NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology Appraisals and Guidance Information Services

Static List Review (SLR) report

Title and TA publication number of static topic:	**TA69; Liquid-based cytology for cervical screening**
Final decision:	The guidance will remain on the 'static guidance list'.

1. Publication date:	October 2003.
2. Date added to static list:	October 2007.
3. Date the last searches were run:	July 2006.
4. Current guidance:	1.1 It is recommended that liquid-based cytology (LBC) is used as the primary means of processing samples in the cervical screening programme in England and Wales. 1.2 There is currently insufficient evidence to recommend one LBC product over another. The NHS Cervical Screening Programme and Cervical Screening Wales may wish to consider evaluating further the different products as the method is introduced.
5. Research recommendations from original guidance:	5.1 It is recommended that high-quality studies be undertaken to compare differences in performance between the ThinPrep and SurePath LBC methods. 5.2 Validation is needed of the number of cells per LBC sample that will be required to

	establish the adequacy of smears. 5.3 For further reviews of LBC, clinical data relating to the sensitivity, specificity and rate of inadequate smears should be provided for EasyPrep, Cytoscreen and any future devices. 5.4 Evaluation of automated technologies for the analysis of cervical samples is needed. In terms of the comparison of ThinPrep and SurePath, there are three relevant papers retrieved in searching. None seem sufficient to materially affect the guidance. One is a cross sectional population study in rural China (Zhao et al, 2011). There is also a study considering the impact of mucus on both these methods (2010). The third looks at both in terms of three performance indicators (Wright et al 2010). There is a recent review / meta-analysis (Fountaine et al, 2012) which suggests SurePath may lead to fewer unsatisfactory smears than ThinPrep, while acknowledging that 'multiple factors affect LBC unsatisfactory rates.' This is consequently unlikely to trigger a review of the guidance. There were no significant relevant hits in the literature search that considered EasyPrep or Cytoscreen. Regarding automated analysis the MAVARIC trial from the RPP paper 2006 is reported on the NHS cervical screening website research page: "A comparison of automated technology and manual cervical screening (MAVARIC) Randomised controlled trial comparing the results of manually read cervical cytology slides with those using automated technology. The trial design will enable two automated devices to be compared with each other in a randomised framework. Double reading of slides will enable large scale direct comparison between manual and automated reading.

	End date: July 2009." The website says: "This trial has now reported and the authors concluded that automation-assisted reading could not be recommended for primary cervical screening."
6. Current cost of technology/ technologies:	Not known.
7. Cost information from the TA (if available):	See section 4.2 of the original guidance.
8. Alternative manufacturers:	None found. Searched the NHS Supply Chain catalogue.
9. Changes to the original indication:	None found. The NHS cervical screening programme is moving into additional HPV triage, but this is not part of the remit for this TA which is 'to review the clinical and cost effectiveness of liquid based cytology for cervical screening'.
10. New relevant trials:	No relevant trials found through clinical trials.gov. The NHS cervical screening website research page has no additional relevant trials listed.
11. Relevant NICE guidance (published or in progress):	There is no relevant NICE guidance on screening, but some on colposcopy and cervical cancer.
12. Relevant safety issues:	None found.
13. Any other additional relevant information or comments:	The NHS completed the move to liquid based cytology in October 2008. The link says the change has 'saved money overall'. See latest screening stats (not costs). Annual report 2011/12.

14. Technical Lead comments and recommendation:	Liquid-based cytology has become the standard method of cervical sample preparation in the NHS, with the 2 most commonly used LBC technologies being SurePath and ThinPrep. Zhao et al. (2011) is a study on a Chinese population to test residual samples from LBC specimen preparation for high-risk oncogenic HPV subtypes. This study is of limited application to the UK because of likely differences in Chinese incidence rates and costs, and differences in the classification systems used to categorise smears. Wright et al. (2010) compared ThinPrep with SurePath LBC in a single UK cytology laboratory using 3 performance indicators, and found that both techniques are equivalent. This paper was available in abstract form only. The meta-analysis by Fountaine et al. (2012) compared 4 head-to-head studies, and it did reveal a statistically significant lower unsatisfactory rate for the SurePath platform (RR 0.44; 95% CI 0.25 – 0.77). However, the authors acknowledged that these differences underscore the fact that multiple factors are associated with overall unsatisfactory rates with the platform used representing only one of these (in fact there is evidence that unsatisfactory rates in LBC are largely reproducible within laboratories but not across laboratories [Haroon et al, 2002]). A limitation of this study is that it considers only one aspect of LBC platform selection (unsatisfactory rate), whereas other factors such as specificity and sensitivity must also be considered. Excessive mucus, as well as blood and inflammation, can be problematic in the processing and screening of liquid-based cervical Pap preparations by interfering in the process of cell retrieval onto specimen filters or slides. Kenyon et al. (2010) is a small study (cells were added to 5 SurePath and 5 Thin-Prep liquid Pap test vials for each of 10 test runs) that compared the capacity of the SurePath and ThinPrep liquid-based Pap tests to handle mucus-rich specimens. The results showed that specimens processed in the SurePath system had effectively no diminution of cellularity with any amount of added mucus. In contrast, the ThinPrep specimens invariably showed a loss

	of cellularity upon the addition of the first aliquot of mucus. The ability of the SurePath System cell enrichment process to handle significantly greater amounts of potentially obscuring blood than the membrane filtration method of the ThinPrep system has also been demonstrated (Sweeney et al., 2006). However, these studies are not randomised and the specimens were artificially created based on the authors' laboratory experience to mimic certain cytological environments. Therefore, the studies do not examine the combined impact of the full range of obscuring factors including blood, inflammation, mucus, cellular debris, and tumour diathesis as it would occur in clinical practice. Section 4.2.4 of the guidance states that the extent of the increase in slide preparation time with LBC (compared with the conventional Pap smear) depended in part on different LBC methods. Slide preparation with LBC was estimated to take 4 minutes and 15 seconds (ThinPrep [semi-automated]), 38 seconds (ThinPrep [fully automated]), or 1 minute and 52 seconds (SurePath system). The average aggregate costs of LBC were £22.99 for ThinPrep (fully automated), £23.15 for ThinPrep (semi-automated) and £20.76 for the SurePath system. On balance, comparative evidence relating to the current methods that use LBC technology is limited and somewhat conflicting. It appears to be some evidence suggesting superiority of SurePath over ThinPrep, particularly for processing specimens containing impurities. However, taking into account the possible confounding factors in the studies, and the fact that the studies were not designed to fully compare the 2 technologies, there is currently insufficient evidence to suggest that one technique should be recommended over the other, or that the cheaper technology would be more cost effective than the other.

Appendix 1 – explanation of options

Options	Consequence	Selected – 'Yes/No'
The guidance will remain on the 'static guidance list'	**The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.**	**Yes**
The decision to review the guidance will be deferred to specify date or trial	NICE will consider whether a review is necessary at the specified date. NICE will actively monitor the evidence available to ascertain when a consideration of a review is more suitable.	No
A full consideration of a review will be carried out through the Review Proposal Process	There is evidence that could warrant a review of the guidance. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No
The guidance will be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No

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