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For cervical cancer screening, which test is better, and for whom?

Edward J Mayeaux Jr,[1] Yun Zhao [2]

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[1]USC School of Medicine Columbia Affiliate Professor of Family and Preventive Medicine, USC School of Medicine Library, Columbia, South Carolina, USA
[2]Peking University People's Hospital, Beijing, China

Correspondence to
Dr Edward J Mayeaux Jr, USC School of Medicine Columbia Affiliate Professor of Family and Preventive Medicine, USC School of Medicine Library, Columbia, South Carolina, USA; edward.mayeaux@lsuhs.edu

In their January 2024 article, Vahteristo *et al* reported the results of their prospective randomised trial comparing human papillomavirus (HPV)-based cervical cancer screening versus cytology screening in Southern Finland.[1] This study examined using high-risk HPV (hrHPV)-based cervical cancer screening in Finland, a country with a well-established, high-quality cytology screening programme and a low incidence of cervical cancer. Over 236 000 individuals were involved in this long-term follow-up of the Finnish randomised HPV screening trial. The authors calculated the cervical cancer incidence and mortality rate ratios using Poisson regression. They found that in the HPV testing arm, the cervical cancer incidence rate ratio was 1.08 (95% CI 0.85 to 1.37) and the mortality rate ratio was 1.01 (95% CI 0.61 to 1.64) compared with the cytology-only arm. This demonstrated that in this setting of high levels of cytology cervical cancer screening, hrHPV and cytology screening showed similar levels of effectiveness. This study fills in an important knowledge gap about cervical cancer screening. It may, however, raise questions in some people's minds about the need to change our screening programmes from cytology to HPV testing in areas of the world with existing systems and which systems to start in areas with no current screening.

In the 2000s, multiple randomised controlled trials demonstrated that hrHPV DNA detection finds cervical intraepithelial neoplasias (CINs) earlier than cytology testing.[2–4] A pooled randomised controlled trial study comparing primary screening tests showed that hrHPV screening provides greater protection against invasive cervical carcinomas compared with cytology.[5] However, with multiple rounds of testing, cytology screening resulted in similar levels of dysplasia and cancer detection.[3] These data are supported by the findings of Vahteristo *et al* and raise the question of why change to primary HPV testing if the infrastructure for cytology is already in place and working? Changing to new systems takes time, planning, equipment investment and training. For this narrowly phrased question, one might think it is not worth the cost and effort of changing.

There are other issues to consider in the broader question of which cervical screening test is best. One consideration for changing to hrHPV screening is that it provides an objective, validated test system as opposed to the more expert-dependent cytology assessment.[6] This allows HPV testing to be standardised for better performance and reduces the requirement for scarce highly trained individuals to screen large numbers of samples. Another advantage to HPV testing is it enables the possibility for self-sampling which can improve screening coverage.[7–9] Many parts of the world are experimenting with different self-sampling devices which may allow for samples to be taken and mailed into central laboratories for processing.[10 11] This plan obviates the need for building more satellite laboratories which can increase screening in resource-limited areas.

What the Vahteristo *et al*'s study does not address is the predictive value of HPV testing versus cytology in the setting of recent abnormal screening tests. Many cervical screening and management guidelines, including the American Society for Colposcopy and Cervical Pathology guidelines, recommend using HPV testing for follow-up of abnormal tests and treatment because of their increased predictive values in this setting.[12] So, regardless of which test may be chosen by national and local screening organisations, HPV testing should be available, if possible, for post-abnormality follow-up. Our focus should be on the advantages and disadvantages of various methods to leverage strengths and avoid weaknesses in application.

Different countries have unique medical systems, economic resources and cultures.

Opportunistic screening remains an important part of cervical cancer screening in many parts of the world including in China, and Vahteristo *et al*'s results should not be generalised to those populations. The West China Second University Hospital study demonstrated that of 161 cervical cancer cases and 1094 CIN 2/3 cases that had available co-test results, hrHPV-negative results were negative in 12.4% of cervical cancer and 10.1% of CIN 2/3 cases compared with cytology-negative results in 15.5% of cervical cancer and 4.3% of CIN 2/3 cases. It is unclear whether these differences are due to differences in the population, the HPV tests or other factors, but these data indicate that co-testing may be the better choice for opportunistic screening in the setting.[13]

The Vahteristo *et al*'s study demonstrated that in settings with long-term cytology screening and low cervical cancer incidence, HPV testing may not offer significant improvements in cervical cancer screening outcomes. For people in low-resource settings or who are starting organised cervical cancer screening programmes, using primary high-risk HPV testing as the screening test offers several key advantages. Its earlier detection of dysplasia and cancer offers advantages to people in under-resourced areas that are also usually underscreened. The potentially lower cost of establishing programmes in these areas may make it easier to establish or expand screening in poorly screened and under-resourced areas. For many parts of the world, hrHPV testing or co-testing will still be the test of choice for cervical cancer screening. How to triage and manage hrHPV-positive people, improve HPV testing and vaccination acceptance, reduce unnecessary anxiety and avoid excessive medical treatment are issues that will also need to be addressed.

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ORCID iD

Yun Zhao http://orcid.org/0000-0002-7945-4464

REFERENCES

1 Vahteristo M, Leinonen MK, Sarkeala T, *et al*. Similar effectiveness with primary HPV and cytology screening - long-term follow-up of randomized cervical cancer screening trial. *Gynecol Oncol* 2024;180:146–51.
2 Naucler P, Ryd W, Törnberg S, *et al*. Human papillomavirus and papanicolaou tests to screen for cervical cancer. *N Engl J Med* 2007;357:1589–97.
3 Ronco G, Giorgi-Rossi P, Carozzi F, *et al*. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomized controlled trial. *Lancet Oncol* 2010;11:249–57.
4 Rijkaart DC, Berkhof J, Rozendaal L, *et al*. Human papillomavirus testing for the detection of high-grade cervical intraepithelial neoplasia and cancer: final results of the POBASCAM randomized controlled trial. *Lancet Oncol* 2012;13:78–88.
5 Sankaranarayanan R, Nene BM, Shastri SS, *et al*. HPV screening for cervical cancer in rural India. *N Engl J Med* 2009;360:1385–94.
6 Li M, Wei L, Sui L, *et al*. Guidelines for cervical cancer screening in China. Gynecol Obstet Clin Med 2023;3:189–94.
7 Polman NJ, Ebisch RMF, Heideman DAM, *et al*. Performance of human papillomavirus testing on self-collected versus clinician-collected samples for the detection of cervical intraepithelial neoplasia of grade 2 or worse: a randomised, paired screen-positive, non-inferiority trial. *Lancet Oncol* 2019;20:229–38.
8 Chou HH, Yang CY, Chao A, *et al*. Consistency in human papillomavirus type detection between self-collected vaginal specimens and physician-sampled cervical specimens. *J Med Virol* 2024;96:e29426.
9 Li J, Wu R, Qu X, *et al*. Effectiveness and feasibility of self-sampling for human papillomavirus testing for internet-based cervical cancer screening. *Front Public Health* 2022;10:938272.
10 Pretsch PK, Spees LP, Brewer NT, *et al*. Effect of HPV self-collection kits on cervical cancer screening uptake among under-screened women from low-income US backgrounds (MBMT-3): a phase 3, open-label, randomised controlled trial. *Lancet Public Health* 2023;8:e411–21.
11 Zhao Y, Zhao L, Wang Z, *et al*. Clinical performance of a dedicated urine-based assay for the detection of human papillomavirus and cervical intraepithelial neoplasia. *Int J Womens Health* 2023;15:1909–16.
12 Perkins RB, Guido RS, Castle PE, *et al*. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2020;24:102–31.
13 Jiang W, Marshall Austin R, Li L, *et al*. Extended human papillomavirus genotype distribution and cervical cytology results in a large cohort of Chinese women with invasive cervical cancers and high-grade squamous intraepithelial lesions. *Am J Clin Pathol* 2018;150:43–50.