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Review article

Public health approach to prevent cervical cancer in HIV-infected women in Kenya: Issues to consider in the design of prevention programs

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ABSTRACT

Women living with HIV in Africa are at increased risk to be co-infected with Human Papilloma Virus (HPV), persistent high risk (HR) HPV infection and bacterial vaginosis (BV), which compounds HPV persistence, thereby increasing the risk for cervical dysplasia. New guidance from WHO in 2014 advocating for a "screen and treat" approach in resource poor settings is becoming a more widely recommended screening tool for cervical cancer prevention programs in such contexts. This review article summarizes the risk factors to be considered when designing a primary and secondary cervical prevention program in a post-vaccination era for HIV-infected women in Kenya.

This review article is based on our prior research on the epidemiology of pHR/HR-HPV genotypes in HIV-infected women and CIN 2 + in Kenya and other sub-Saharan contexts. In order to contextualize the findings, a literature search was carried out in March 2017 by means of four electronic databases: PUBMED, EMBASE, SCOPUS, and PROQUEST.

Risk factors for potential (pHR)/HR HPV acquisition, including CD4 count, HAART initiation, Female Sex Worker status (FSW) and BV need to be considered. Furthermore, there may be risk factors for abnormal cytology, including FSW status, multiple potential (p)HR/HR HPV genotypes, which may require that HIV-infected women be subjected to screening at more frequent intervals than the three year recommended by the WHO. The quadruple synergistic interaction between HIV, HPV and BV and its related cervicitis may need to be reflected within a larger prevention framework at the community level. The opportunities brought forth by the roll out of HAART could lead to task shifting of HIV-HPV-BV care to nurses, which may increase access in poorly-served areas.

1. Background

Kenya is home to the world's fourth-largest HIV epidemic. In 2013, an estimated 1.6 million people were living with HIV and roughly 57,000 people died from AIDS-related illnesses (UNAIDS, 2013). In 2007, the World Health Organization (WHO) included Invasive Cervical Cancer (ICC) to stage "4" of the HIV/AIDS clinical classification of staging for resource-constrained settings (WHO Department of Immunization, Vaccines and Biologicals, World Health Organization; Geneva, 2007).

More than 200 types of human papillomaviruses (HPV) have been identified, of which 40 can progress to high-grade precancerous squamous intraepithelial lesions (HSILs) and subsequent invasive cervical cancer (ICC) (de Villiers et al., 2004). Although most HPV infections clear without intervention within 1 year, certain High Risk HPV (HR-HPV) genotypes have a propensity to persist and are consequently the chief risk factor for the development of ICC (Koshiol et al., 2008). The 15 HR oncogenic viral strains, which have been identified, can be broken down into different species: the HPV 16 group (alpha-9) of the alpha-papillomavirus genus (HPV 31, 33, 35, 52, and 58), the HPV 18 group (alpha-7; HPV 39, 45, 59, and 68) and the alpha-6, genotype *HPV 56* (Li et al., 2011; Rodríguez-Cerdeira et al., 2009).

Sexually transmitted infections (STIs) have been associated with longer HR-HPV persistence in previous studies (King et al., 2011). The prevalence of Bacterial Vaginosis (BV) in African women, characterised by an overgrowth of vaginal anaerobic flora and reduction of H_2O_2-

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producing lactobacilli, is among the highest worldwide (Morris et al., 2001). The high BV prevalence is of particular concern as there is evidence that BV is a risk factor for acquisition and transmission of many STI's, including HIV and HPV (Cohen et al., 2012; Martin et al., 1999). A meta-analysis also suggested a positive association between BV and cervical pre-cancerous lesions (Gillet et al., 2012a). Cervical inflammation has been associated with cervical intraepithelial neoplasia (CIN) and may be a cofactor for high-grade cervical lesions in HPV-infected women (Castle et al., 2001a). BV frequently coexists with cervicitis (Sweet, 2000a) and was found to be an independent risk factor for cervicitis (Marrazzo, 2006; Platz-Christensen et al., 1994; Sweet, 2000b), which may be a risk factor for cervical dysplasia in its own right (Castle et al., 2001b; Liu et al., 2016).

The WHO recommends the inclusion of HPV vaccination in national immunization programs as HPV represents a public health priority, and vaccine delivery is feasible and cost-effective (World Health Organization (WHO), 2014a). Whilst immunogenicity trials have shown the effectiveness of a two-dose HPV vaccine against HPV 16 and HPV 18 in HPV-naive girls aged 9–14 (Markowitz, 2016), the WHO still recommends that immunocompromised/HIV-infected girls aged 9–14 be administered a third dose (World Health Organization, 2017a). However, this will not obviate the need for secondary prevention in Kenya, where our recent meta-analysis (2016) on the distribution of pHR/HR HPV genotypes in HIV-infected women in Kenya found a pooled estimated prevalence of HPV 16 and 18 of 61% in HIV-infected women with ICC (Menon et al., 2016a). This finding underscores a need for a broader primary prevention program than the quadrivalent vaccine (Gardasil™) that protects against HPV genotypes 6, 11, 16 and 18 that is currently being rolled out (Garland & Smith, 2010). In addition, in light of the limited vaccine uptake in Kenya (Vermandere et al., 2015) in tandem with poor cervical cytology infrastructure, Kenyan women with undiagnosed or untreated severe cervical lesions may be at high risk of developing ICC (Crum et al., 2003).

The more feasible, and WHO-approved, strategy for cervical cancer screening in low resource settings, like Kenya is visual inspection with acetic acid (VIA) or visual inspection with Lugol's iodine (VILI), although cytological screening is available in Kenyan urban settings. Women with HIV infection are recommended by the Centers of Disease Control (CDC) to have more frequent screening with cervical cytology: twice in the first year after diagnosis of HIV and, if normal, annually thereafter (CDC, 2010). However, the WHO recommends that women living with HIV be screened within 3 years if tested negative by VIA or cytology (World Health Organization (WHO), 2014b).

The regular immunological and/or virological followup that accompanies the latest WHO recommendation to initiate HAART regardless of the CD4 count provides a golden opportunity to increase cervical screening. However it is expected that Kenya will need to utilize more public health resources to expand laboratory facilities to monitor HIV viral load and, by default, CD4 count to monitor treatment efficacy (Menon, 2010). As a corollary, this may leave even fewer resources for cervical cancer preventive measures while HIV-infected women will live longer, thereby potentially experiencing an increased incidence of ICC. This review firstly discusses clinical, virological and behavioural risk factors for pHR/HR-HPV genotypes to take into consideration when designing a triage-based cervical cancer prevention programme; secondly, it discusses programmatic issues related to implementation.

2. Methodology

We contextualized our prior research on Kenya and on the sub Saharan African continent, consisting of systematic reviews, meta analyses, and cross sectional studies, by carrying out a literature search in April 2017 by means of four electronic databases: PUBMED, EMBASE, SCOPUS, and PROQUEST.

2.1. Association between BV and cervical pre-cancerous lesions in Africa

Relevant studies on the association between BV and cervical pre-cancerous lesions were identified through an extensive search of the electronic databases based on the following key words: 'bacterial vaginosis', 'bacterial infections and vaginitis' in combination with 'cervical intraepithelial neoplasia' (CIN), 'squamous intraepithelial lesions' (SIL), 'cervical lesions', 'cervical dysplasia', and 'cervical screening AND Africa'.

2.2. Distribution of HPV genotypes in HIV-infected women in Kenya

The domains of the search terms were HIV, HPV, cervical cancer, incidence or prevalence, and Kenya. We combined HPV and cervical cancer with the Boolean operator "OR", and the result was combined with the other terms with "AND".

2.3. Association between BV and alpha 9 related HPV genotypes

'Bacterial vaginosis', 'bacterial infections and vaginitis' in combination with alpha 9 related HPV genotypes.

2.4. Association between vaginal inflammation and VIA specificity

'Vaginal inflammation' AND VIA OR visual inspection with acetic acid AND specificity.

2.5. Task shifting of cervical cancer prevention in Africa

Task shifting AND cervical cancer screening OR prevention AND HIV treatment infrastructure AND Africa.

2.6. Treatment of bacterial vaginosis in HIV-infected women

Metronidazole OR treatment AND Bacterial vaginosis OR 'bacterial infections and vaginitis' AND HIV.

2.7. Self-sampling of HPV in Africa

HPV self-test AND sub Saharan Africa.

3. Results

Fifteen studies were included, one of which is still in press.

3.1. Risk factors for HPV acquisition

3.1.1. Triage according to HIV, HAART and CD4 count

Our meta-analysis demonstrated a high burden of HR-HPV genotypes with 64% (95%CI: 50%–77%) in a general HIV population in Kenya (Menon et al., 2016a), significantly higher than a recent meta-analysis on pooled HPV prevalence in the general female population in eastern Africa (42.2%) (Ogembo et al., 2015). This finding suggests that a compromised immune system may be a risk factor for HR-HPV acquisition. Our recent systematic review of HAART and its association on the presence of HPV, pre-malignant and malignant cervical lesions in Sub-Saharan Africa suggests that there is evidence that duration of HAART treatment along with the CD4 count may reduce the prevalence of high–risk HPV (HR-HPV) (Menon et al., 2017a).

However, the immuno-epidemiology of each HPV genotype remains inadequately elucidated. This can be prone to variations based on the culturally different follow-up algorithms and endpoint evaluations, quality of cytological specimens and biopsies taken along with heterogeneous HPV genotyping methods available (Padalko et al., 2015). In Kenya, our exploration of the association between different levels of immunosuppression and pHR/HPV genotypes suggests that the (WHO,

2013) recommendation to initiate HAART regardless of CD4 count may offer opportunities to prevent HPV 53 and multiple HPV infections, and thereby reduce the potential for cervical dysplasia in HPV-vaccinated women (Menon et al., 2016b). However, the significant association between CD4 count ≥ 350 μl and HPV 16 we observed suggests that for HIV positive unvaccinated women, a CD4 based triage may not be as effective as they may still be at risk for this oncogenic genotype (Menon et al., 2016b).

3.2. Synergistic interactions

3.2.1. BV-based triage - association between BV and alpha 9 related genotypes

Our research in the clinical epidemiology of pHR/HR-HPV genotypes indicates the vulnerability of HIV-infected women with BV. Our findings suggest a potential beneficial impact of BV treatment to reduce the risk of HR-HPV genotype acquisition. In line with a study in Spain having found BV to be a predictor for alpha 9 related genotypes (Rodriguez-Cerdeira et al., 2012), we have found BV to be a predictor of the HPV 16 genetically related HPV 58 in HIV-positive women (Menon, 2010; Menon et al., 2017b). This finding underscores the need to consider a potential synergistic effect between BV and phylogenetically related HPV 16 genotypes. It may be hypothesized that treatment of BV may be an effective intervention to prevent subsequent HPV infection.

3.3. Risk factors for abnormal cytology

3.3.1. A bacterial Vaginosis-based triage

Apart from its benefits for preventing HR-HPV acquisition in HIV-infected women, a BV based initial triage can be an effective component of a secondary cervical cancer prevention program. The vaginal inflammation caused by BV may result in increasing HIV viral load, which in turn can lead to enhanced cervical dysplasia progression (Cardillo et al., 2001). This relation may accentuate the positive association that a meta-analysis suggested between BV and cervical pre-cancerous lesions (pooled OR: 1.51) (Gillet et al., 2012b).

Moreover, in a clinical setting, inflammation may result in a false positive VIA if the appearance of leukocytes in the submucosa mimics white epithelium (Davis-Dao et al., 2008). A BV-based primary triage for HR-HPV acquisition in HIV-infected women and treatment thereof may have the additional benefit of diminishing cervicitis, which studies have shown its confounding nature on VIA results, resulting in women with cervicitis being more likely to have false positive VIA results than women without cervicitis (Davis-Dao et al., 2008; Vedantham et al., 2010).

Our study on HIV-infected women in Kenya, which found a cervicitis prevalence of 15% (Menon et al., 2016b) highlights the impact that BV-related cervicitis might have on diagnosis by rendering VIA interpretation less specific. In turn, a VIA based “screen and treat” approach without histological confirmation may be too sensitive, leading to overtreatment of women (WHO, 2013). A study of a HIV-infected population in Uganda reported that a VIA based “see and treat” strategy may have resulted in overtreatment by 72% (439 out of 625) (Mutyaba et al., 2010).

In contrast to the significant association (OR 4.0; 95% CI, 1.07–15.1) (Kharsany et al., 1993) observed between BV and abnormal cytology in HIV-negative women in South Africa, our study did not find a statistically significant association between BV and abnormal cytology (Menon et al., 2017b). It may be that the vulnerability of our FSW clandestine population exposed them to competing risk factors, which in turn may have diluted the association between BV and abnormal cytology. Furthermore, BV in the South African study was diagnosed using the Amsel criteria, which had lower sensitivity and higher specificity than the Nugent scoring system, the gold standard (RangariAmit et al., 2013) that we have used.

3.3.2. Triage based on HIV-infected Female Sex Workers (FSW)

In light of the financial constraints that preclude universal screening, as well as the high pooled prevalence of pHR/HR-HPV genotypes among the HIV-infected population of 64% (95%CI: 50%–77%) (Menon et al., 2016a), enhanced screening may need to be devised for certain groups.

A borderline statistically significant difference in our recent meta-analysis in Kenya between pooled estimates of HR-HPV genotypes in FSW and the general HIV population suggested that a cost-effective approach for cervical cancer prevention may warrant a triage based on this risk factor (Menon et al., 2016a). Moreover, our study found that of the 192 HIV-infected FSW, 27.1% (95% CI: 20.9–34.0%) had abnormal cytology (Menon et al., 2017b). However, given the penal code specifically penalising prostitution in Kenya (International Models project on women's right, 2011), failure to guarantee anonymity of this group may preclude the implementation of prevention programmes targeting this population at risk (Musyoki et al., 2015). Also, the non-randomness of snowball sampling of FSW, which is used in most of the research for this group, precludes generalizing findings to the larger FSW population in Western Kenya, as the sampling strategy may have excluded FSWs without any social networks.

3.3.3. Immunosuppression

According to our systematic review, in sub Saharan Africa, the CD4 count, rather than HAART coverage or its duration, plays a central role in the prevalence of CIN 2 and CIN 3, which suggests the importance of earlier immune reconstitution (Menon et al., 2017a). Therefore, with CD4 count appearing in the causal pathway between HAART and CIN2 +, HAART may have an indirect effect on decreasing the prevalence of CIN2 +.

3.3.4. Multiple pHR/HR-HPV genotypes

Our meta-analysis on Kenya found that the prevalence of multiple pHR/HR-HPV genotypes was very prominent not only in normal to abnormal cytology but also in ICC (48%; 95% CI: 37%-60% and 35%; 95% CI 0.25%–45%, respectively) (Menon et al., 2016a). This association suggests that a triage for further cytological screening based on the presence of multiple HPV genotypes may be warranted.

3.4. Programmatic issues of preventive programmes

Whilst early diagnosis and treatment of cervical pre-cancerous lesions prevent up to 80% of cervical cancers in high resource countries where cervical cancer screening is routine (Sankaranarayanan et al., 2001), in sub Saharan African, regular follow up of cervical cytology is not feasible. A study in Kenya found that a significant percentage of women (56–80.6%) (Maranga et al., 2013) is only identified once their cervical cancer is at an advanced stage. Furthermore, a study in Tanzania reported that women co-infected with HIV are less likely to be treated (Mosha et al., 2009).

A roll out of cervical preventive programmes throughout underserved rural setting Kenya will necessitate a change in the cervical cancer prevention landscape. Such a programme should be designed considering the limited resources. Indeed, a recent survey among health care workers found that the main barriers to service provision were staffing shortages and insufficient staff training (Rosser et al., 2015).

3.4.1. Task shifting of cervical cancer prevention using HIV care

While in sub-Saharan Africa nurses greatly outnumber doctors and are often on the frontline in primary care services, their expanded role in the post-HAART roll out era has been redefined. The decentralization process of HIV care launched in Kenya has considerably increased services from 15 health facilities in 2003 to over 700 facilities by December 2008 (National AIDS and STI control Programme, Ministry of Health, 2009). A crucial aspect of this process has been the establishment of HIV clinics at health centres and dispensaries, close to those in

need, as well as the integration of HIV programs with other services provided at the health facilities. Concurrently, the roll out of HAART access to underserved communities gave impetus to a task shifting approach in HIV care to deal with the severe shortage of health workers in the front line.

Albeit poor access to services has resulted in the low cytological screening coverage rates in Africa, new strategies facilitate screening in resource-limited settings. Screening services have been expanding since the WHO 2014 guideline advocating for a VIA or HPV-based "screen and treat" approach, with mobile units reaching more rural areas and cervical cancer prevention integrating HIV and family planning services (Huchko et al., 2011). This approach contrasts with the previous screening and diagnosis by the standard sequence of cytology, colposcopy, biopsy, and histological confirmation of CIN.

Building on previous successful public health initiatives, which integrated TB and antenatal care within HIV care, studies have shown how the use of the HIV care infrastructure in sub-Saharan Africa has been capitalised to integrate cervical cancer prevention in HIV-infected women. In rural Mozambique, clinics were characterised by shortages of human resources, equipment, poor paper record systems and a limited ability to follow-up with patients. These rural clinics managed to piggyback on prior HIV infrastructure to implement chronic disease screening and management for cervical screening (Moon et al., 2012). In Zambia, a study demonstrated the feasibility of implementing a referral and management system for cryotherapy-ineligible women in a "screen-and-treat" cervical cancer prevention program targeting HIV-infected women (Pfaendler et al., 2008).

In Kenya, where there are only 40 registered and 81 enrolled nurses per 100,000 people, outpatient treatment services, where cryotherapy and loop electrosurgical excision procedure are performed, are largely unavailable throughout the country (Ministry of Public Health and Sanitation and Ministry of Medical Services, 2012). In a rural setting in Western Kenya, a recent study showed that the established infrastructure of an HIV treatment program was successfully used to build capacity for cervical screening (Khozaim et al., 2014).Task-shifting and population-based cervical screening was found to be feasible, nevertheless loss to follow-up and poor cytology infrastructure remained important obstacles (Khozaim et al., 2014).

However, the availability of doctors in Kenya, which is 10 per 100,000 inhabitants (World Health Organization, 2017b), is even lower than the availability of nurses and mostly concentrated in urban areas. These barriers to cervical cancer prevention will undoubtedly hamper the enhanced responsibility that nurses should be granted in cervical cancer prevention in HIV-infected women within a high BV prevalence setting. Sufficient and well trained human resources are necessary to optimise investments made in diagnostic and treatment equipment and infrastructure. In Sub Saharan Africa, diagnostic testing for STIs and BV is often not available and most pregnant women are managed using syndromic algorithms (Marx et al., 2010). However, a study in Kenya reported poor detection of BV using syndromic diagnostic algorithms in HIV-infected women by health care workers (Marx et al., 2010). This underscores the need to enhance microscopy proficiency or Amsel reading of BV in HIV-positive women, who possibly harbour several co-infections. In addition, there is a need to develop nurses' skills in applying a management algorithm for BV associated cervicitis.

4. Discussion

Secondary prevention programs in Kenya will need to be tailored to the local epidemiology of cervical dysplasia and ICC within the HIV-infected Kenyan female population. In light of some shortcomings of primary prevention for HIV-infected women in Kenya, risk factors for pHR/HR HPV acquisition, including CD4 count, HAART use, FSW status and BV presence may need to be considered when determining who requires a more intense follow up. Furthermore, there may be risk factors for abnormal cytology, including FSW status, multiple pHR/HR HPV genotypes, which may require HIV-infected women to undergo screening at more frequent intervals than the once every three years WHO 2014 recommendation for HIV-infected women with negative VIA and cytology tests. Until the advent of rapid, point of care and low-cost HPV screening options, regular BV monitoring and its treatment may also be sought to improve the specificity of VIA.

4.1. Strength and limitations

The studies used to draw our recommendations have the strength of stemming from a wide array of settings, which enabled us to capture a more representative HIV positive female population. However, our recommendations are subjected to the limitations of the cross-sectional study design, which does not allow the fulfillment of the temporal criterion for causality.

4.2. Generalizability

Our recommendations may be extrapolated to other clinical environments where women present similar levels of immunosuppression. However, our recommendations may not be generalizable to HIV-infected women who have scarce access to health care, as being of poorer socio-economic status, they may be more at risk for co-infection of poverty, including other STIs, TB, malaria, and helminthic infections. These are infections, which may affect persistence of certain pHR/HR HPV genotypes and/or cervical dysplasia progression (Menon et al., 2017a).

In order to determine a tailored screening interval, there are first a number of epidemiological, clinical and then programmatic research gaps, which need to be addressed.

4.3. Research gaps

4.3.1. Research gaps for risk factors for pHR/HR HPV acquisition

Longitudinal studies should be undertaken to determine if treatment of BV may reduce pHR/HR-HPV in genotype acquisition and/or cervical dysplasia progression in HIV-infected women. Furthermore, the epidemiology of BV recurrent BV within this population is still poorly elucidated. A recent study on the epidemiology of BV in a cohort of women at high risk for STI and HIV infection in Kampala, Uganda, showed that of the HIV + women who were treated for BV, 72% had a second episode within 3 months (Francis et al., 2016).

Since the bivalent vaccine covers species α7 and α9, the burden of HPV carcinogenesis in a fully vaccinated population might shift to the potentially high-risk genotypes that are not currently covered by either vaccine. Given the relatively high prevalence of HPV 53 as stand-alone and in pairings in HIV-infected FSW with abnormal cytology, its potential public health impact has yet to be estimated.

FSW are a major risk group for HPV, STIs and HIV. At the same time, it is very difficult to conduct methodologically-sound research for this group due to the difficulties encountered in sampling methods and to avoid exposing them to stigma and legal actions. It is therefore recommended that innovative methods to conduct epidemiological research for FSW are explored, tested and validated.

If a causal relationship between treatment of BV and prevention of HPV infection can be assumed, the population attributable fraction of BV due to synergistic interactions with HIV and HPV should be estimated. Although it has been shown that HAART use may reduce the prevalence of various HPV genotypes, it is still unclear whether this effect is also valid for HPV16, which is, among all the genotypes, the one with the highest potential to induce ICC. Due to the increasing number of HIV-infected women accessing HAART at any CD4 count, it is essential that this hypothesis is confirmed.

4.3.2. Risk factors for abnormal cytology

Prospective studies need to be carried out to establish the

relationship between BV and abnormal cytology within sub Saharan HIV-infected women.

The high prevalence of concomitant STIs in HIV-infected women warrant that their biological interactions and their subsequent capacity to induce progression of cervical dysplasia be further explored. Furthermore, the synergistic effect of multiple pathogens implicated in cervicitis must be elucidated.

While one of our studies in Kenya, (Menon et al. in press) has found a propensity to cluster between phylogenetically similar α9 genotypes in HIV-infected women with CIN 2 + /HSIL, another study exhibited a prominent role for non-alpha 9 and 7 genotypes, HPV 51 and 53 (Menon et al., 2017b). In order to target HIV-infected women harbouring more than one pHR/HR HPV genotype most at risk for progression, a large prospective study should be undertaken to investigate clustering between phylogenetically similar or dissimilar phylogenetic groups in HIV-infected women with CIN 2 + /HSIL so that a less crude triage than one based merely on the presence of more pHR/HR HPV genotypes can be designed.

The screening of the pHR/HR-HPV genotypes 26, 53, 67, 70, 73 and 82 are currently not included in any HPV DNA screening protocols in sub-Saharan Africa. The emergence of these serotypes will need to be monitored as well as their synergistic/antagonistic interactions with other HR-HPV genotypes. At the population level, affordable point of care nucleic acid amplification methods to detect pHR HPV genotypes are required throughout Kenya to explore how these genotypes will behave in post-vaccination era. A personal level approach for secondary prevention may be used if pHR HPV gentoypes as stand alone genotypes are a risk factors for ICC.

4.3.3. Programmatic research gaps

Once there is a wider body of scientific evidence, there are a number of programmatic research gaps which should be addressed.

In Kenya, a cluster randomised non-inferiority trial should be undertaken in rural HIV management clinics to explore whether task shifting to nurses of symptomatic management of BV and cervicitis in HIV-HPV co-infected women is at least as effective as when carried out by physicians in secondary health care facilities. Moreover, a cost-benefit analysis should be undertaken to estimate whether bacterial ecology monitoring by nurses in the front line may be a valuable component of a primary cervical cancer prevention program.

Additionally, the population attribution fraction of STI due to synergistic interactions with BV, as well as their increased combined cervical dysplasia genesis capacities, should be estimated. A cost-benefit analysis should be undertaken to assess whether there may be a need to scale up STI prevention and management within the FSW population, in addition to BV prevention within a cervical cancer prevention framework.

As HIV self-testing has been found to be an acceptable method among the general population and FSWs (Ochako et al., 2014), several countries are beginning to introduce HIV self-testing as a promising innovation to achieve faster scale up, prompting the WHO to develop enabling guidelines (World Health Organization, 2016). A recent study found that tampon-based self-collection for hrHPV mRNA, based on molecular diagnostics aimed at detecting hrHPV viral integration, via the production of oncogenic E6 and E7 messenger-RNA, in South Africa could function as a viable method for cervical cancer screening among HIV-infected women in low-resource settings (Adamson et al., 2015). Provided the linkage between HIV and cervical cancer care in Kenya is established, the acceptability and success of HIV self-testing may set the stage for a concurrent roll out of HPV self-testing kits in this hard to reach population, if it can be shown that there is an overall positive public health impact.

5. Concluding remarks

The new WHO guideline to rescreen HIV infected women for HPV within three years if tested negative by VIA or by cytological screening may be more effective if BV and its related cervicitis management becomes an integral component of primary and secondary prevention.

With earlier HAART initiation requiring regular immunological and virological follow up, there are opportunities for a more regular cervical screening provided that front line nurses are better equipped to deal with challenges. The quadruple synergistic interaction between HIV, HPV and BV and its related cervicitis may need to be reflected within a larger prevention framework at the community level. The potential synergistic interactions between BV, HIV, and HPV beg for an integrative cervical cancer prevention framework, with algorithms easy to follow.

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Competing interest

The authors declare that they have no competing interest.

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Authors' contribution

SM: Conception of the study, writing and editing the paper, validation of the final version.
RR: writing and editing the paper, validation of the final version.
SH: editing the paper, validation of the final version.
HM: interpretation and validation of the final version.
SC: writing and editing the paper, validation of the final version.

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