



Rostrum

Cervical cancer screening opportunities for Guinea-Bissau

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ABSTRACT

Guinea-Bissau is a severely resource constrained country, in search of political stability and development in every sector of public life. International aid is permanent and healthcare is one of the most targeted fields, focusing mostly on infectious diseases, maternity, infant malnutrition, access to healthcare and gender inequality in health. As in the rest of Sub-Saharan Africa, cervical cancer is gathering increasing attention from the community and ruling officers. The potential of screening for control of cervical cancer raised the interest of adapting screening methods to low-resource settings. This started the search for the best resource-adapted strategies, which promoted several trials that currently shape the development of screening programs in these countries. Prevention and control strategies are also being adapted taking into account the availability of human Papillomavirus vaccination. Nonetheless, several barriers are still in place for widespread vaccination programs, and cervical cancer screening and treatment remain central in the control of cervical cancer in low-resource settings.

We intend to discuss current cervical cancer screening approaches in low-resource countries and opportunities for their implementation in Guinea-Bissau.

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Cervical cancer

Cervical cancer is the third most frequent cancer in women worldwide, after breast and colorectal cancers, with an estimated 527,624 new cases in 2012, corresponding to an age standardized incidence rate – world reference population (ASIR-W) of 14 per 100,000 women. It is also responsible for a high mortality rate, accounting for an estimated 266,000 deaths (age standardized mortality rate – world reference population [ASMR-W]: 6.8/100,000).¹ In Sub-Saharan Africa, cervical cancer is the most frequent cancer, accounting for an estimated 57,381 deaths in 2012 (ASMR-W: 22.5/100,000) corresponding to 22% of the number of deaths due to cervical cancer worldwide.¹

Abbreviations: ASIR-W, age standardized incidence rate – world reference population; ASMR-W, age standardized mortality rate – world reference population; HPV, human Papillomavirus; HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; Pap test, Papanicolaou test; VIA, visual inspection with acetic acid; LEEP, loop electrosurgical excision procedure; CIN2, cervical intraepithelial neoplasia grade 2.

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Infection with human papillomavirus (HPV) infection is central in the epidemiology of cervical cancer and development of strategies for its prevention and control. On the one hand, HPV is estimated to cause nearly all cases of cervical cancer,²⁻⁴ making vaccination against HPV a tool of paramount importance for the prevention of cervical cancer. On the other hand, persistent HPV infections (approximately 10% of all infections) are estimated to take ten or more years to develop into cervical cancer, which allows for early detection, through screening, of highly curable lesions caused by the infection.⁵

Cervical cancer is considered to be a defining disease of acquired immune deficiency syndrome (AIDS).⁶ Human immunodeficiency virus (HIV)-positive women have a greater incidence of HPV infection, overall and with multiple HPV types, and present a faster progression to cervical cancer, as well as a higher risk of recurrence after treatment.⁷ Since time from infection to cancer can be considerably shorter among HIV-positive women, more frequent screening is very important to detect and cure early lesions.⁸

Screening

The development of effective HPV vaccines brought a new paradigm for prevention of cervical cancer.⁹ However, in developing countries, scarce resources and failure to complete full dosage

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schemes constitute barriers to the implementation of effective vaccination programs.¹⁰ Therefore, screening will expectedly remain an essential tool for the prevention and control of cervical cancer in the next decades.¹¹

For the last 60 years and mostly since the implementation of organized screening programs based on cytology with the Papanicolaou test (Pap test), cervical cancer mortality has been largely reduced in developed countries.¹² However, screening programs are lacking in most low-income countries, which results in a large proportion of the patients presenting with large invasive tumours, who frequently need multimodal treatments including surgery, chemotherapy and radiotherapy.^{13,14} Many developing countries do not have the capability for complex surgery, radiation therapy or chemotherapy, and often have shortage of chemotherapy agents, which highlights the importance of screening in these settings to identify lesions at stages amenable to more effective treatment, and with lower risks and costs.¹⁵

Screening programs based on the Pap test showed a high effectiveness, decreasing by 80% cervical cancer mortality in some countries.¹² However, this is a costly method requiring highly trained professionals and the ability to obtain, store and transport samples, which are not easily available in many developing settings.¹⁶ Moreover, screening with the Pap test requires a follow-up visit for treatment of patients with lesions. In some studies conducted in developing countries, one-third or more of women did not return for test results, rendering this screening method ineffective.⁸ Therefore, "test & treat" strategies were developed to overcome these shortcomings, and are currently proposed by World Health Organization for the screening and treatment of cervical pre-invasive lesions in low-income settings.¹⁷

Test & treat

Test & treat involves screening and treatment in the same visit.¹⁷ It is usually based on visual inspection with acetic acid (VIA) followed by cryotherapy. These procedures are easy to learn, may be performed by non-physicians, are less dependable on well-equipped facilities and therefore have a high potential for widespread use even in settings where human resources are scarce.¹⁸ The loop electrosurgical excision procedure (LEEP) can be used if the eligibility criteria for cryotherapy are not met.¹⁷ Several countries use this approach and in Zambia, for instance, a national scale-up program was possible using test & treat.^{19,20}

Test – VIA

VIA uses acetic acid to highlight intraepithelial cervical lesions (pre-invasive lesions) caused by HPV infection.¹⁷ The specificity and sensitivity of VIA for the detection of cervical intraepithelial neoplasia grade 2 or worst (CIN2+) have been evaluated in several studies in low resource settings and VIA showed a higher sensitivity for CIN2+ lesions when compared to the Pap test.^{21–23} In a pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India, sensitivity and specificity estimates of VIA for CIN2+ were 79.2% (95% confidence interval [95%CI]: 73.3–94.9) and 84.7% (95%CI: 80.7–88.8), respectively. On the other hand, the pooled sensitivity and specificity estimates of the Pap test were 57.0% (95%CI: 37.6–76.3) and 92.8% (95%CI: 88.7–96.8), respectively.²⁴

Test – digital cervicography

VIA can be combined with digital cervicography to increase its accuracy. Cervicography uses a magnified photograph of the cervix to evaluate abnormalities in detail.²⁵ Cervicographs may be shown to women for active education, while reassuring them about the results. It also makes quality assurance possible by reviewing photos with the providers.^{26,27} Cervicography is currently used

for screening in some countries, including Zambia, Botswana and Ethiopia.^{19,28,29}

One study in Zambia evaluated different point-of-care screening methods showing a sensitivity and specificity of 59% (95%CI: 41–76) and 88% (95%CI: 82–93), respectively, for digital cervicography, while for VIA alone, the corresponding figures were 48% (95%CI: 30–67) and 92% (95%CI: 86–95).³⁰ However, other studies have not shown improved results in terms of accuracy when compared to VIA.³¹

Test – HPV test

HPV detection can be used for screening. In western countries, HPV testing is now part of screening programs because of its high sensitivity, over 90%, for the detection of CIN2+ lesions.³² However, it has a suboptimal specificity, ranging from 85% to 90%, which results in a high proportion of women being unnecessarily referred for colposcopy.³³ In addition, women younger than 30 years have a higher rate of transient HPV infections that do not evolve to pre-invasive lesions. This decreases specificity even more, limiting the usefulness of the test in this age group.³⁴ HPV testing is currently being evaluated for cervical cancer screening in low-income settings. It can be combined with other tests, such as VIA, to increase specificity while still using a resource-adapted, same-day visit methodology.³⁵ HPV testing is evolving to be a fully resource-adapted screening method: rapid point-of-care tests that do not need to be performed in a lab and do not require complex training are already available³⁶; different methods for sample collection that do not need to be performed by a health provider such as self-sampling or based on urine samples are being evaluated.³⁷ However, HPV tests are not yet ready for a widespread use, namely due to their high cost.¹¹

Treat – cryotherapy

Cryotherapy is the most frequently used treatment procedure in the test & treat approach. It relies on the destruction of cervical lesions by frost, using pressured carbon dioxide or nitrogen dioxide. It is very fast and easy to learn, requiring simple equipment that can be used by non-medical personnel and serious side effects are very rare. In addition, cryotherapy showed a high acceptability in low-income settings.^{35,38} In eligible lesions, cryotherapy produces similar results to electrosurgical procedures in terms of lesion destruction³⁹; however, it destroys cervical tissue and samples will become unavailable for histopathological evaluation to confirm complete excision.¹⁷ Finally, it requires a supply of pressured gas, which can be challenging in some settings.⁴⁰

Treat – LEEP

Electrosurgical removal of the transformation zone is one of the most effective procedures for treatment of cervical lesions. However, it is technically challenging when compared with cryotherapy, must be performed by a trained doctor, is expensive and relies on electricity. In the test & treat approach, patients should be referred for LEEP when lesions are ineligible for cryotherapy.^{17,41}

Guinea-Bissau

The Republic of Guinea-Bissau is a small country located in the west coast of the African continent. It has 36,125 km² and an estimated population of 1,520,830 inhabitants according to the 2009 census.⁴² It is a severely resource constrained country with considerable economic difficulties and 44% of the inhabitants live with less than a dollar per day. Development is threatened by a persistent political fragility that arises from the innumerable coups in the past. According to the Human Development Index, Guinea-Bissau ranks 178th out of 188 countries, having an average life expectancy

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