NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence

Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

VibraTip for testing vibration perception in the detection of diabetic peripheral neuropathy

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from Newcastle upon Tyne Hospitals (NUTH) and York Health Economics Consortium (YHEC) External Assessment Centre to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 4pm, **Wednesday April 30th 2014** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

28/04/2014

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P6. The study by Bowling *et al.* (2012) (1) was performed in a population who had had DPN pre-diagnosed, and reported on the target condition of 'at risk' feet. This study was considered to be of limited value because use of VibraTip or its comparators is not routinely used to detect DPN in this very high risk population.	Propose this conclusion is reconsidered….	What is used to detect DPN in high risk populations?	The EAC's meaning here is that, following the clinical pathway from NICE CG10, patients in the general diabetic population are screened for DPN during their annual review, using monofilament or vibration perception test. Those with detected DPN are referred on to the services of a foot protection team according to 'increased risk' (3 to 6 month checks) or 'high risk' (1 to 3 month checks) of foot ulceration. We have been advised by our Clinical Experts that once the initial DPN diagnosis is made, then it is not standard practice to repeat DPN checks at these more frequent foot protection appointments, as it is rare for the condition to regress. Extent of spread and severity of neuropathy (up the leg) may be assessed, but this is not the same as detection. *Action: None.*

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P.6 The study by Nizar *et al*. (2014) (8) used a modified reference standard, that of a neurothesiometer set to 20 V rather than the usual threshold of 25 V. This difference in vibration perception threshold is clinically significant, and for this reason, this study was judged not to be generalisable to the decision problem.	…This difference in vibration perception threshold may be clinically \significant and could make the study more relevant to the decision problem.	As stated by the study authors.. We used a lower threshold of 20Volts for the confirmation of peripheral neuropathy compared to 25Volts used in the previous study.8 This loss of vibration sense could therefore be recognised at a much earlier stage, providing opportunity to prevent complications.	In critique of this paper, the EAC judged that the ability to detect a vibration stimulus of 20V is more representative of a healthier population than the reference standard of 25V for vibration perception threshold of DPN used elsewhere in the published literature. Nizar et al. do not define a hypothesis to explain their choice of 20V in this study. 20V is therefore not considered a 'reference standard' which can be generalised to the decision problem in NICE scope. *Action: None.*

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P.8 Using technical papers on the useful life of VibraTip (6) and the durability of the Bailey's 10g monofilament	Using technical papers on the useful life of VibraTip (4) and the durability of the Bailey's 10g monofilament (12), the EAC estimated the cost range per examination	Ref 4 not 6 Ref 4 authors showed VibraTip	Ref 4 authors showed that under conditions that mimic clinical use, the VibraTip has a consistent **frequency** output for up to 5000 activations

(12), the EAC estimated the most likely cost per examination using Vibratip would be between 4.0 pence and 10.0 pence. The corresponding figure for the 10g monofilament would be between 3.04 and 7.6 pence, which these ranges overlapping. The EAC could not estimate the per examination cost for the 128 Hz tuning fork using this methodology because it has an indefinite shelf life. The EAC concluded that the economic case for VibraTip had not been made.	using Vibratip would be between 0.4 pence and 10.0 pence. The corresponding figure for the 10g monofilament would be between 17.7 pence and 22.9 pence. On this basis the economic case for VibraTip has been made.	output consistency up to 5,000 activations. EAC used the very conservative number of 1,000 activations with 10 sites tested per patient to arrive at 10 pence cost. The 5,000 activations number associated with 2 sites per patients provides the low end of the range 0.4 pence. Ref 12 authors state "At best, monofilaments…would remain within a usable range for 7-10 days or to evaluate 70-90 patients." EAC estimate of monofilament cost is £16 (Table 4.3) therefore cost range per examination is 17.7 pence to 22.9 pence. (Based on section 4.5 below the estimated cost per examination using a Baileys monofilament is 13.3p)	(Figure 4A), however, VibraTip has a consistent **amplitude** output for up to 1000 activations (Figure 4B). We have been advised by our Clinical Experts that it is the amplitude of the vibration stimulus that is more important than the frequency in terms of vibration perception. In Ref 4 (Horsfield and Levy) the authors stated that VibraTip would provide a very consistent source of vibration to test at least 100 patients, if not considerably more. We have exactly cited this sentence in the critique. For reference 12 (Lavery et al.) we used the actual data from Table 1 for our estimates rather than the modelled data which was very conservative in its definition of life time use (Table 3). It should be noted that the steady state value for the Bailey monofilament is 8.82g (95% CI 8.5 to 9.2), which is very close to the accepted value of 9g (and within confidence intervals). It is unclear if a drop of 0.18g below 9g

			would be of any clinical significance, and this decrease in amplitude is much less than that seen with VibraTip after 2000 activations (25% drop). From Figure 4B of Horsfield and Levy, the EAC estimates >10% drop in amplitude around 1300 activations, and beyond 1000 activations the device cannot be considered to be providing consistent amplitude, which the 10g monofilament arguably can. The Clinical Experts advised us that there is no standard number of sites per foot to test for vibration, therefore the suggestion that only one site per foot would be used is debateable (and covered in the sensitivity analysis regarding per-examination costs calculated by the EAC.) *Action: the EAC will amend the text to reflect the facts discussed above and include an estimate of costs for monofilament based on Lavery's conservative conclusion (70 to 90 patients treated with 10g monofilament) in section 4.5 of the report. However, the EAC maintains approximately 2000 uses is a more plausible scenario (see below), so the conclusion and summary will not*

			be changed.

Issue 4

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
P.111 Section 4.5 However, it is known that the useful life of the 10g monofilament is limited, and this issue has been addressed in the literature. A technical study performed by Lavery *et al.* (2012) on several brands of monofilaments showed considerable variation on their durability after repeat testing (12). However, the Bailey's 10g monofilament (used widely in the NHS) fared comparatively well, with the results indicating the device produced a buckling force within the limits of acceptability (between 9 and 11 grams) after 1800 to 2400 tests. If the device is used 5 times on both	However, it is known that the useful life of the 10g monofilament is limited, and this issue has been addressed in the literature. A technical study performed by Lavery *et al.* (2012) on several brands of monofilaments showed considerable variation on their durability after repeat testing (12). However, the Bailey's 10g monofilament (used widely in the NHS) fared comparatively well, with the results indicating the device consistently produced a buckling force within the limits of acceptability (between 9 and 11 grams) upto 1200 tests. If the device is used 5 times on both feet, this suggests the Bailey's monofilament would have a useful life of approximately 120 patients before requiring replacement. NB – Table 4.5, section 4.6 and section 5 would need to be re-written if above amendment accepted.	Study confirms that Baileys monofilament first falls outside usable range (11g-9g) after 1200 cycles.	In Table 1 in the study of Lavery et al., the buckling force of the monofilament drops to 8.82 (standard deviation 0.4) at 1400 (not 1200) cycles. However, the confidence intervals of this value appear to cross the 9g value, and also this seems to be a 'blip', with following values at 1600, 1800, 2200, and 2400 all being over 9g (8.91g at 2000 loading cycles). This suggests to the EAC that the Bailey's monofilament performs within acceptable limits for at least 2000 load cycles but possibly a lot more, and therefore the EAC has been conservative in its estimates. *Action: the EAC will make text amendments as described for response 3 above.*

feet, this suggests the Bailey's monofilament would have a useful life of approximately 200 patients before requiring replacement.			