HPV-Only Screening Misses More Cervical Cancers in Women 30 and Older Than Pap-Only or Pap-HPV Co-testing, Finds National Study

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As many as 19% of women received false negatives for cervical cancer when HPV-only tested, finds Quest Diagnostics Health Trends™ study published in Cancer Cytopathology of 256,648 women, one of the largest of different screening tests for cervical cancer

MADISON, N.J., April 14, 2015 /PRNewswire/ -- HPV-only screening is less likely to accurately detect cervical pre-cancer and cancer than testing that includes a Pap test in women 30-65 years of age, according to a new study published online today in *Cancer Cytopathology*, a peer reviewed journal of the American Cancer Society. The study, by researchers at Quest Diagnostics (NYSE: DGX) and the University of Pittsburgh Medical Center (UPMC), reinforces medical guidelines recommending women in this age group be screened with both Pap and HPV tests to rule out cancer risk, but which have come into question following FDA approval of an HPV-only screening test last year.

The study is believed to be one of the largest to examine the effectiveness of HPV and Pap screening for cervical pre-cancer and existing cervical cancer, based on approximately 8.6 million women 30-65 years of age who received concurrently performed Pap and HPV tests (co-testing) by Quest Diagnostics laboratories in the United States. Of these, 256,648 women also received a biopsy to detect cancer and 526 had confirmed cases of cervical cancer.

According to the analysis, 18.6% of women with confirmed cervical cancer received a negative test for human papillomavirus (HPV), compared to 12.2% that had a negative Pap test and 5.5% that had a negative co-test result. Of 169 women with confirmed cervical adenocarcinoma, the most difficult form of cervical cancer for which to screen, 26.6% received a negative HPV test, compared to 20.7% that had a negative Pap test and 8.3% that had a negative co-test result.

"Our study arrives at a crucial moment in the evolution in cervical cancer screening for millions of women in the United States," said co-author R. Marshall Austin, M.D., Ph.D., professor of pathology at Magee-Womens Hospital of UPMC. "Our large-scale, real-world patient data provides convincing evidence that HPV-only testing would tragically miss many cervical cancers that would be detected if co-testing were employed. In fact, our study showed that Pap reliably detected more cervical cancers than HPV-only, an incredibly important finding in light of the current debate about the use of HPV-only as a primary cervical cancer screen. Cervical cancer screening has been one of the great success stories in cancer prevention, and we hope that the medical community takes these findings seriously as it considers the best screening approach to promote favorable health outcomes for women."

Medical guidelines have recommended that women 30-65 years of age be screened periodically for cervical cancer with HPV-Pap co-testing. HPV tests identify the presence of the virus that causes most cervical cancers, while Pap tests identify cellular abnormalities in the cervix caused by HPV infection that could indicate the presence of cancer or precancerous cellular changes. Cervical cancer, particularly when detected in early stages, can typically be treated with a variety of measures.

In April 2014, the FDA approved an indication for the cobas® HPV test to be used alone as a primary cervical cancer screen in women 25 years of age and older. The FDA approval was based on a clinical trial that compared HPV testing to Pap testing and involved eight confirmed cervical cancer cases. While the American Congress of Obstetricians & Gynecologists (ACOG) continues to recommend co-testing in women 30-65 years of age, the Society of Gynecologic Oncology and the American Society for Colposcopy and Cervical Pathology issued interim guidance in January 2015 citing HPV-only testing as a viable alternative to Pap-HPV co-testing or Pap alone.

"Cervical cancer was the leading cancer killer of women in the United States before the introduction of the Pap test. Our latest Quest Diagnostics Health Trends study involving one of the largest populations of co-tested women shows that the Pap test should continue to play a front-line role in the battle against cervical cancer," said Douglas S. Rabin, M.D., medical director, women's health, Quest Diagnostics.

Large Study Finds Unreliable HPV Test Results in Women with Cervical Cancer

The investigators analyzed results of HPV tests and Pap tests in samples of women 30-65 years of age for differences in rates of positive and negative tests results in women who were co-tested, tested only by Pap and tested only by HPV. Of the 256,648 women whose de-identified test results were analyzed for the study, 1.6%, or 4,090, had intraepithelial neoplasia stage 3 (CIN3), a premalignant condition, or more severe biopsy results. Proactive management of CIN3 is recommended to minimize the risk of cancer.

Key findings:

- HPV alone missed more confirmed cancers than Pap alone. Among 526 women with diagnoses of cervical cancer in the study, 18.6% were HPV negative, compared to 12.2% that were Pap-test negative and 5.5% that were co-test negative, an approximately three-fold improvement in the cancer detection rate of co-testing compared to HPV only. In addition, 26.6% of women with cervical adenocarcinomas tested HPV negative.
- Co-testing identified more cases of CIN3 and more severe results. Co-testing detected 98.8% of women with CIN3 or more severe cervical biopsy results, compared to 94.0% for HPV-only testing and 91.3% for Pap-only testing. Among women who had an abnormal Pap test result, a negative HPV result, and a CIN3 or more severe cervical biopsy result, 35.4% had cervical cancer.
- Older age associated with HPV-negative test results in women with cervical cancer. The average age of women in the study who had a Pap test was 45.8 years of age. Women with HPV-negative cervical cancer were 52-53 years of age on average compared to 43-44 years of age on average for all HPV-negative patients studied.

The study, "Comparison of cervical cancer screening results among 256,648 women in multiple clinical practices," is available at http://onlinelibrary.wiley.com/doi/10.1002/cncy.21544/full

"This study highlights that up to 19%, or about 2,400, of the approximately 12,400 women diagnosed with cervical cancer each year could be falsely reassured of a negative screening result were they screened by HPV-only testing. As early detection and treatment of cervical cancer are critical to a favorable outcome, it is important that the best and most sensitive diagnostic tools for cancer detection be identified and made available to all women. Our data support co-testing in women 30–65 years of age as the most effective screening test for cervical cancer detection," Dr. Rabin said.

According to the American Cancer Society, nearly 12,400 women are diagnosed with cervical cancer annually, and more than 4,000 will die of the disease. The incidence of cervical cancer deaths has declined dramatically in the United States "due to early detection as a result of screening with the Pap test." More than half of new cervical cancer cases occur among women who have never or rarely been screened, according to the Centers for Disease Control and Prevention.

The present study's strengths are its size, national scope and use of unselected patient results rather than a control study as well as the use of quality laboratory methods. The HPV tests in the study may not share the precise performance characteristics as the cobas® HPV test and are not intended to be used as HPV-only screens. The study was performed in compliance with applicable privacy regulations and the company's strict privacy policies, and was determined to be exempt from Western Institutional Review Board.

About Quest Diagnostics Health Trends
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