

Human Papillomavirus DNA versus Papanicolaou Screening Tests for Cervical Cancer

Marie-Hélène Mayrand, M.D., Eliane Duarte-Franco, M.D., Isabel Rodrigues, M.D., Stephen D. Walter, Ph.D., James Hanley, Ph.D., Alex Ferenczy, M.D., Sam Ratnam, Ph.D., François Coutlée, M.D., Eduardo L. Franco, Dr.P.H., for the Canadian Cervical Cancer Screening Trial Study Group

Abstract

Background To determine whether testing for DNA of oncogenic human papillomaviruses (HPV) is superior to the Papanicolaou (Pap) test for cervical-cancer screening, we conducted a randomized trial comparing the two methods.

Methods We compared HPV testing, using an assay approved by the Food and Drug Administration, with conventional Pap testing as a screening method to identify high-grade cervical intraepithelial neoplasia in women ages 30 to 69 years in Montreal and St. John's, Canada. Women with abnormal Pap test results or a positive HPV test (at least 1 pg of high-risk HPV DNA per milliliter) underwent colposcopy and biopsy, as did a random sample of women with negative tests. Sensitivity and specificity estimates were corrected for verification bias.

Results A total of 10,154 women were randomly assigned to testing. Both tests were performed on all women in a randomly assigned sequence at the same session. The sensitivity of HPV testing for cervical intraepithelial neoplasia of grade 2 or 3 was 94.6% (95% confidence interval [CI], 84.2 to 100), whereas the sensitivity of Pap testing was 55.4% (95% CI, 33.6 to 77.2; $P=0.01$). The specificity was 94.1% (95% CI, 93.4 to 94.8) for HPV testing and 96.8% (95% CI, 96.3 to 97.3; $P<0.001$) for Pap testing. Performance was unaffected by the sequence of the tests. The sensitivity of both tests used together was 100%, and the specificity was 92.5%. Triage procedures for Pap or HPV testing resulted in fewer referrals for colposcopy than did either test alone but were less sensitive. No adverse events were reported.

Conclusions As compared with Pap testing, HPV testing has greater sensitivity for the detection of cervical intraepithelial neoplasia. (Current Controlled Trials number, ISRCTN57612064.)