



Is the HPV test effective as the primary screen for cervical cancer?

YES In a large, randomized trial from Finland, the HPV test functioned effectively as the primary screen for cervical cancer and was more sensitive than conventional cytology for detecting cervical intraepithelial neoplasia grade 3 (CIN 3) or higher.

Anttila A, Kotaniemi-Talonen L, Leinonen M, et al. Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomised study within organised screening programme. BMJ. 2010;340:c1804.

► EXPERT COMMENTARY

J. Thomas Cox, MD, Associate Emeriti, University of California, Santa Barbara, and past-President of the American Society for Colposcopy and Cervical Pathology. Dr. Cox serves as a Contributing Editor to OBG MANAGEMENT. Dr. Cox is a consultant to Gen-Probe and Roche, and serves on the Data and Safety Monitoring Committee for Merck HPV vaccine trials.

Until now, the HPV test has been evaluated primarily as an adjunct to the Pap test and not as the primary screen for cervical cancer. In this randomized trial from Finland, 58,076 women 30 to 60 years old were invited to participate in a routine, population-based screening program for cervical cancer. Participants were randomized to primary screening with the HPV DNA test (hybrid capture 2) or to conventional cytology. In the group undergoing HPV testing, women who had a positive result were triaged to conventional cytology.

The HPV and conventional-cytology arms involved 95,600 and 95,700 woman-years of follow-up, respectively, and detected 76 and 53 cases of CIN 3 or higher. Six and eight cases, respectively, involved cancer.

The relative risk (RR) of CIN 3 or higher in the HPV arm versus conventional cytology was 1.44 (95% confidence interval [CI], 1.01–2.05) among all women invited for screening and 1.77 (95% CI, 1.16–2.74) among those who

attended. Among women who had a normal or negative HPV test, the RR of subsequent CIN 3 or greater was 0.28 (95% CI, 0.04–1.17).

The greatest strengths of this study are the 1:1 randomization of just over 58,000 women and the ability to link study participants to outcomes, over a 5-year period, using the comprehensive Finnish population database and cancer registry.

One concern that clinicians may have is whether the findings are applicable to a US population that is now rarely screened using conventional cytology (liquid-based cytology is the norm). That concern should be allayed by a large meta-analysis that found no difference in the sensitivity of liquid-based cytology versus conventional Pap testing.¹

Although nearly one third of women invited to participate in screening did not do so, the two groups had comparable numbers of women deciding not to participate (9,588 in the HPV arm versus 9,818 in the conventional-cytology arm).

One variable limiting applicability to a US population is the lack of an organized

FAST TRACK

In a well-organized cervical cancer screening program, the HPV test is more sensitive than conventional cytology for detecting CIN 3 lesions and cancer

WHAT THIS EVIDENCE MEANS FOR PRACTICE

I recommend that you follow current US guidelines and screen women 30 years and older with both the Pap and HPV tests and extend the screening interval to 3 years for women who have a negative result on both tests. Numerous studies support the overwhelming conclusion that HPV testing in primary cervical cancer screening significantly increases detection of CIN 3 or higher and should reduce the woman's subsequent risk of developing cervical cancer.

» J. THOMAS COX, MD

screening program like the one in Finland.

Despite its large size, the study had limited statistical power to show the impact of the two screening modalities on the rate of cervical cancer, primarily because that rate is so low in the population screened. To determine that impact, the screening options need to be repeated for another round, with follow-up extended to 10 years.

Co-testing is the standard

US guidelines from the American Cancer Society (2002) and ACOG (2003, 2009) offer clinicians the option of screening women 30 years and older using both cytology and HPV testing—an approach known as “co-testing.” However, even though about 90% of the women who have a negative response to both tests can safely forgo further screening for at least 3 years, many clinicians screen them more frequently with co-testing, decreasing the cost-effectiveness of this option.²

The findings of Antilla and coworkers are in line with those of other authors. For example, Naucler and colleagues found that

using the most sensitive test first (the HPV test), followed by reflex testing of positive HPV findings using the most specific test (the Pap), increased the sensitivity of screening for CIN 3 or greater by 30%, compared with screening with the Pap test alone.³ Other authors, including Ronco and coworkers and Sankaranarayanan and colleagues, have pointed to the superiority of either co-testing or HPV testing to use of the Pap test alone.^{4,5} 

References

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