Human papillomavirus testing versus repeat cytology for triage of minor cytological cervical lesions


Low-grade cytological abnormalities of the cervix can be challenging to manage; while most will clear without intervention, between 10% and 20% could harbour high-grade lesions. Furthermore, low-grade abnormalities represent the largest category of abnormal results. In Scotland, of the 409 000 cervical screening tests that were performed in 2011–2012, 90.9% had a negative result, 1.3% had high-grade cellular changes and 7.8% had low-grade cellular changes.1

The high sensitivity and negative predictive value of human papillomavirus (HPV) DNA testing has been exploited for the risk-stratification of low-grade abnormalities (often referred to as ‘triate’) with practice of this approach varying between and sometimes within countries. In the USA, HPV triage of atypical squamous cells of undetermined significance (ASCUS) is recommended by the American Society for Colposcopy and Cervical Pathology and has been practised for several years, whereas in the UK it was rolled out only last year in England with no definitive plans for introduction in Wales and Scotland.

This article by Arbyn and colleagues represents a comprehensive review of the global evidence related to HPV triage of low-grade abnormalities using the most established HPV DNA assay, the Hybrid Capture 2™ (HC2) test (Qiagen). Accuracy of HPV triage was assessed for ASCUS and low-grade squamous intraepithelial lesions (LSIL) separately and also directly compared to repeat cytology for the detection of cervical intraepithelial neoplasia (CIN) disease at two thresholds: CIN2+ and CIN3+. The review provides an update of the previous meta-analyses on the subject obviously via the interrogation of additional literature but also through the imposition of multilevel models, adapted by the Diagnostic Test Accuracy Working Group of the Cochrane Collaboration. Of the nearly 3000 studies that were initially assessed, 39 separate studies (incorporating 13 196 women) and 24 separate studies (incorporating 9983 women) were assessed to determine the accuracy of HPV triage in women with ASCUS and LSIL, respectively. The sensitivity of HPV testing was significantly higher than repeat cytology (at a cut-off of ASCUS+) to detect CIN2+ in the triage of ASCUS and LSIL. Furthermore, the specificity of HPV testing for detection of CIN2+ in ASCUS was equivalent to that of repeat cytology, although it was significantly lower in LSIL when compared to repeat cytology. In addition to the above key clinical performance measures, the authors also assessed (where possible) the influence of additional variables and study characteristics on performance including sampling device transport medium, the continent where the study was undertaken and age. Notable findings were that HC2 was less sensitive when a sample was collected with a brush rather than a broom and less specific when the transport medium was PreservCyt® (Hologic) rather than specimen transport medium. With respect to between-continent differences, for ASCUS triage (to detect CIN2+) repeat cytology was less sensitive but more specific in European rather than American studies. HPV triage of LSIL was also more specific in European compared to American studies. Age-specific information was absent from the majority of studies and the relative accuracy of HPV triage for ASCUS could not be assessed due to insufficient data. However, for LSIL, the sensitivity of HPV triage was unaffected by age, although the specificity (for the exclusion of CIN2+) increased significantly with increasing age and was 18.0% in women younger than 30 years of age compared to 43.7% in women aged 50 years or older.

Although the review is lengthy and spans over 200 pages, much of these comprise detailed data tables and citations – the core of the review is both concise and clear and the conclusions are objective and avoid overstatement. In terms of novelty, this work effectively confirms previous observations in relation to ASCUS but presents new insights into LSIL with respect to the higher sensitivity of HPV triage compared to repeat cytology (in previous analyses the sensitivity of these approaches were equivalent). The other most noteworthy, albeit confirmatory, finding is the poor specificity of HPV testing for LSIL, which would appear particularly low in younger women. Given that several programmes (including England) have taken the pragmatic route and incorporated HPV triage for all low-grade abnormalities, there is room to improve the performance of this approach. Whether this is achieved through age stratification and/or the application of more sophisticated markers of clinically significant HPV infection such as restricted typing, measurement of viral load, assessment of cellular and viral biomarkers (or combinations thereof) is an area that warrants further investigation.

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