BCIS Comments on the Economic Model

As requested The British Cardiovascular Intervention Society has now carefully reviewed LRiG economic model..

The model is a basic health economic model that depends for its value on the accuracy of the figures imputed into it. The model as such is exquisitively sensitive to some key parameters . The decision regarding cost efficacy appears thus to be dependant on the choice of the various absolute values used – why certain values were chosen and used in this model continues to remain unclear. We continue to be perplexed as to why the values used are different from those from published data or indicated as valid by the N.I.C.E committee

Yet again we wish to bring to the attention of the N.I.C.E executive the falure by the N.I.C.E committee to use apprpropriate and accurate data in deriving the Guidance on DES

1. Absolute Risk of Repeat Revascularisation

- It is unclear why the absolute risks of repeat revascularisation with BMS have been set at 10% for elective patients and 13% for non-elective patients, averaging to 11% for all patients. This is inconsistent with the Appraisal Committee's previous request that LRiG update the economic model with absolute risk of repeat revascularisation taken from the Scottish registry (Addendum 3' page 48). The submission to NICE by NHS QIS (dated 13th January 2006) states:

  "*The Scottish Coronary Revascularisation Register Report for 2003-04 reports a repeat revascularisation rate at 12 months of* ***12.9%*** *(95%CI 12.1-13.7; n=6525 vs 7.79% in Liverpool) for patients undergoing elective PCI and* ***16.6%*** *(15.7-17.6; n=5921 vs 10.15% in Liverpool) for patients undergoing PCI for unstable coronary syndromes.*"

  It is clearly perverse to request that specific data be used in the economic model and to then ignore those data. If one combines the Scottish data submitted by NHS QIS (above) using the correct national proportion of ACS patients (44%), then the overall unselected population absolute risk of repeat revascularisation is **14.5%**.

- BCIS has always argued that a value of 13% for absolute risk is justified from the randomised trials and registries in the worldwide literature, However if we were to follow the NICE recommendation of Jan 2006 **14.5%** would be the correct starting point in the economic model for the unselected population. We would continue to support and be happy to justify (as we have done previously) the 13% figure despite this , since we believe this is a true reflection of the current clinical scenario.

- There is **no** justification on any grounds (scientific, evidence based, or clinically reported) to reduce the base rate with BMS to less than 13%

2. Relative Risks for the Independent Risk Factors

- It is unclear why the relative risks for the independent risk factors remain solely based on the CTC database when BCIS have previously presented all relevant data and repeatedly from the literature. Whilst the CTC relative risks for small vessels and long lesions are within the literature range, the relative risk for diabetes is outside the lower range (CTC 1.19, Addendum 6', literature mean 1.52, range 1.34-1.18). LRiG's low value is driven by the use of a relative risk of 0.90 for non-elective patients and is clearly a spurious result for this positively-predictive factor. Further it is clear form the CTC database that the population is a low risk one with wa low incidence od diabetes.

- The economic models accuracy and robustness would be improved significantly if BCIS's previously submitted relative risks (shown below in Table 1) were used when evaluating the excess risk associated with long lesions, small vessels and diabetes.

- These values are not derived from "BCIS" They come from peer reviewed published data and contain angiographically driven but more importantly non angiographically driven RCT and registries including the N.I.C.E –favoured BASKET study.

Sub-group	Relative Risk	Comment	Source
Small vessels			
	1.55	12m non-MI related TVR, stents <3mm diameter	BASKET trial, Kaiser et al 2006
	1.17	12m TLR, vessels <2.75mm vs vessels >2.75mm	SIRIUS trial, Holmes et al 2004
	2.09	24m TLR, minimum lumen diameter <3mm	Stent design trial, Elbaz et al 2002
	1.79	9m revascularisation, vessels <2.75mm vs >2.75mm in lesions <20mm length (estimate)	Clinical database, Ellis et al 2004
	1.52	12m reintervention, vessels <2mm, elective patients	Assessment Report Addendum 3"
	2.62	12m reintervention, vessels <2mm, non-elective patients	Assessment Report Addendum 3"
	1.78	12m TVR, vessels <3mm vs vessels >3mm (estimate)	Clinical database, Gotschall et al 2006
	1.33	12m TLR (estimate)	Clinical database, Kornowski et al 1999
	1.71	6m TLR, mimimum lumen diameter <3mm	Clinical database, Kastrati et al1997
	1.84	9m TLR, <3mm vs vessels >3mm (estimate)	ENDEAVOR II trial, Fajadet et al 2006
	1.85	12m TLR, longer stent length	TAXUS IV trial, Stone et al 2004
Mean	***1.75***		
Long lesions			
	1.10	12m TLR (estimate) per 5mm lesion length increase, no angiographic follow up	Trial meta analysis, Cutlip et al 2002
	1.18	12m TLR, lesions >13.5mm vs lesions < 13.5mm	SIRIUS trial, Holmes et al 2004
	1.02	12m TVR, per unit (undefined) increase	Clinical database, Agema et al 2003
	2.11	9m revascularisation, lesions >20mm vs <20mm in vessels >3.25mm diameter (estimate)	Clinical database, Ellis et al 2004
	1.01	12m revascularisation, per 1mm increase in stent length	Clinical database, Wu et al 2004
	1.20	12m reintervention, lesions >20mm, elective patients	Assessment Report Addendum 3"
	1.19	12m reintervention, lesions >20mm, non-elective patients	Assessment Report Addendum 3"
	2.15	12m TVR, lesions >20mm vs lesions <20mm (estimate)	Clinical database, Gotschall et al 2006
	1.42	12m TVR, lesions >20mm vs lesions <20mm (estimate)	PRESTO trial, Singh et al 2005
	1.41	9m TLR, lesions >16mm vs lesions <16mm (estimate)	ENDEAVOR II trial, Fajadet et al 2006
	1.04	12m TLR, longer stent length	TAXUS IV trial, Stone et al 2004
Mean	***1.35***		
Diabetes			
	1.81	12m TVR	RESEARCH registry, Lemos et al 2004
	1.51	12m TLR	SIRIUS trial, Holmes et al 2004
	1.80	12m TVR	TAXUS IV trial, Pinto et al 2006
	1.42	12m TLR (estimate), no angiographic follow up	Meta analysis, Cutlip et al 2002
	1.57	12m TVR	Clinical database, Agema et al 2003
	1.52	12m revascularisation by CABG	Clinical database, Wu et al 2004
	1.38	12m reintervention, elective patients	Assessment Report Addendum 3"
	1.36	12m TVR (estimate)	Clinical database, Gotschall et al 2006
	1.35	12m TLR (estimate)	Clinical database, Kornowski et al 1999
	1.34	6m TLR (estimate)	Clinical database, Kastrati et al1997
	1.73	12m TLR (estimate)	Clinical database, Jilaihawi et al 2005
	1.39	9m TLR	ENDEAVOR II trial, Fajadet et al 2006
Mean	***1.52***		

Table 1. Relative risk for repeat revascularisation for the independent risk factors of small vessels, long lesions and diabetes.

Using these appropriate relative risk adjustments will result in the following values for TVR needing to be inserted in the model for these higher risk patients:

Small Vessels: 1.75 x 13% = 23%
Long Lesions: 1.35 x 13% = 18%
Diabetes: 1.52 x 13% = 20%

Of course if we started with a 14.5% absolute risk as suggested by NICE then these figures would be higher still.

(3) Relative Risk Reduction for DES

- The 55% risk reduction used in one of the model scenarios is an under-estimate of the true 60-70% reduction shown by the randomised trials. The model scenario that employs a 65% risk reduction is more representative of the randomised trials, but the model would be more reliable if the literature-based risk reductions previously presented by BCIS were used in the model (reproduced in Table 2). Again these are a large set of data from peer review publication including both angiographically driven and non angiographically driven outcomes.

Sub-group	DES Risk Reduction	Comment	Source
Base case			
	0.67	12m TVR	RESEARCH registry, Lemos et al 2004
	0.75	12m TLR	SIRIUS trial, Holmes et al 2004
	0.65	12m TVR, no angiographic follow up	TAXUS IV trial, Pinto et al 2006
	0.53	9m TVR	TAXUS VI trial, Dawkins et al 2005
	0.56	9m TLR, no angiogram subset	ENDEAVOR II trial, Fajadet et al 2006
	0.41	12m non-MI related TVR (estimate)	BASKET trial, Kaiser et al 2006
Mean	***0.60***		
Small vessels			
	0.67	12m TVR, vessels </= 2.5mm	RESEARCH registry, Lemos et al 2004
	0.76	12m TLR, vessels 2.5-3.0mm in non-diabetics	SIRIUS trial, Holmes et al 2004
	0.83	9m TLR, vessels <2.5mm	TAXUS VI trial, Dawkins et al 2005
	0.61	12m non-MI related TVR, stents <3mm	BASKET trial, Kaiser et al 2006
	0.57	9m TLR, vessels <2.5mm	ENDEAVOR II trial, Fajadet et al 2006
	0.71	12m TLR, vessels <3mm (estimate)	TAXIS IV trial, Stone et al 2004
Mean	***0.69***		
Long lesions			
	0.59	12m TVR, lesion >/= 33mm	RESEARCH registry, Lemos et al 2004
	0.78	12m TLR, lesions >15mm in non-diabetics with vessels >3mm	SIRIUS trial, Holmes et al 2004
	0.83	9m TLR, lesions >26mm	TAXUS VI trial, Dawkins et al 2005
	0.57	9m TLR, lesions >16mm	ENDEAVOR II trial, Fajadet et al 2006
	0.75	12m TLR, lesions > 20mm	TAXIS IV trial, Stone et al 2004
Mean	***0.70***		
Diabetes			
	0.28	12m TVR	RESEARCH registry, Lemos et al 2004
	0.77	12m TLR, in vessels >3mm, lesions 12-15mm in length	SIRIUS trial, Holmes et al 2004
	0.88	9m TLR	TAXUS VI trial, Dawkins et al 2005
	0.51	9m TLR	ENDEAVOR II trial, Fajadet et al 2006
	0.63	12m TLR	TAXIS IV trial, Stone et al 2004
Mean	***0.61***		

Table 2. Relative risk gained from DES for the independent risk factors of small vessels, long lesions and diabetes.

4. Drug Eluting Stent Price Premium

- The model investigates the cost effectiveness of DES across a range of price premium. A key decision for the Appraisal Committee will be what premium is realistic. Comments from BCIS members leads us to conclude that £300 is a realistic premium and most appropriate to use in the model. This is consistent with previous evidence presented to the committee and within the range previously publically acknowledged by the Committee.

We would also have the following comments which we have not expressed previously:

NHS Reference Costs

- The reference costs used in the model date from 2003-04 and are not representative of costs for 2008 onwards when the new guidance will apply. Table 3 shows the latest and most up to date NHS reference costs for 2005-06. As these are higher, the 2003-04 costs currently used in the model work to the disadvantage of DES cost efficacy. The model we believe reflect true cost efficacy and therefore must be re-run using the most bcontemporary 2005-06 reference costs.

Cost Item	Current Model Input (2003-04 Costs)	2005-06 Reference Cost
Cardiology out-patient visit	£134	£148 (code 320F)
Cardiac surgery out-patient visit	£208	£274 (code 172F)
Angiography	£724	£838 (day case E14)
Unstented PCI	£1453.40	£1937.40
CABG	£7066	£8172
Cardiology out-patient f/up visit	£94	£104 (code 320F)
Cardiac surgery out-patient f/up visit	£156	£182 (code 172F)

Table 3. Revised cost inputs based on 2005-06 reference costs.

Waiting Times for PCI and CABG

- In order to calculate QALY loss awaiting repeat revascularisation, the model employs a 16 week wait for PCI, a 9 week wait for CABG and assumes a 4 week wait prior to joining the list. A methodology that more realistically reflects real-world UK practice was reported by Hawkins, Sculpher and Rothman (2005), who considered the total wait to be made up of three elements: time waiting for first consultant appointment, time waiting for coronary angiography and time waiting for the revascularisation procedure.

- Table 4 shows the latest available NHS data inputs to this calculation. The current LRiG model understates the waiting time assumptions by 5.1 weeks for PCI and 13.4 weeks for CABG and the model should therefore be re-run using the data in Table 4.

	Weeks				Mean weeks	Mean days	Mean years	Source
1st OP visit	**0 to 4**	**4 to 8**	**8 to 13**	**>13**				
Cardiology patients (n)	35,260	20,996	20,059	985	6	42	0.11499	NHS waiting time stats
Cardiac surgery patients (n)	401	112	38	1	6	42	0.11499	NHS waiting time stats
Angiography					11.1	78	0.21355	HES 2005-06
Procedure								
PCI					8.0	56	0.15332	HES 2005-06
CABG					9.3	65	0.17796	HES 2005-06
Overall								
PCI					25.1	176	0.48186	HES 2005-06
CABG					26.4	185	0.50650	HES 2005-06

Table 4. Calculation of overall waiting times for PCI and CABG according to the method of Hawkins, Sculpher and Rothman (2005). *The mean waiting time for 1st out-patients visit is estimated to be 6 weeks. Overall = 1st OP wait + angiography wait + procedure wait.*

Combination of Elective and Non-elective Datasets

- The model combines the incremental costs and utilities from the elective and non-elective models according to the proportion of patients in each of these two categories in the CTC dataset. The CTC proportion of 32.35% non-elective is low compared with the national picture in which 48.5% (BCIS audit figures for 2006) present as acute coronary syndromes. Thus, LRiG's combination of data, based on a single centre, is not representative of the national picture. Thus, in order to ensure accuracy, the model should be revised to include at least a 49% non-elective contribution.

- Combination of the two datasets according to the proportions of elective and non-elective is not ideal and has the hallmarks of a 'quick fix'. This appears to have led to some inconsistency between the number of stents used given in Table A of Addendum 6' and the number of stents used shown in the separate elective and non-elective datasets in Table A of Addendum 5'. The number of stents per procedure in Addendum 6' should be the same as that resulting from the combination of the separate datasets in Addendum 5' in the proportions of elective and non-elective patients, but it is not. BCIS have re-calculated the mean stents per procedure and the discrepancies are shown in Table 5.

	Elective	Non-elective	LRiG Combined	BCIS Calculated
Proportion	0.6765	0.3235		
Stents per patient				
No risk factors	1.54	1.43	1.54	1.50
Long lesions	1.63	1.42	1.53	1.56
Diabetes	1.56	1.52	1.56	1.55
Small vessels	2.30	2.00	1.66	***2.20***
Long+ Diabetes	1.72	1.54	1.73	1.66
Long + Small	2.53	2.50	2.24	***2.52***
Small + Diabetes	2.67	2.00	2.57	2.45
Long + Small + Diabetes	3.00	2.00	2.63	2.68
Overall	**1.615**	**1.467**	**1.571**	**1.567**

Table 5. Comparison of LRiG's combined 'number of stents per patient' dataset with BCIS's calculation of the same from the separate elective and non-elective groups.

- Table 5 shows that there are particular differences for small vessels and long lesions + small vessels. It is our belief that the model reflects the stents per patient shown in the column 'BCIS calculated', in which case LRiG's combined parameter values table shown in Addendum 6' is wrong. However, if the combined parameter values in Addendum 6' correctly describes the mean stents per patient for the total elective + non-elective dataset, then ***the model substantially over-estimates the ICER for small vessels and small vessels + long lesions***. LRiG should be asked by N.I.C.E to

investigate these questions and issue a clarification. Again wrong imput will result in wrong oconclusions from the model

- If the separate datasets prove to be correct, they should be combined in the proportions of 52% elective and 48% non-elective as above and the model re-run on this basis. If the Addendum 6' combined dataset is correct, the model should be re-run using these data.

Acute Coronary Syndromes

- BCIS note that NICE are now consulting on a clinical guideline development for the management of patients with acute coronary syndromes (ACS). It would therefore be appropriate and helpful for the Appraisal Committee to consider ACS patients as a sub-group who may benefit from DES.
- The Committee will be aware that ACS patients who receive BMS are already prescribed Clopidogrel for 12 months, so this cost essentially drops out of the model for ACS and is likely to have a considerable impact on the cost-effectiveness of DES. Whilst BCIS do not agree with 'elective' or 'non-elective' as a clinical categorisation of patients, those presenting with ACS tend to do so in the non-elective setting thus 'non-elective' relative risks, costs and resource use are the most appropriate inputs for an ACS model.

Summary

- Whilst the LRiG model structure is appropriate to address the cost effectiveness question, a considerable number of data inputs are either questionable, unrepresentative or out of date. The inappropriate use of such inputs, as they currently stand, make any conclusions base don the model wholly unreliable. This is not a good way to construct a National policy – on flawed data

- LRiG's model should be re-run using the following data inputs:

    1. A 13% repeat revascularisation rate for an unselected population (although it would be possible to argue for a 14.4% level based on the Scottish registry).
    2. The literature-based relative risks for the risk factors of long lesions (1.35), small vessels (1.75) and diabetes (1.52).
    3. The trial-based DES risk reductions for the overall population (0.60), long lesions (0.70), small vessels (0.69) and diabetes (0.61).
    4. DES price premium of £300, reflecting current national pricing.
    5. The 2005-06 reference costs.
    6. Up to date waiting times, calculated according to the UK-based methodology published by Hawkins, Sculpher and Rothman (2005).
    7. LRiG elective and non-elective datasets combined in the nationally-appropriate proportions of 52% elective and 48% non-elective.
    8. Clarified and/or corrected inputs for the mean number of stents per patient.

- The cost-effectiveness of DES in patients with acute coronary syndromes should also be modelled to inform the clinical guideline development. The above points on data inputs should be implemented into this model.

References

Department of Health (2007). England Summary - Outpatient First Attendances, Q4 2006-07. www.performance.doh.gov.uk/waitingtimes/2006/q4/qm08_y00.html. (Accessed 21st September 2007).

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