

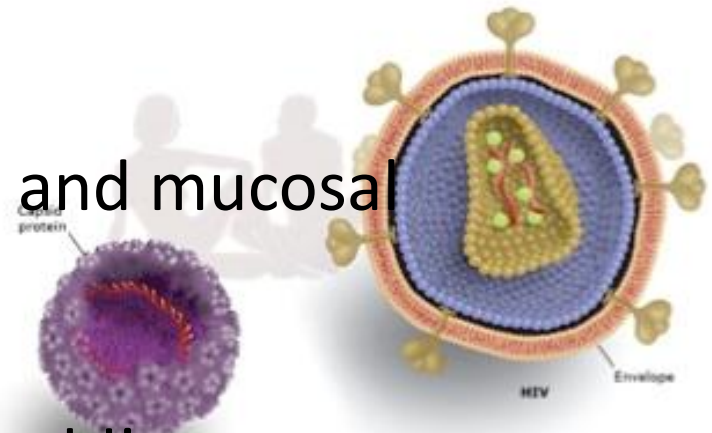
HPV and HIV (A DUAL BURDEN); Does vaginal dysbiosis make it a dreadful trio?

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What is Human papilloma virus (HPV)?

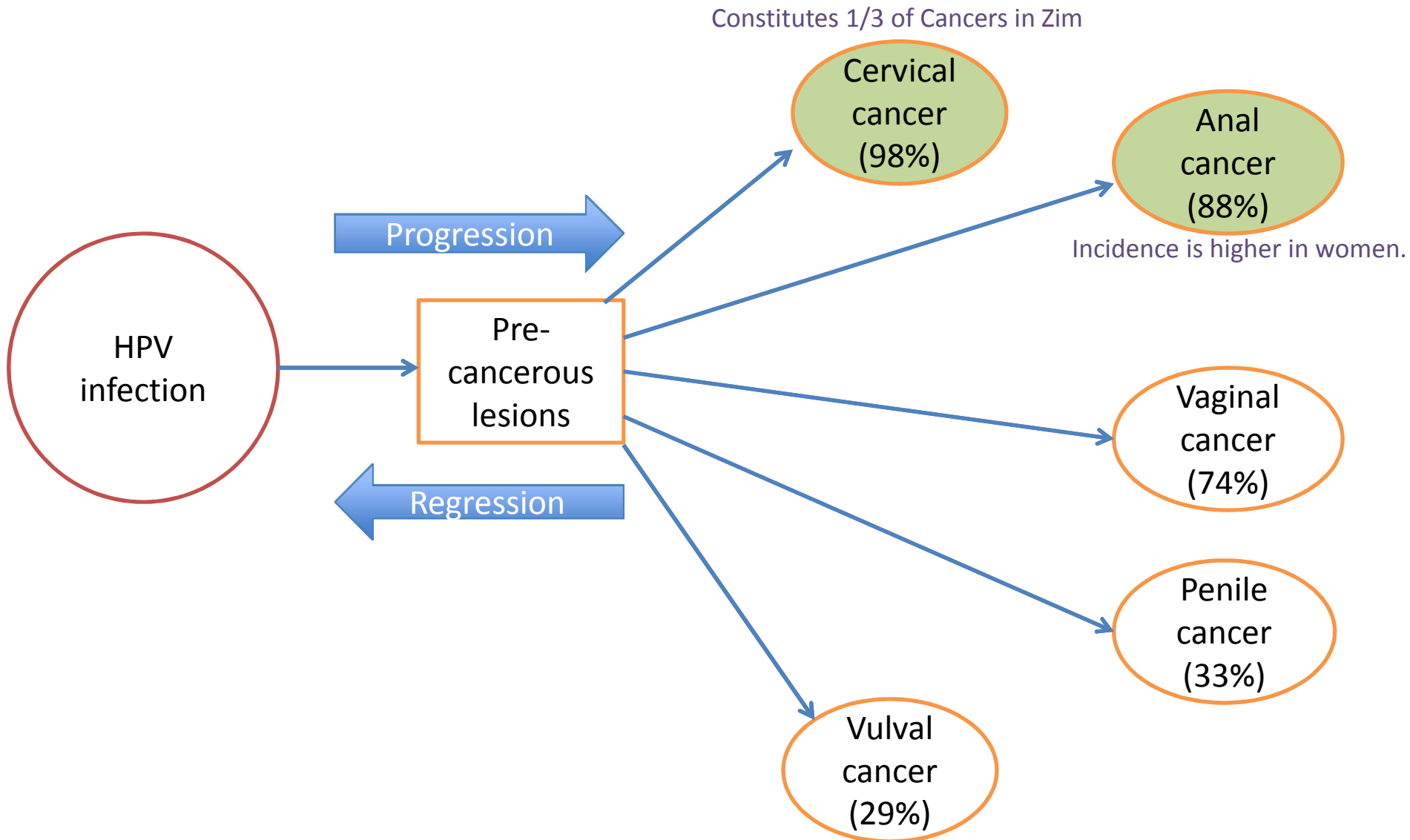
- A DNA virus that causes cutaneous and mucosal proliferations
- Genital infection with HPV is the world's most common STI
- 206 HPV types
- 60 infect mucosal epithelia & 13 have oncogenic potential
 - High-risk (HR)-include 16, 18, 31, 33, 45, 52, 58
 - Low-risk (LR)-6, 11, 40, 42, 70



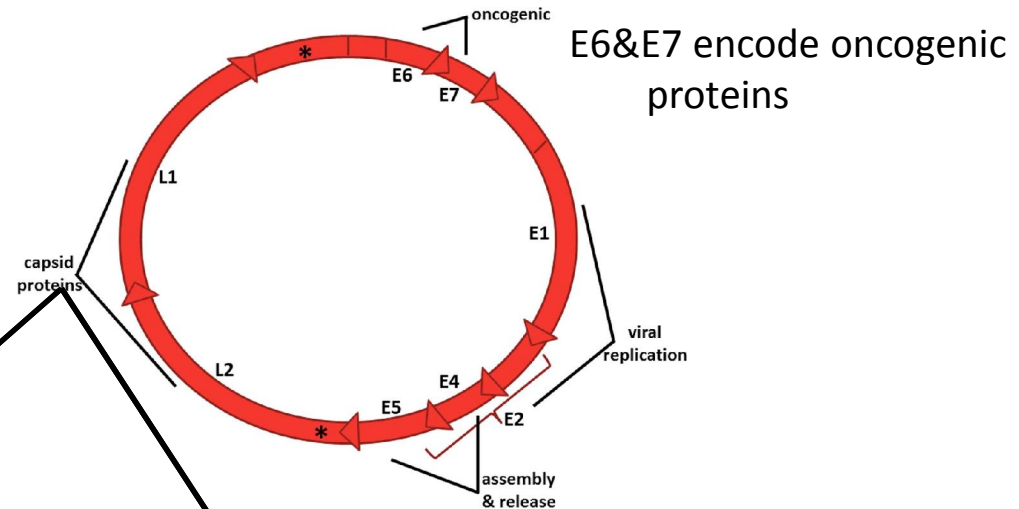
Cause ~70% of cervical cancers

Cause ~90% of anogenital warts

HPV and the associated anogenital diseases



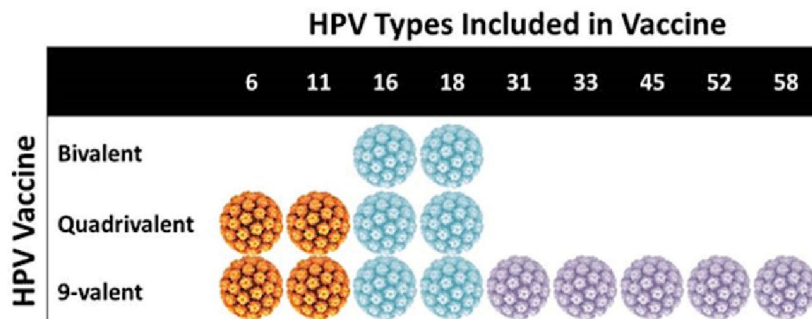
(Nomenclature and vaccine)



Vaccine design

L1 viral proteins

Nomenclature (variability on L1)
2-10% =HPV genotype
<2%=HPV variant



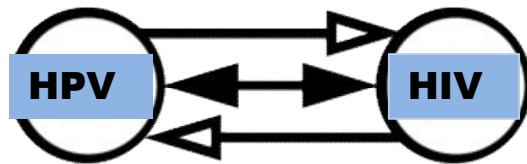


HIV and HPV- A dual burden

Integration of **HIV** and **HPV** is quite complex and bidirectional

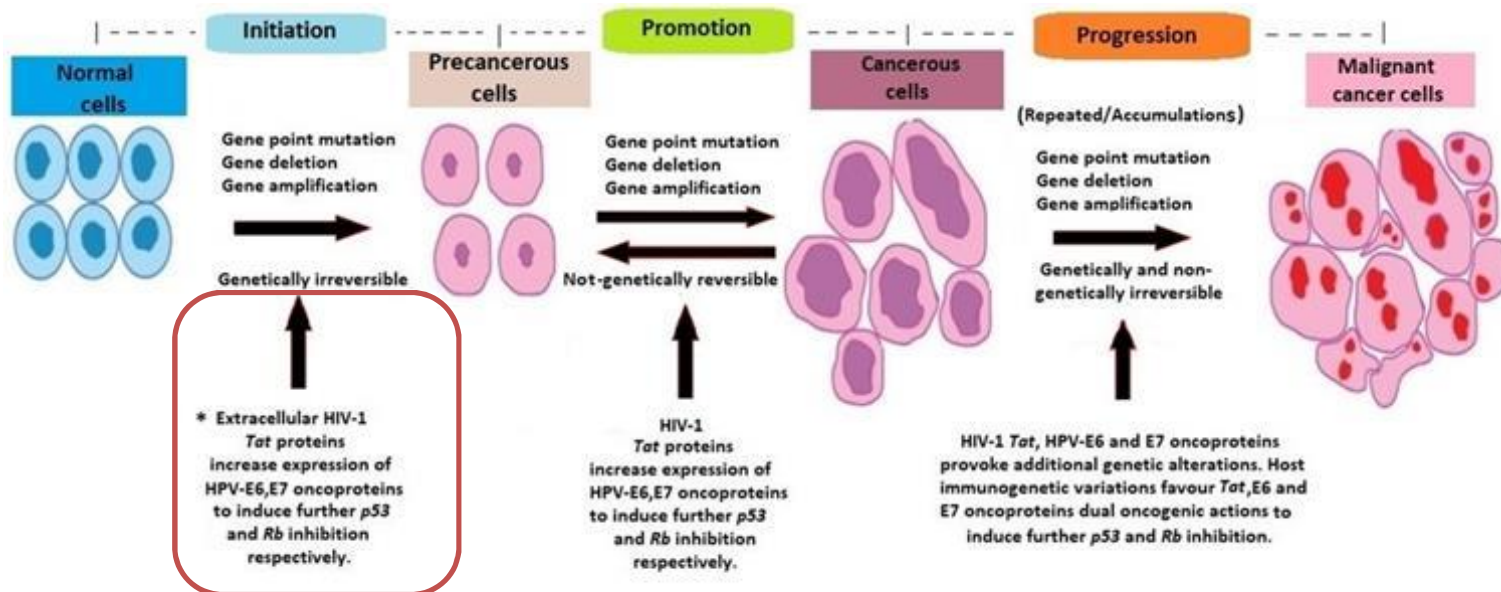


Both classified as carcinogens



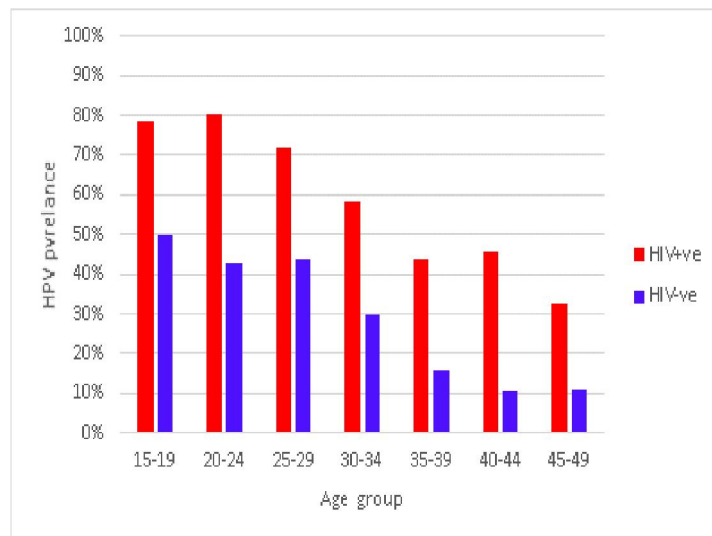
Multiple HR-HPV genotypes infection predisposes the individual to increased susceptibility of HIV infection

HIV infected individuals are more likely to have HPV infection

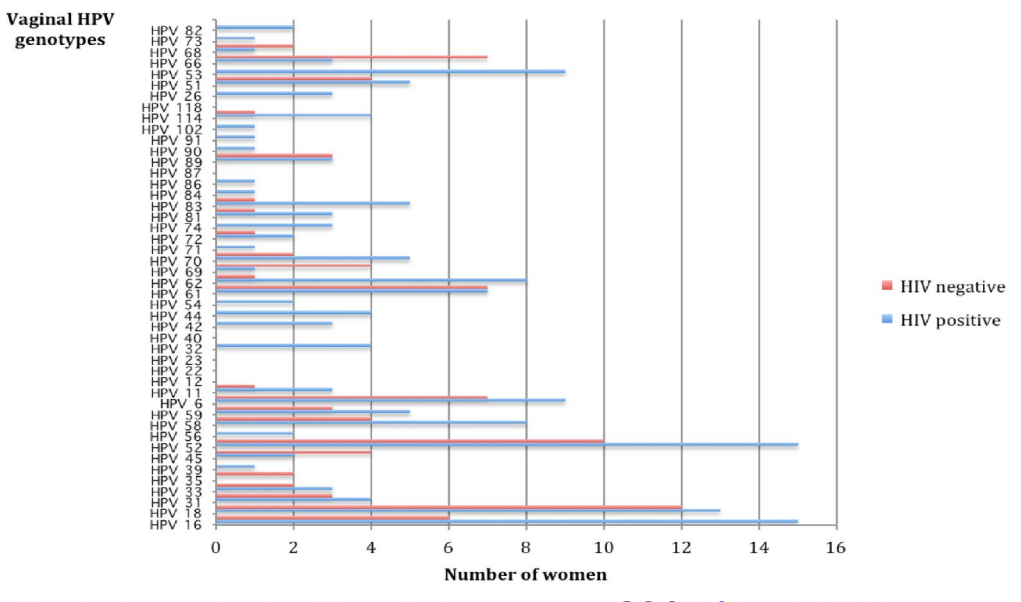


* HPV alone is sufficient but HIV-1 exacerbates and accelerates the effects of HPV on early cervical carcinogenesis.

S1 Fig: Age-specific of Hr-HPV prevalence among reproductive aged women by HIV status, Swaziland



Swaziland- Ginindza et al 2017-HIV infection was associated with hr-HPV infection (Adjusted OR = 4.9, 95%CI: 3.043–7.8, p<0.001)



Zimbabwe: Dube-Mandishora et al 2017-(Anal HPV OR=4.8; CI 2.4-9.8, P<0.001) and (Vaginal HPV OR = 2.9; CI 1.3-6.4, P = 0.005)

SA: Mbulawa et al 2012-“HIV infection increases the risk of new HPV detection and decreases the rate of HPV clearance in both women and men”

Zimbabwe: Averbach et al 2010-“The odds of acquiring HIV were 2.4 times higher in women with prior cervical HPV”

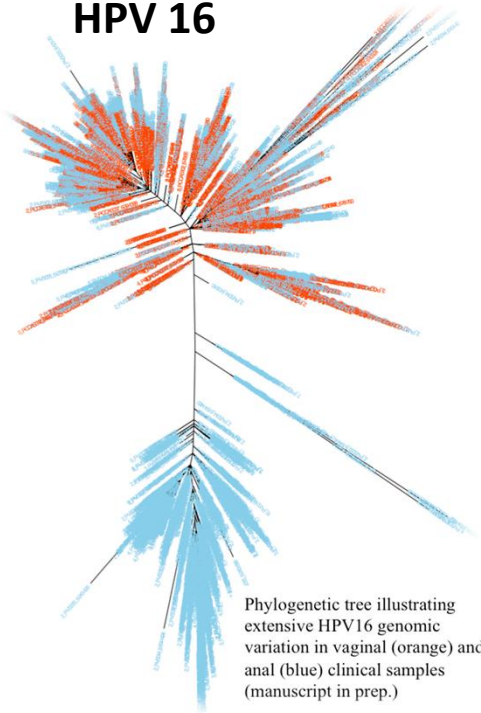
LMIC & US review-Joel Palefsky 2017-“HPV-related cancers are likely to remain an important problem in HIV-infected men and women for the foreseeable future, even among those on effective ART”.



Intra-host sequence variability in human papillomavirus

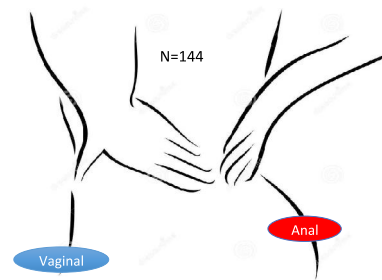
Racheal S. Dube Mandishora^a, Kristina S. Gjøtterud^b, Sonja Lagström^{b,c}, Babill Stray-Pedersen^d, Kerina Duri^c, Nyasha Chin'ombe^a, Mari Nygård^b, Irene Kraus Christiansen^c, Ole Herman Ambur^{c,f}, Mike Z. Chirenje^g, Trine B. Rounge^{b,*}

HPV 16



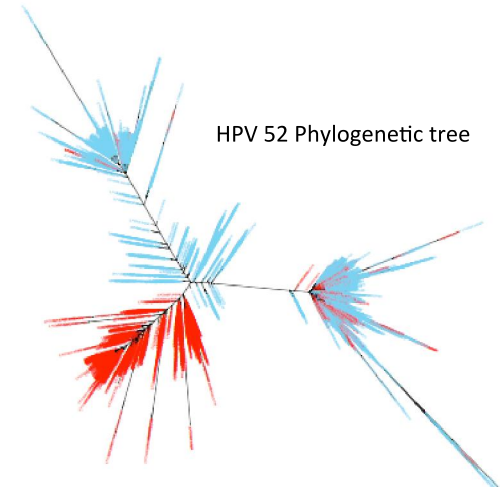
HPV 52 intra individual hyper-variability

*23% prevalence



Illumina sequencing of
HPV L1 region.

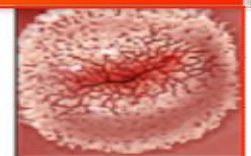
HPV 52 Phylogenetic tree



HPV genomic events

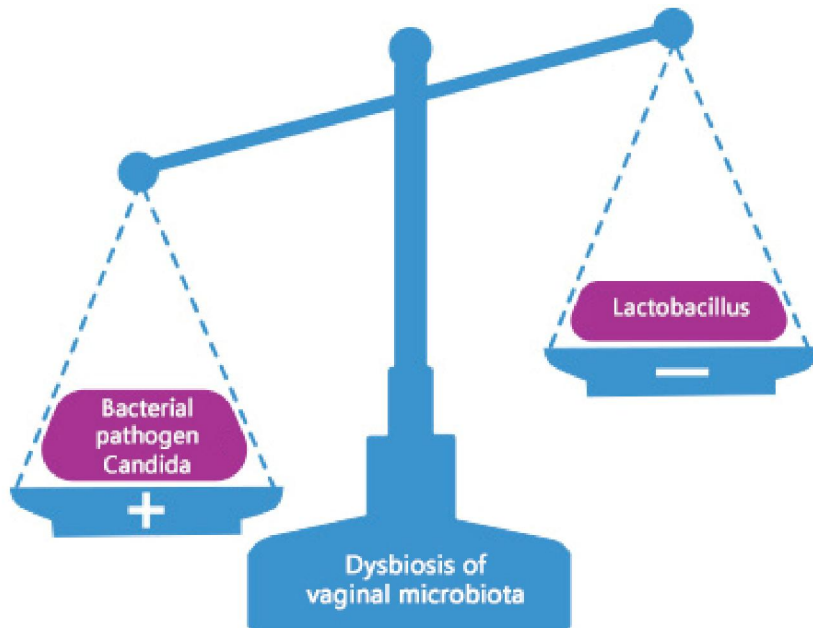


Normal
tissue



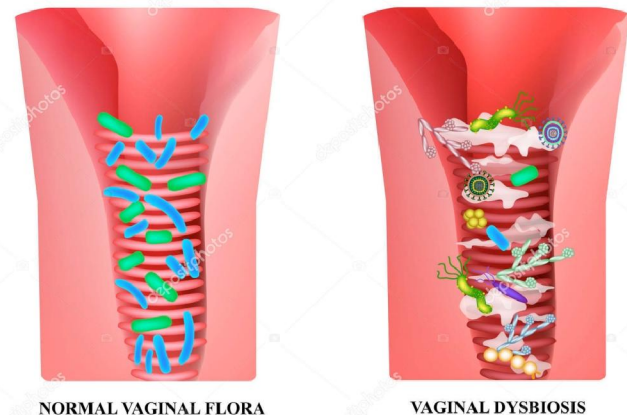
Low- and high grade
cervical lesions and cancer

Vaginal microbiome



- Both “good” and “bad” bacteria live in the vagina, and if a delicate balance between them is disturbed, then **Vaginal dysbiosis** occurs, also called bacterial vaginosis.

VAGINAL DYSBIOSIS



*Just as an Example: Zim CHIC:
impact of contraceptive initiation
on vaginal microbiota-S.Hiller,
Z.M.Chirenje et al 2017*

Vaginal microbiome and HIV

**Altered vaginal
Microbial
composition**

=



**Markers of
inflammation
and HIV
transmission risk.**

HPV, HIV and vaginal dysbiosis

- A dreadful trio?

- Is it a research priority?

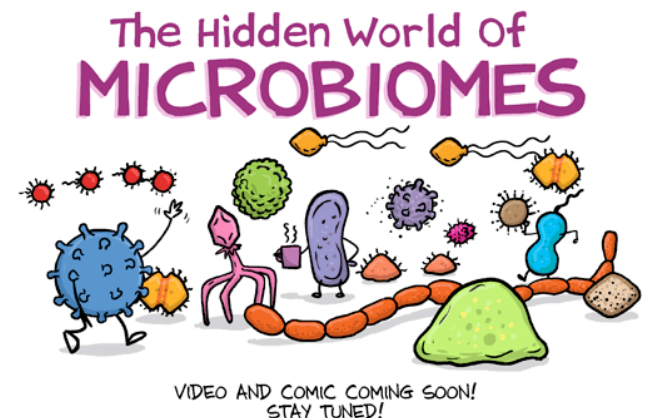
- Red Flags?

- increased diversity of vaginal microbiota and **reduced abundance of *Lactobacillus* spp.** is involved in HPV acquisition and persistence and the development of cervical precancer and cancer. Mitra et al 2016

- vaginal **microbiome may affect pre-exposure prophylaxis (PrEP).** Klatt et al CROI 2018

- **Difference in diversity** of vaginal microbiome taxa in blacks vs white women . Gosman et al 2017

YES



Conclusion and Way forward

- Does **vaginal dysbiosis** affect **HPV acquisition, persistence, and progression** to related cervical premalignancy?
- What are the potential **mechanisms** for the involvement of **vaginal microbiome** in the **evolution of CIN and cervical cancer**, in **HIV** infected women?
- Take advantage of **Next-generation sequencing** (NGS) techniques based upon the analysis of bacterial 16S rRNA genes; **in-depth study of vaginal microbiota**.
- Use of **DL-Lactic ring** to treat recurrent BV, rebalance the microbiome, and potentially prevent or **help clear HPV**

THANK-YOU FOR LISTENING

Acknowledgements

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