THE COMPREHENSIVE CERVICAL CANCER PREVENTION IN TANANIA (CONCEPT) PROJECT

Research update V

PERFORMANCE OF HPV TESTS AND VISUEL INSPECTION

Partners

The CONCEPT study is an international research collaboration project between Denmark and Tanzania, funded by the Danida Fellowship Centre.

The Tanzanian partners are Ocean Road Cancer Institute (ORCI) and Kilimanjaro Christian Medical Centre (KCMC).

The Danish partners are the University of Southern Denmark (SDU) and the Danish Cancer Society Research Center.

Danida Fellowship Centre
- sustaining development through research and learning

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Key findings: Performance of HPV tests and visuel inspection

- A total of 3640 Tanzanian women were eligible to be included in this CONCEPT sub-study.
- *Care*HPV tests and Hybrid capture 2 (HC2) HPV tests had a higher positivity rate than VIA, 23.6%, 19.1% and 6.3% respectively.
- All three tests had higher positivity rates among HIV-positive women than among HIV-negative women.
- The sensitivity for *care*HPV and HC2 were 88.9%, 91.1%, respectively. In contrast, it was only 31.1% for VIA. However, VIA had higher specificity than the other tests.
- When using VIA as a triage test among *care*HPV positive women, the sensitivity dropped to 27.4% whereas the specificity increased to 98.3%.

Introduction

This research update describes the performance of *care*HPV, HC2, and visuel inspection with acetic acid (VIA) for detection of cytologically diagnosed cervical high-grade lesions or cancer among women enrolled into the research project CONCEPT (***Comprehensive Cervical Cancer Prevention in Tanzania***).

Cervical cancer is one of the most common malignant diseases in low and middle income countries (LMIC), more than 86% of new cases diagnosed in 2012 were from LMICs [1,2]. Persistence infection with high-risk HPV (HR HPV) is the main cause of high-grade cervical lesions and cervical cancer. Further, it has been proven that women who are HIV-positive have increased risk of HPV infection and increased risk of high-grade cervical lesions and cervical cancer [3,4].

The fact that LMICs has a high incidence of cervical cancer, reflect low coverage of cervical cancer screening and high prevalence of HPV and HIV [5]. Most LMICs use VIA as primary screening method as it is affordable and easily accessible at all facility levels, however, it is subject to the provider's interpretation of the findings [6]. In contrast, most high-income countries use HPV testing technology as primary screening method followed by cytology or histology [6].

HPV DNA testing such as hybrid capture 2 (HC2) has a good sensitivity and specificity, however, the technology is expensive and requires skilled staff. As a response, *care*HPV has been developed, which is a derivative of HC2. It can be purchased at a price that is affordable for most LMICs and does only require minimal lab facilities [7].

***Care*HPV machine**

While the performance of *care*HPV has been evaluated in a few selected countries, it is not yet established how the test perform in a routine screening setting in a Tanzanian context.

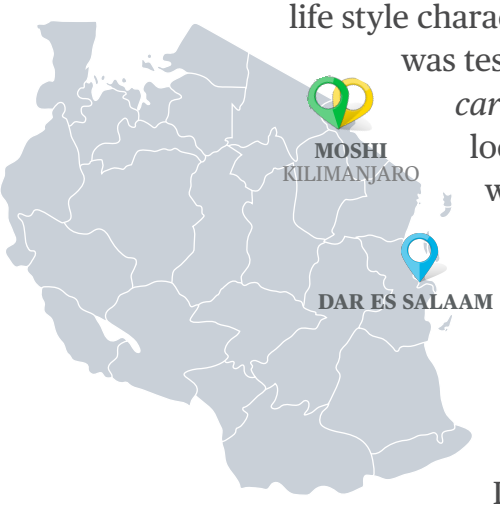
The aim of this study was to examine,

1. *The performance of careHPV, HC2, and VIA for detection of cytologically diagnosed cervical high-grade lesions or cancer, overall and according to age and HIV status.*
2. *The value of VIA as a triage strategy following careHPV testing.*

Methods

Data for the CONCEPT project were collected from Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Kilimanjaro Christian Medical Centre (KCMC) and Mawenzi regional hospital in the Kilimanjaro region. All women who were attending routine screening were invited to participate in the study.

Eligible women were voluntarily tested for HIV and underwent face-to-face interview with structured questionnaires to capture socio-demographic and life style characteristics. One cervical sample was tested for HPV DNA using the *care*HPV machine and testing kit, located at ORCI and KCMC. A test was considered positive if one or more of the following 14 HR HPV types were detected: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68. Another cervical sample was transported to Pathology Department at Lillebaelt Hospital, Vejle, Denmark for cytological analysis. The results were reported according to Bethesda nomenclature. After the cytological assessment, the samples were sent to the Section for Experimental Virology, Tubingen University in Germany for HC2 testing. A test was considered positive if one or more of the following 14 HR HPV types were found:

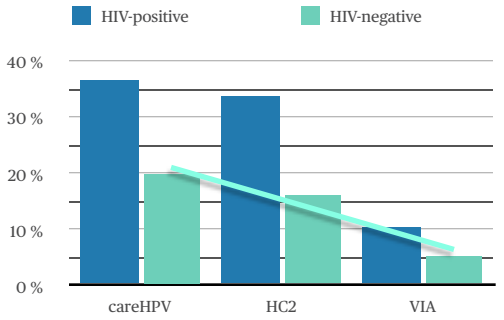


HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68. The final element of screening involved VIA, which was done as per the Tanzanian protocol. A cotton wool on bamboo stick was soaked in acetic acid and applied on the cervix and changes were observed. Women with well-defined aceto-whites lesion were termed as VIA-positive and if no changes occurred they were termed as VIA-negative. All women who were found to be HIV-positive or to have precancerous/cancerous lesion were referred for further medical proceedings.

Main findings

A total of 4043 were included in the CONCEPT cohort, and 3640 were eligible to be included in this sub-study. It was found that *Care*HPV overall had a higher positivity rate than the other tests. More specifically, 23.6% (859/3640) women tested *care* HPV-positive, 19.1% (696/3640) tested HC2-positive, and 6.3% (231/3640) tested VIA-positive.

Further, it was found that the positivity rate varied with HIV status. Women who were HIV-positive had increased rates of positivity with 36.4% being *care*HPV-positive, 33.8% being HC2-positive, and 10.6% being VIA-positive. For HIV-negative women,

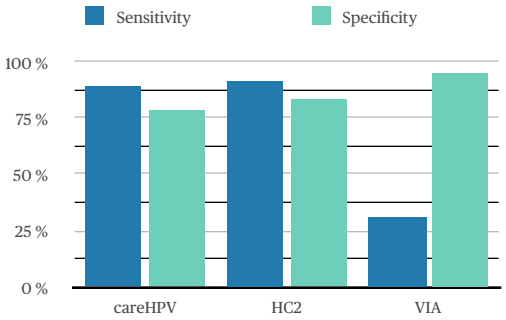


Positivity rates

the corresponding figures were 20.0%, 15.9%, and 5.4% respectively.

Test performance

The performance of *care*HPV, HC2 and VIA in detection of high-grade lesions was assessed against cytology results. Both *care*HPV and HC2 testing performed better than VIA. For example, *care*HPV had a sensitivity of 88.9% (95% CI, 82.4 - 93.6) and a specificity of 78.9% (95% CI, 77.5 - 80.3), HC2 had a sensitivity of 91.1% (95% CI, 85.0 - 95.3) and a specificity of 83.7% (95% CI, 82.4 - 84.9) whilst it was found that VIA had a lower sensitivity of 31.1% (95% CI, 23.4 - 39.6) but a higher specificity of 94.6% (95% CI, 93.8 - 95.3). The sensitivity of careHPV and HC2 were higher among HIV-positive than among HIV-negative women whereas the sensitivity of VIA did not vary with HIV status.



Triage of VIA with *care*HPV

A total of 859 women tested *care*HPV-positive, and the performance of VIA as a triage among these women was analysed. Overall, 98 women were *care*HPV-positive and VIA-positive and among these women, 37 (37.7%) had high-grade lesions. Among the 761 women who were *care*HPV positive but VIA-negative, 83 women (10.9%) had high-grade lesions. When using VIA as a triage test, the

sensitivity dropped to 27.4% whereas the specificity increased to 98.3%.

Future perspectives

This study demonstrated that *care*HPV and HC2 HPV tests had high sensitivity whereas VIA had much lower sensitivity in detecting cytologically diagnosed high-grade lesions or cancer (HSIL+). A triage of *care*HPV with VIA might be a promising way of introducing the new technology in the routine cervical cancer screening program in Tanzania.

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