



Title	Decision-Analytic Modeling Study to Evaluate the Long-Term Effectiveness and Cost Effectiveness of HPV-Based Primary Cervical Cancer Screening in Germany
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Aim

To perform a decision analysis to systematically evaluate the long-term effectiveness and cost effectiveness of HPV-based primary cervical cancer (CC) screening in the German healthcare context.

Conclusions and results

Human papillomavirus (HPV)-based screening was more effective than cytology alone, with 71% to 97% (depending on screening intervals) reduction in CC compared to 53% to 80% for cytology. The incremental cost-effectiveness ratios (ICER) ranged between 2600 euros (EUR)/LYG (cytology, 5-year interval) and EUR 155 500/LYG (annual HPV-testing age 30 years, cytology 20 to 29 years). Annual cytology, the recommended screening strategy in Germany, was dominated by other strategies. Increasing the starting age to 25 years had no relevant loss in effectiveness, but resulted in lower costs. Considering long-term effectiveness and cost effectiveness, biennial HPV testing at age 30 years preceded by biennial cytology at age 25 to 29 years could be an optimal screening strategy (ICER: EUR 23 400/LYG). With increased screening adherence (>75%), or a substantial reduction in HPV incidence in the population (>70%), a longer screening interval (and with low adherence a shorter interval) would be more cost effective. In a scenario analysis with data for test accuracy from a German study (increased relative sensitivity for HPV testing compared to cytology) HPV-based screening in screening intervals of 1, 2, or 3 years were more effective than annual cytology.

Recommendations

- HPV-based primary screening for CC is more effective than cytology when considering long-term outcomes, eg, life expectancy and reduction in cervical cancer risk and mortality.
- Introducing HPV-based primary screening in Germany could extend the screening interval to 2 years for women of average risk.

- For women who undergo regular screening, the interval could be extended to >2 years. The same applies if the relative sensitivity increase with HPV testing is higher.
- For women with average risk, the starting age of screening can be increased to 25 years without a relevant loss in effectiveness.
- Screening at short intervals is recommended in populations with low screening adherence.
- An optimal screening strategy in Germany would be biennial HPV testing in women aged 30 years and older preceded by biennial cytology between ages 25 and 29 years.

Methods

A Markov model simulating the natural history of CC was developed and validated for the German context. Different screening intervals and strategies were evaluated, eg, cytology alone, HPV testing alone, or combined with cytology or cytology triage for HPV-positive women. German clinical, epidemiological, and economic data were used. Test accuracy data were retrieved from international meta-analyses. Predicted outcomes were a reduction in CC cases and deaths, life expectancy, and discounted ICER. A healthcare system perspective and 3% annual discount rate were adopted. Extensive sensitivity analyses were performed to evaluate the robustness of results.

Further research/reviews required

Research is needed to acquire evidence-based information on adherence patterns, the impact of screening on quality of life and on decision-analytic evaluation of different integrated screening strategies in mixed vaccinated and unvaccinated populations, and systematic evaluation of different practice patterns in diagnostic work-up and treatment after initial screening results.