National Institute for Health and Clinical Excellence

390 – Percutaneous laser revascularistion for refractory angina pectoris

Consultation Comments table

IPAC date: Thursday 12th March

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Private Sector Professional	**1**	Bupa agrees	Thank you for your comment
2	Consultee 1 Private Sector Professional	**2.1**	?CBT?	Thank you for your comment. The Committee considered this comment but decided not to change the guidance to include cognitive behavior therapy. Section 2.1.2 of the guidance will be changed to remove reference to treatments.
3	Consultee 1 Private Sector Professional	**2.2**	No comment, thank you	Thank you for your comment.
4	Consultee 1 Private Sector Professional	**2.3**	Exercise capacity and overall survival are key outcomes, surely?	Thank you for your comment. These outcome measures were analysed in the systematic review on which the guidance is based. Mortality is included in section 2.3.1 and 2.4.1 of the guidance; exercise tolerance is included in section 2.4.3 of the guidance.
5	Consultee 1 Private Sector Professional	**2.4**	No comment, thanks.	Thank you for your comment.

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6	Consultee 2 on behalf of BCIS and BCS	**General**	Consultation document for NICE entitled "Percutaneous laser revascularisation for refractory angina pectoris" The systematic review has identified the relevant trials and observational studies, to our knowledge. There are two methodological concerns and some issues of interpretation that we would like to draw attention to. First, not all of the percutaneous myocardial laser revascularisation (PMR) trials have used the same control arm. Five trials compared PMR to medical therapy and one trial compared PMR to spinal cord stimulation (SCS).[1] If SCS is more effective at controlling anginal symptoms than medical therapy, then the inclusion of the SCS trial in the meta-analysis may result in an underestimate of the benefits of PMR. However we note that the weighting attached to the results of this trial in the meta-analysis, with regard to the outcomes of exercise time and anginal symptoms was relatively low, and so even in the absence of formal sensitivity testing it would appear that this methodological concern is not likely to have significantly impacted upon the final results.	Of the 7 studies identified, 3 used medical management as a control, 2 used sham therapy and one used spinal cord stimulation as a control. The Committee were aware of the variation in control arms between studies and accounted for this when considering their recommendations. Meta-analysis was further stratified by comparator stratum (as above). No significant effect favouring the PMR intervention was observed in any of the stratified models, in fact for mortality in the model comparing PMR with medical management the results favour the latter (OR 2.26, 95%CI 1.05-5.05). The stratified models now form Appendix 5 figures 1, 2, 3, 4 and 5.
7	Consultee 2 on behalf of BCIS and BCS		Second, there has been no apparent consideration given to the different laser systems utilised in the different trials. All were Holmium:YAG lasers, but one trial 2 employed a different system: so-called direct myocardial laser revascularisation (DMR), intended to be a non-penetrative stimulation of angiogenesis. It may not be appropriate to group together these different technologies in a meta-analysis. Nevertheless, because the effect measures of the DMR trial were generally favourable with regard to mortality, exercise capacity and anginal symptoms, the inclusion of this trial will not have contributed to any underestimate of the potential benefits of PMR.	The IP programme issues guidance on procedures rather than individual devices, and the scope of the systematic review therefore addressed the procedure rather than individual pieces of equipment. No additional sensitivity analysis was carried out in relation to this specific issue, because it was seen as low priority. As the consultee suggests, the inclusion of this study was conservative, i.e. favouring the PMR group, and, in general, we believe issues of heterogeneity were handled appropriately, by using random (as opposed to fixed) effect models in the meta-analyses.

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8	Consultee 2 on behalf of BCIS and BCS		The expectation that adenosine SPECT perfusion imaging, in patients who almost invariably had multi-vessel coronary disease, could detect small improvements in myocardial perfusion would appear very optimistic. We have similar concerns regarding the use of global ejection fraction. Despite the meta-analysis demonstrating clear benefit in symptom control, the authors perform a non-specified sensitivity analysis of blinded studies and appear to conclude that there is no significant benefit yet fail to clarify whether this lack of significance is a consequence of inadequate power resulting from widening of the confidence intervals due to a removal of a significant (and unspecified and unknown) proportion of the sample size, or whether the effect measure is truly lessened.	The importance of blinding in the respective trials was a major concern of the Committee and was pivotal in drawing up recommendations. Further iterations of meta-analysis models were carried out and the results are now better stipulated in appendix 5 figure 6. In addition to loss of significance, the central estimate of effect moved substantially towards parity (from 2.32 to 1.53) indicating both loss of effect, as well as loss of power.
9	Consultee 2 on behalf of BCIS and BCS		These methodological issues are worthy of consideration prior to release of the final NICE recommendations. McNab D, Khan S, Sharples L, et al. An open-label, single centre, randomized trial of spinal cord stimulation vs. percutaneous myocardial laser revascularization in patients with refractory angina pectoris: the SPiRiT trial. European Heart Journal 2006; 27:1048-1053. Leon M, Kornowski R, Downey W, et al. A blinded, randomized, placebo-controlled trial of percutaneous laser myocardial revascularization to improve angina symptoms in patients with severe coronary disease. Journal of American College of Cardiology 2005; 46:1812-19.	Noted, thank you.