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Cervical cancer screening using tests that provide same-day results: a study of test accuracy

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The WHO in 2020 called for the Elimination of Cervical Cancer as a public health problem,[1] in recognition that cervical cancer is a preventable disease afflicting middle-aged, socioeconomically disadvantaged women living in the most under-resourced countries of the world. It is a classic disease of 'inequity of access', where its incidence may be up to 20-fold greater and deaths rates more than four times of women living in high-income countries. And of course, women living with HIV, even those on treatment, have the highest rates of cervical cancer morbidity and mortality.

Leveraging Universal Health Coverage and the Sustainable Development Goals, the elimination strategy has three pillars: 90% of girls under 15 years of age must be vaccinated, 70% of women aged 35 years and again at age 45 years to be screened with a high-quality screening test and 90% of women with either precancer or invasive cancer to receive appropriate treatment. Using modelling, it is estimated that if these goals are achieved by 2030, nearly 62 million lives will be saved in the next century. Highly ambitious and there is already evidence that many countries are not on track to reach these goals, but there are some very successful stories.[2 3]

In this edition of the journal, Taghavi *et al*[4] report on a study performed in Zambia, where women aged 18–65 years and known to be HIV positive were recruited and all women were screened with three tests: visual inspection with acetic acid (VIA), portable colposcopy and molecular testing for 14 high-risk types of human papillomavirus (hr-HPV) (GeneXpert platform, Cepheid). Key aspects of the study design were to link same-day testing to a treatment decision in women living with HIV and interventions taken to minimise verification bias. All women underwent testing for the reference standard, which was histology. Women with visible lesions underwent a minimum of two biopsies and those without a lesion had four biopsies taken from the cervix at clock positions of 3, 6, 9 and 12 o'clock, within the transformation zone.

Their findings provide important information: of 371 women who had a valid histological diagnosis 101 (27.2%) had CIN2+ and 1 had invasive cancer. Of these, only 64/101 received treatment, mostly due to failure to return for follow-up. This is an ongoing problem globally, but especially in low-income and middle-income countries. Failure to treat women with abnormal screening tests is widely reported, hence the quest to provide treatment at the screening visit, so-called single visit screen and treat. HPV testing using the PCR-based GeneXpert platform provides a result within 1 hour of the sample being processed and has been validated. It is robust and reproducible and can be performed in a primary care clinic and run by a trained community health worker, without laboratory training. In this study, the prevalence of hr-HPV was 163/371 (43.5%). The point estimate of sensitivity of hr-HPV testing for CIN 2+was 67.3% and specificity 65.3% and women with CIN2+ were four times more likely to be hr-HPV positive. The portable colposcope had a sensitivity of 52% with a specificity of 89% and VIA had the lowest sensitivity of 22.8%, with highest specificity of 92.6%. Another concerning finding was that hrHPV testing, gynocular colonoscopy and VIA performed poorly as standalone tests with 23% of cases not detected in any of the tests.

The most striking finding from these test accuracy results is that none of the tests achieved a sensitivity above 70%, and using tests in combination did not improve accuracy, particularly if the first test had a low sensitivity. The sensitivity of hrHPV testing increased from 65.3% to 85.7% when only biopsies from visible lesions were considered.

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The fact that more than one biopsy is likely to detect more disease has been shown in a number of studies, including that by Wentzensen *et al*[5] where they demonstrated sensitivities for detecting CIN2+ increased from 61% in a single biopsy to 86% with two biopsies to 96% with three biopsies.

Nearly 40% of women screened and diagnosed with histologically proven CIN2+ in this study did not receive treatment. This has major implications for the use of resources and these women remain at risk of disease, despite having undergone screening. The cumulative incidence of cervical cancer can only be achieved if precancerous lesions are successfully treated and those that persist or recur post-treatment, are detected and managed appropriately. In this study, women were not treated on the same day, although a decision for future treatment was made and presumably conveyed to the women. The long delay in receiving treatment was associated with women not receiving treatment. The COVID-19 pandemic most likely also had a major impact on women not going for treatment.

There are a lot of data on the accuracy and test performances of a variety of primary screening tests, including randomised controlled trials. Based on these data, the WHO recommends transition to hrHPV testing as the primary screening test where affordable, feasible and sustainable.[1] This study, however, indicates that more work and larger studies need to be performed to improve test accuracy in women living with HIV, as well as the need to develop high-quality, reliable triage tests.

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