Posttreatment human papillomavirus testing for recurrent cervical intraepithelial neoplasia: a systematic review
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CRD summary
This review concluded that human papillomavirus hybrid capture 2 testing identified approximately 91% of women with residual or recurrent cervical intra-epithelial neoplasia grade 2 or worse, but that around 30% of these women would test positive and undergo colposcopy in follow-up evaluation. These conclusions may be stronger than the evidence warrants.

Authors' objectives
To evaluate human papillomavirus testing for post-treatment detection of cervical intra-epithelial neoplasia.

Searching
MEDLINE was searched from 1992 to 2007; search terms were reported. References of relevant articles and review articles were scanned for additional studies.

Study selection
Studies in which women were treated for cervical intra-epithelial neoplasia by conization, loop excisional procedures, laser ablation or cryotherapy, and subsequently tested for human papillomavirus (HPV) within 12 months, were eligible for inclusion. Valid human papillomavirus tests included hybrid capture 1 (HC1), hybrid capture 2 (HC2), and polymerase chain reaction (PCR). Eligible studies were required to have a 12 month follow-up period with less than 30% loss to follow-up. All positive results had to be colposcopically evaluated with biopsy to determine recurrence. Cervical intra-epithelial neoplasia grade 2 or worse was the primary outcome measure.

The included HC1 and HC2 studies used a cohort design and were conducted in Spain, South Korea, Austria, France, USA, Brazil, Belgium and the Netherlands. Mean ages of participants ranged from 24 to 40 years. Most patients were treated with loop electrosurgical excision procedures. Included PCR studies were described as being heterogeneous, a mixture of prospective cohort and retrospective case-control studies; the tests used varying numbers of viral types from two to 25.

Studies were selected independently by two reviewers.

Assessment of study quality
Quality indicators assessed included blinded assessment and whether follow-up was influenced by human papillomavirus test results.

Validity assessment data were extracted by two reviewers.

Data extraction
Two reviewers independently extracted data on human papillomavirus test details, type of initial treatment, results from human papillomavirus tests, cytological tests, colposcopy, and biopsy. Sensitivity and specificity results were extracted for each study as a 2x2 table. A continuity correction of 0.5 was added to each cell with a zero count. Discrepancies were resolved by consensus. Authors were contacted for additional data where necessary.

Methods of synthesis
Pooled sensitivity and specificity, and associated 95% confidence intervals (CI), were calculated where possible using a bivariate normal model. Studies were grouped according to type of human papillomavirus test. Heterogeneity was assessed using the Q and I² statistics; where heterogeneity was present, study characteristics were assessed.
Results of the review
A total of 20 studies were included in the review; human papillomavirus HC1 test (one study), HC2 test (eight studies), polymerase chain reaction (PCR) test (11 studies). Mean follow-up duration ranged from 12 to 31 months.

Only five of the HC2 studies were deemed suitable for pooling; all used a positive cut-off of 1pg/mL. Of the HC2 studies, only one used blinded assessors, most trials used follow-up colposcopy, and six out of eight trials did not use the human papillomavirus test to influence follow-up.

Pooled sensitivity for the HC2 test was calculated as 90.7% (95% CI 75.4 to 96.9) and pooled specificity as 74.6% (95% CI 60.4 to 85.0). Heterogeneity was not present for sensitivity, but I² for specificity was 80%. One study seemed to contribute most of the variation, and was excluded for a sensitivity analysis, which did not produce markedly different sensitivity or specificity values.

Four HC2 studies also reported cervical cytological results, giving an overall sensitivity of 76.6% (95% CI 62.0 to 86.8%) and specificity of 89.7% (95% CI 22.7 to 99.6); heterogeneity was not reported.

Further results were also reported.

Authors' conclusions
Human papillomavirus hybrid capture 2 testing identified approximately 91% of women with residual or recurrent cervical intra-epithelial neoplasia grade 2 or worse, but around 30% of these women would test positive and undergo colposcopy in follow-up evaluation.

CRD commentary
This review addressed a clear question with partially defined inclusion criteria. The searches were limited, covering only one database and reference checking. No mention was made of foreign language or unpublished papers, so publication and language biases could not be ruled out. Appropriate procedures to include, assess and data extract the primary studies were used to minimise reviewer error and bias.

The quality assessment was not reported in detail and, although it seemed likely that poor quality studies would have been excluded at the inclusion stage, the lack of assessor blinding cast doubt on the quality of the included trials. Analysis and pooling appeared to have been appropriate, but there was a lack of useful narrative synthesis where meta-analysis was not possible. Heterogeneity was not reported for all major analyses and may have been statistically significant.

The conclusions offered by the authors may be stronger than the evidence from a small number of cohort studies warrants.

Implications of the review for practice and research
Practice: The authors did not make any recommendations for practice.

Research: The authors suggested that well-designed randomised controlled trials comparing human papillomavirus testing with cytological testing or colposcopy are indicated; alternatively large prospective cohort studies with standardised outcomes and a simultaneous reference standard would be of benefit.

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Bibliographic details
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.