



Medical Services Advisory Committee Public Summary Document
Reference No. 39 – Human Papilloma Virus (HPV) Triage for Pap Smear

Sponsor: Referred from the Pathology Services Table
Committee, Department of Health and Ageing

Date of MSAC consideration: 44th MSAC meeting, 20 March 2009, Canberra

1. Purpose of Application

The hybrid capture II (HC-II) human papilloma virus (HPV) deoxyribonuclease (DNA) test is a nucleic acid hybridisation assay used to detect HPV subtypes that are associated with cervical cancer. It is undertaken using cervical cells collected during a vaginal speculum examination by a medical practitioner in the same way that a conventional Papanicolaou (Pap) cytology test is performed. The assay is then performed in a pathology laboratory.

The test is commercially available as a standardised testing kit which includes a cervical brush for collecting cell samples, a vial with a specimen transport medium and the solution hybridization assay. Cell samples can also be collected using liquid-based cytology (LBC) protocols.

2. Background

Applications to MSAC undergo an eligibility step that includes an assessment of the application's compliance with any required Therapeutic Goods Administration (TGA) listing, conformity with MSAC's Terms of Reference and consistency with Government policy.

MSAC receives a report from expert independent evaluators on the strength of the evidence of the safety, effectiveness and cost-effectiveness of the requested procedure and related technology, which is produced under the guidance of an Advisory Panel consisting of MSAC members, clinical experts, and consumer representatives. The applicant is consulted at the initial research protocol stage and at the final draft report stage of the production of this report.

At its 44th MSAC meeting, MSAC considered the strength of the evidence for the safety, effectiveness and cost-effectiveness for human papilloma virus (HPV) triage for Pap smears. Members considered the final report of the evaluation of the evidence (as endorsed by the Advisory Panel), the applicant's response and evaluator's rejoinder, as well as presentations/input from the 1st discussant (independent MSAC member), 2nd discussant (MSAC Advisory Panel Chair), and the MSAC Economics Sub-Committee.

3. Safety

The HC-II HPV test is a technically safe procedure. Women may experience mild discomfort from the use of the cervical brush to collect cells for testing. The same risks are associated with routine screening cervical cytology testing which uses the same collection procedure.

4. Clinical effectiveness

No published clinical studies were identified which compare the impact of the HPV triage test on cervical cancer incidence or mortality versus repeat cytology.

The immediate HPV triage test as a replacement to repeat cytology

If a strategy of HPV testing is adopted for triage of all women with low-grade intra-epithelial lesions, its relative effectiveness will depend on the relative proportion of women with a possible low grade squamous intra-epithelial lesion (pLSIL) versus definite low grade squamous intra-epithelial lesion (dLSIL).

The absolute specificity of the HPV triage test varies by age (Level II accuracy evidence) and does not support its use in young women.

The delayed HPV triage test as an addition to repeat cytology at 12 months

The published evidence was inadequate for conclusions about the accuracy of performing the HPV test with repeat cytology at the 12 month follow-up visit compared to the current strategy of performing repeat cytology alone.

5. Cost effectiveness

The economic considerations of HPV are also considered in relation to the MSAC assessment of Application 1122 Automated Liquid Based Cytology (LBC).

The evaluation found that when compared to current practice with conventional cytology, the most cost-effective options are strategies involving immediate triage either with conventional cytology and co-collection; or reflex manual LBC testing (assuming a \$2.40 incremental price compared to conventional cytology). For both of these technology options, increasing the age range for triage testing would increase both costs and effectiveness - as the age group for triage testing is extended from 35+ years down to 30+ years and then to 23+ years, the absolute costs and absolute effectiveness increase.

The evaluation found that performing immediate HPV triage offers substantially better value for money than delaying triage testing until a 12-month follow-up visit, for all types of cytology (conventional with co-collection, manual LBC and Auto LBC). However, at the current level of reimbursement for the HPV test, all HPV triage strategies have high and somewhat unfavorable cost-effectiveness ratios, compared to current practice.

If immediate HPV triage testing were implemented in women aged 30+ in the context of conventional cytology with co-collection of samples for HPV DNA testing, there would be approximately 41,000 HPV DNA tests performed and 21,000 fewer cytology tests performed per annum. This would involve an additional cost of \$2.6M for HPV DNA testing, but a cost saving of \$0.4M due to fewer cytology tests. If this strategy were to be implemented, a total incremental increased cost to the health system of \$4.9M is predicted, taking into account all factors considered in the modelled evaluation of the evaluation report.

If immediate HPV triage testing were implemented in women aged 30+ in the context of manual LBC (\$2.40 incremental cost compared to conventional cytology) with reflex HPV DNA testing, there would be approximately 50,000 HPV DNA tests performed and 4,000 fewer cytology tests performed per annum. This would involve an additional cost of \$4.5M for cytological testing (even though fewer tests are performed), and an additional cost of \$3.2M for HPV DNA testing. If this strategy were to be implemented, a total incremental

increased cost to the health system of \$8.1M is predicted, taking into account all factors considered in the modelled evaluation of the evaluation report.

The economists on MSAC queried the use of a “willingness to pay” threshold for cost per life-year saved in the report and advised that there was no established basis for the use of such a threshold.

MSAC agreed that reference to a willingness-to-pay threshold should be removed from the report as reference to a threshold amount in MSAC reports could be misconstrued as Australian Government policy (noting that the Evaluator’s rejoinder also mentioned the threshold).

MSAC discussion and advice on cost effectiveness proceeded on the basis of advice from the Advisory Panel Chair that removal of the reference to a willingness-to-pay threshold would be agreed by the Panel. After the MSAC meeting the Secretariat sought the Advisory Panel’s agreement to remove the reference to a willingness-to-pay threshold from the report, before providing MSAC’s advice and final report to the Minister.

6. *Rationale for MSAC’s Advice*

Compared with repeat recall cytology at one year, MSAC finds that HPV triage testing:

- is safe,
- is effective,
- is not cost effective in the Australian setting at the current price of HPV testing.

MSAC does not support public funding for HPV triage testing in cervical cancer.

7. *Context for Decision*

This advice was made under the MSAC Terms of Reference:

- Advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported.
- Advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness.
- Advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures.
- Undertake health technology assessment work referred by the Australian Health Ministers’ Advisory Council (AHMAC) and report its findings to the AHMAC.

8. *Linkages to Other Documents*

The MSAC Advisory Panel Report is available at
<http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Completed-References1-40>