CABG and repeat revascularisation. See: Section 1 (3) • identify additional utility values in the first six weeks following CABG or PCI. See: Section 3 (14) • identify the parameter values for the base-case scenario accordingly using data from the Scottish registry for absolute risks, relative risks for the two sub-groups (small vessels and long lesions) from the trial data, additional utility values and price premium. See: Sections 6 (29) and 7 (39)

Specification summary	Details of specification (with reference to location of further analyses within this Addendum)
	• identify from the literature and review whether diabetes is an independent risk factor for restensosis. See: Section 6 (29) • develop a model, containing these new parameters with an appropriate time horizon, for example 12 months See: Section 7 (39) • synthesise the available information and calculate the degree of uncertainty around the cost effectiveness estimate using sensitivity analysis. See: Section 7 (39)
Relevant new evidence requested	• Data in literature regarding mortality and morbidity of CABG and angiography • Data on absolute risk of revascularisation from the Scottish registry data • Clinical evidence regarding whether diabetes is an independent risk factor for restenosis.

Specification text taken (unedited) from: http://www.nice.org.uk/page.aspx?o=293164

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