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Prevention of cervical cancer through use of liquid-based cytology and supplementary HPV testing in population-based screening

AKADEMISK AVHANDLING
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ABSTRACT

The aim of this project is to evaluate an alternative screening strategy using liquid-based cytology (LBC), and supplementary detection of human papillomavirus (HPV) in cases of minor cytological abnormalities (atypical squamous cells of undetermined significance, ASCUS, and low-grade squamous intraepithelial lesion, LSIL).

Within population-based screening in Stockholm, Sweden, we alternated screening using LBC with supplementary HPV testing in ASCUS and LSIL (LBC+HPV testing, using Linear Array HPV genotyping Assay, Roche diagnostics) and conventional cytology (CC), from September 2005 to December 2006. LBC+ HPV testing (n=6075) and CC (n=4261) screening performance were compared. LBC+ HPV testing was evaluated over time (September 2005- December 2007). Diagnostic performance of HR-HPV detection as a triage test to identify high-grade precancerous lesions (CIN2+) in cases of ASCUS and LSIL was assessed, and age-specific HPV prevalence was studied. To assess the cost-effectiveness of HPV triage compared with immediate colposcopy or repeated cytology as a follow-up strategy for ASCUS and LSIL, an economic analysis was carried out from the perspective of the Swedish healthcare system, based on data from previous studies.

Comparing LBC+ HPV testing with CC, the adjusted OR for detecting CIN2+ and CIN3+ were 0.89 (95% CI: 0.64-1.25) and 1.02 (95% CI: 0.67-1.54) respectively. Detection of CIN2+ improved significantly over time for both methods. Positive predictive values were similar between methods for all endpoints. High-risk (HR-) HPV was found in 71% of LSIL and 49% of ASCUS cases (p=0.001) with similar prevalence between groups in women >30 years. HR-HPV prevalence was age-dependent in LSIL (p=0.01), with decreasing prevalence until age 50 years, followed by a slight increase. The negative predictive value of HR-HPV detection for histologically confirmed high-grade lesions was 100%. For women with ASCUS >30 years, HPV triage is the least costly alternative, whereas immediate colposcopy with biopsy provides the most effective option at a modest additional cost.

No obvious advantages of the LBC+ HPV testing strategy over CC were shown. However, detection of high-grade precancerous lesions improved significantly over time for both strategies. This finding suggests that introduction of LBC+ HPV testing may have lead to general improvement of expertise and increased vigilance in cytological interpretation. Observed changes underscore the importance of continuously monitoring rates of abnormal cytology to ensure balance and to guard against overdiagnosis or overconfidence in cytological evaluation. By using HPV reflex testing, additional extensive workup can safely be avoided in about 50% of all cases of ASCUS and LSIL among women ≥30 years. With highly sensitive HPV testing techniques at lower costs, HPV triage could become a cost-effective alternative. Cervical cancer screening will need to continuously adapt as HPV-vaccinated women reach screening ages and new potentially superior screening strategies are identified.