

# Vaginal Microbiome & Susceptibility to HIV

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# Disclosures

Dr. McClelland has worked as a consultant for Lupin Pharmaceuticals and receives research funding, paid to the University of Washington, from Hologic Corporation

# Objectives

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- Understand the science linking the vaginal microbiota to women's risk of acquiring HIV
- Recognize the types of interventions that might be used to mitigate this risk

# Outline

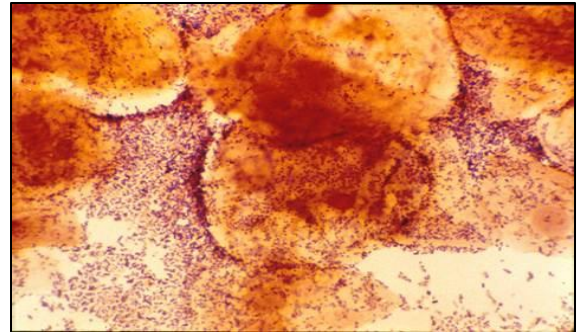
- BV and susceptibility to HIV infection
- Molecular studies of the vaginal microbiota and HIV acquisition
- Mechanisms through which the vaginal microbiota may influence HIV susceptibility
- Possible interventions to reduce HIV risk by manipulating the vaginal microbiota

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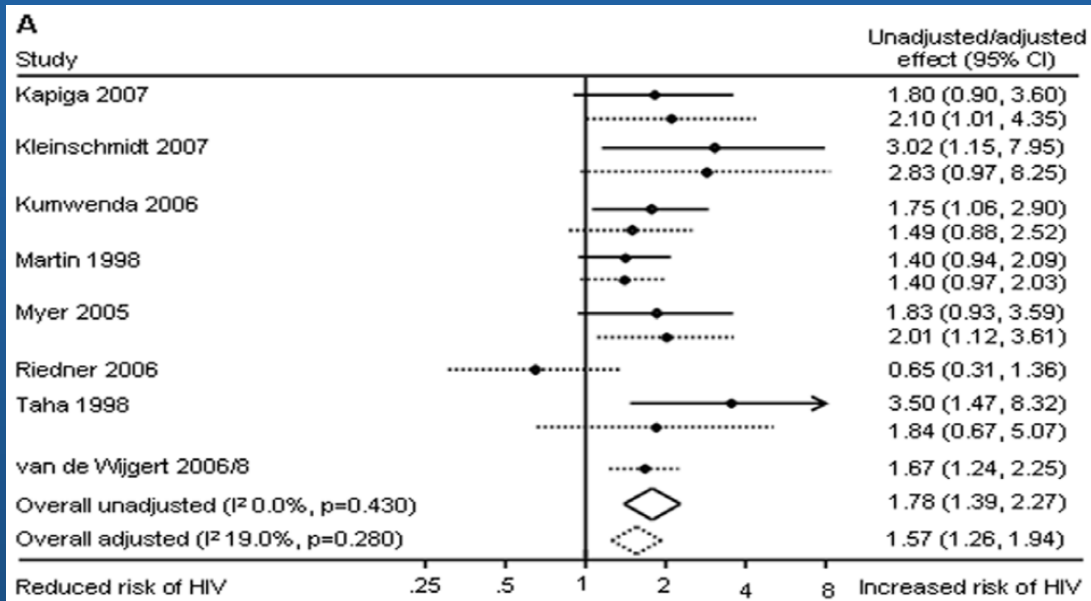
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# Bacterial vaginosis

- Diagnosis by clinical (Amsel's) criteria
- Diagnosis by Gram stain (Hillier & Nugent's) criteria



# Bacterial vaginosis and HIV acquisition

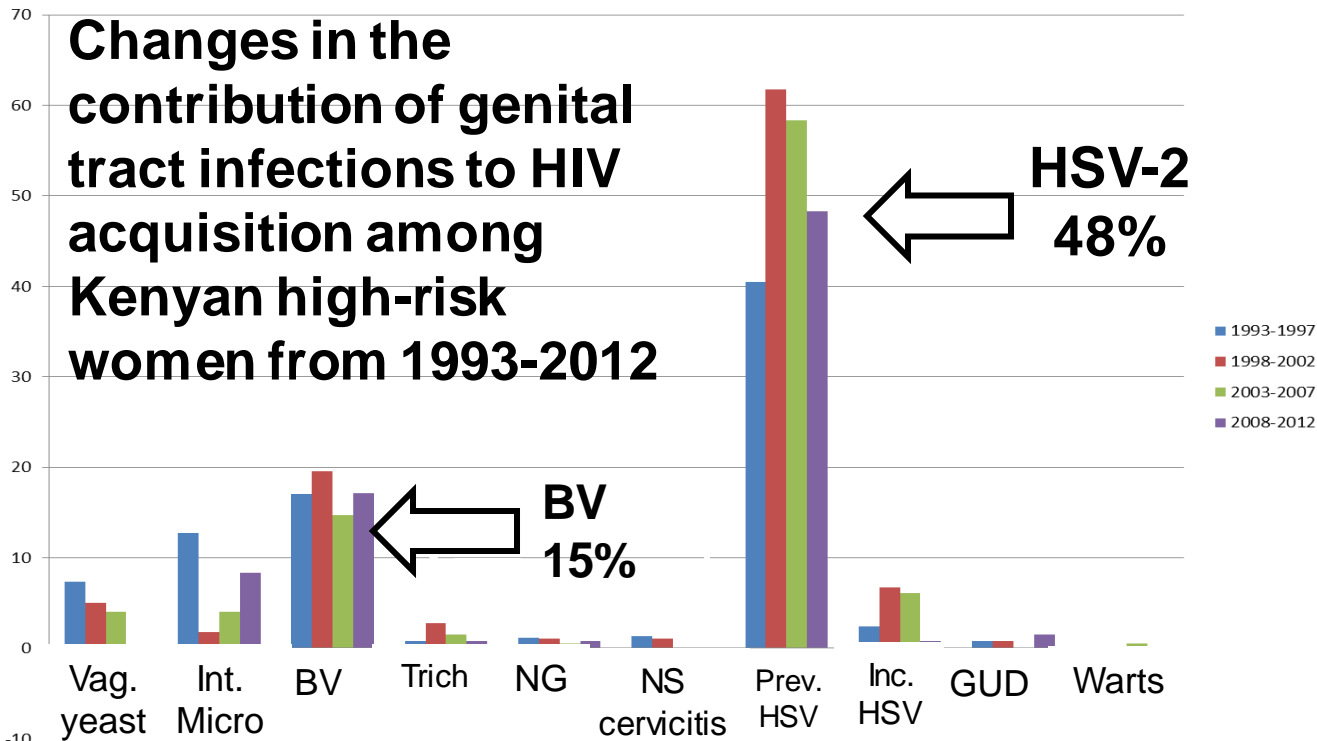


# BV & HIV infection in women: independent participant data meta-analysis

	<b>aHR (95%CI) for HIV acquisition</b>	<b>Joint p value</b>
Gram stain		<0.001
Normal	REF	
Intermediate	1.41 (1.12–1.79)	
BV	1.53 (1.24–1.89)	



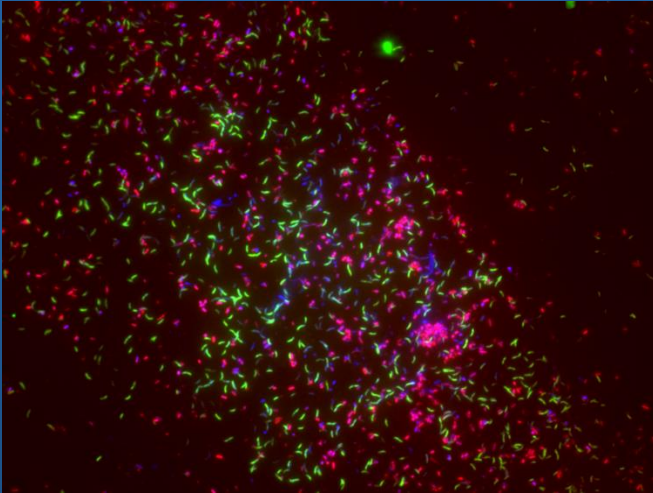
# Changes in the contribution of genital tract infections to HIV acquisition among Kenyan high-risk women from 1993-2012



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# Molecular characterization of vaginal microbiota



- Lactobacillus-dominated microbiota is associated with healthy vaginal microenvironment
- *L. crispatus* is more beneficial than *L. iners*
- BV is a polymicrobial dysbiosis, and its extent correlates with Nugent's score and vaginal pH

*Fredricks N Engl J Med 2005; 353:1899-911.*

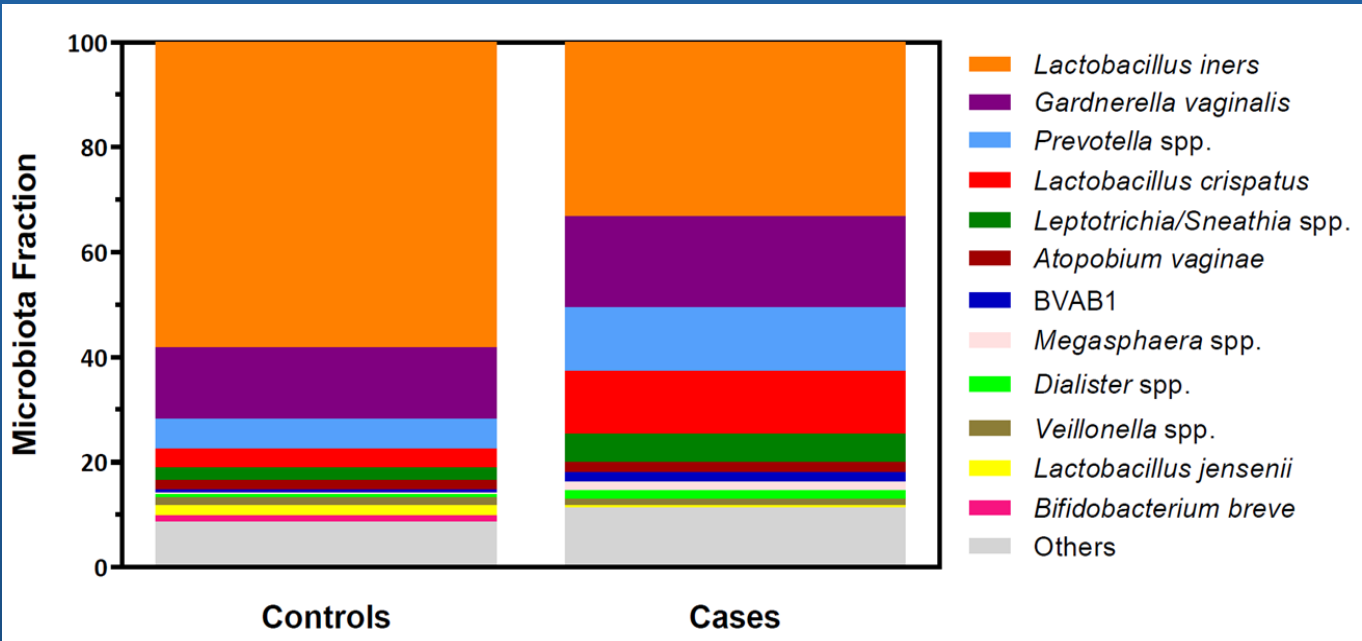
*van de Wijkert PLoS ONE 2014; 9:e105998*

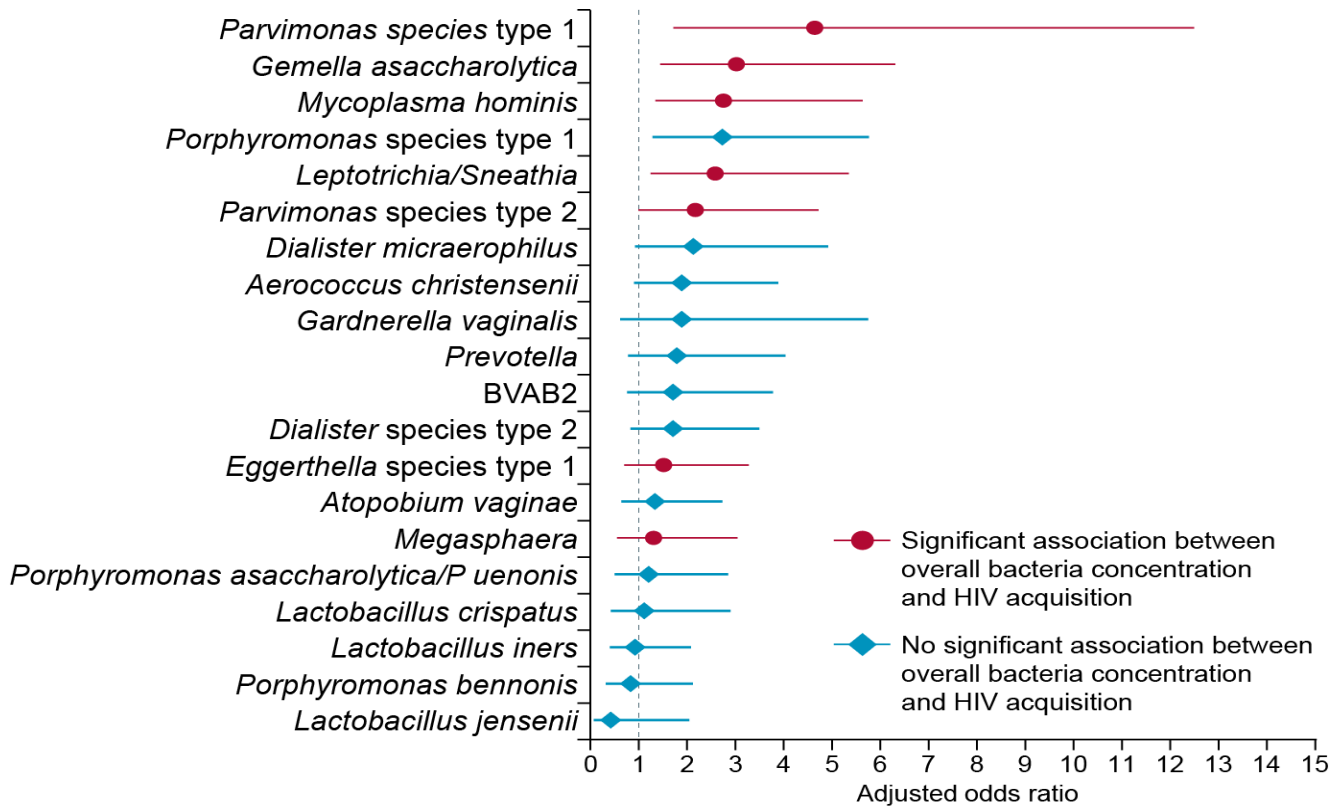
**Do high-risk vaginal bacterial communities  
or taxa increase women's susceptibility to  
HIV infection?**

# Vaginal microbiome cluster associated with inflammation and HIV risk

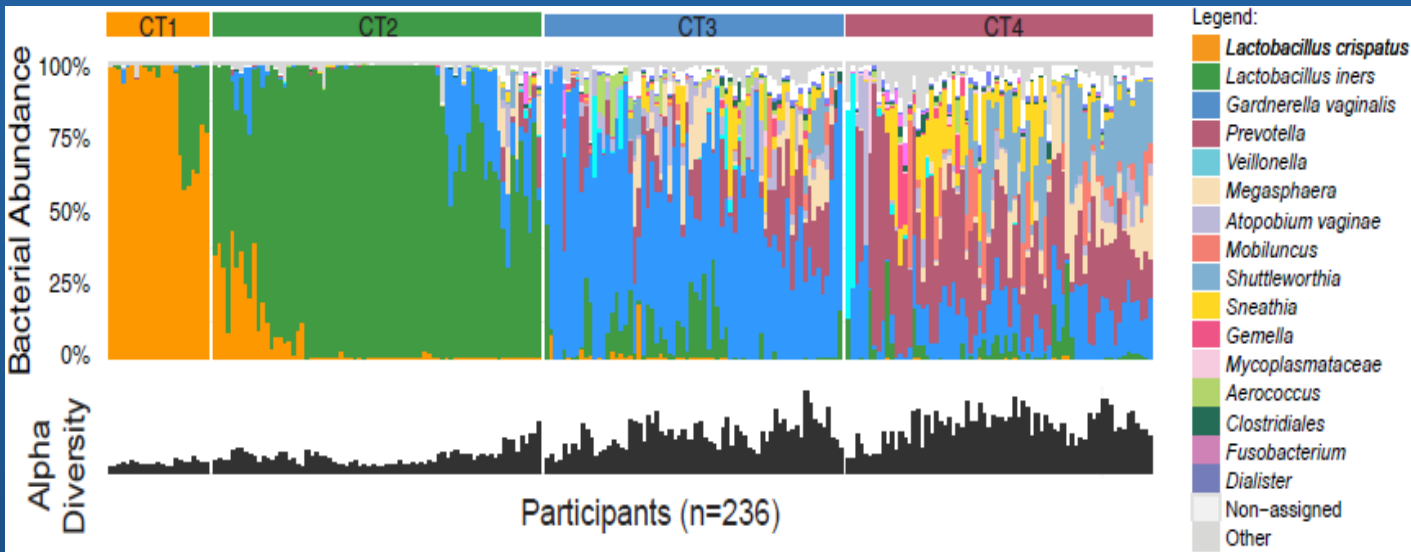
- Vaginal microbiome with high relative abundance of *P. bivia* was associated with inflammatory cytokine profile and HIV risk
- aOR for HIV acquisition 12.7, 95%CI 2.1-77.8,  $p=0.006$

# Bacterial relative abundance in cases & controls



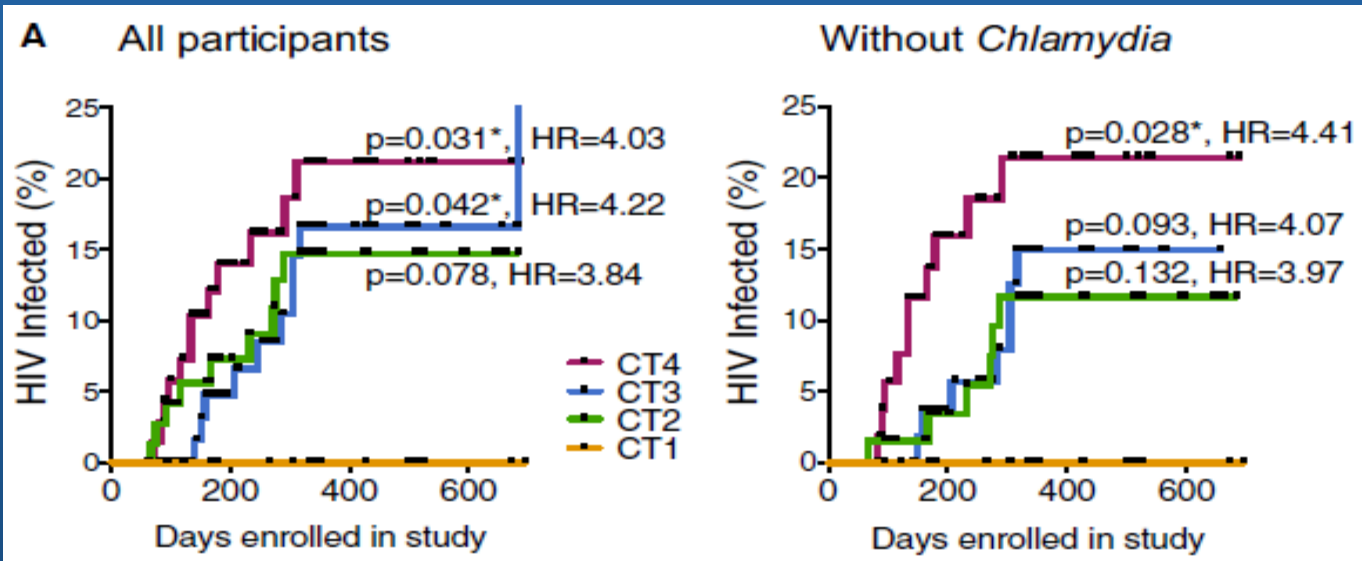


# *Lactobacillus*-deficient vaginal bacterial communities & HIV Risk





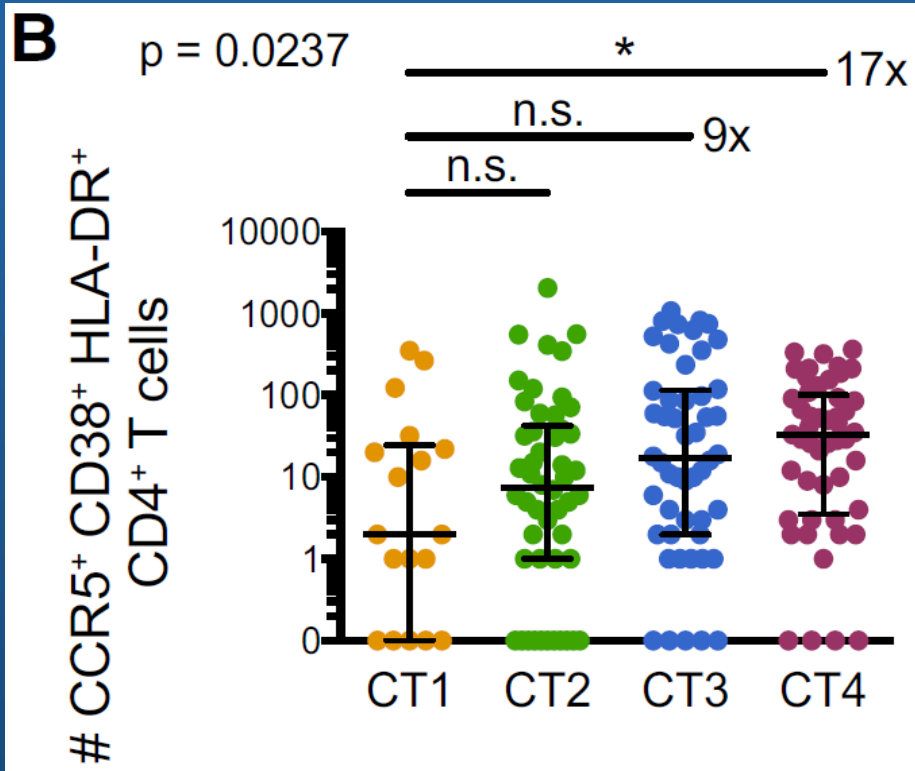
# *Lactobacillus*-deficient vaginal bacterial communities & HIV Risk



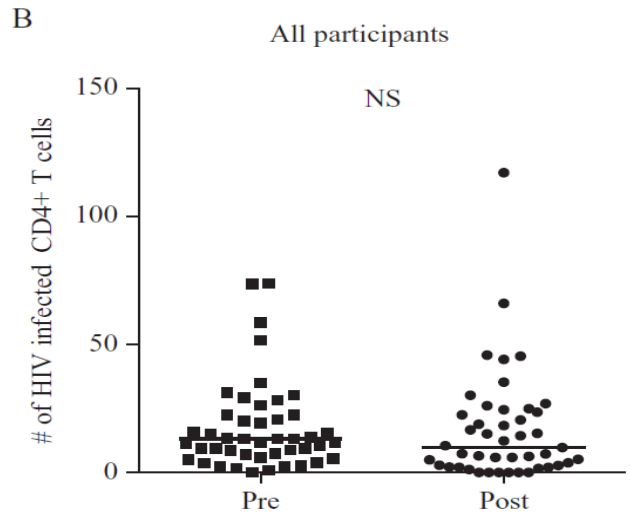
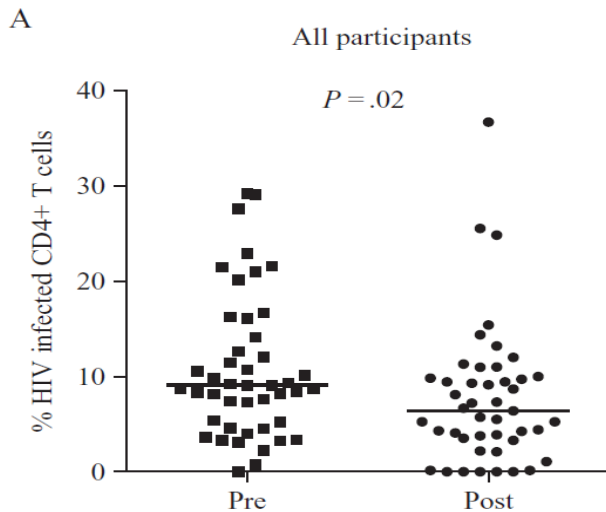
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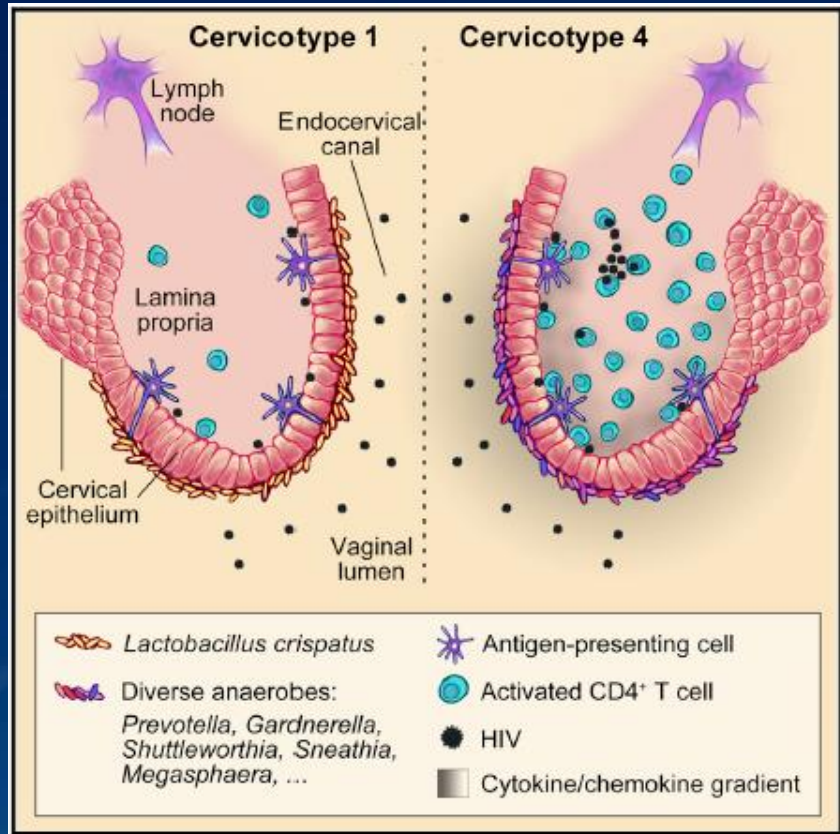
# *Lactobacillus*-deficient vaginal bacterial communities & CD4<sup>+</sup> T cells



# Treatment of BV and HIV infection of endocervical CD4<sup>+</sup> T-cells



*Lactobacillus*-deficient vaginal bacterial communities, mucosal CD4<sup>+</sup> T-cells, and HIV susceptibility



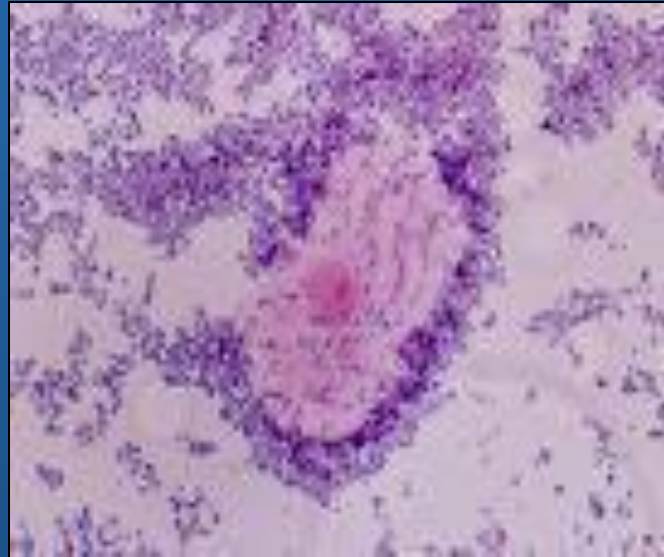
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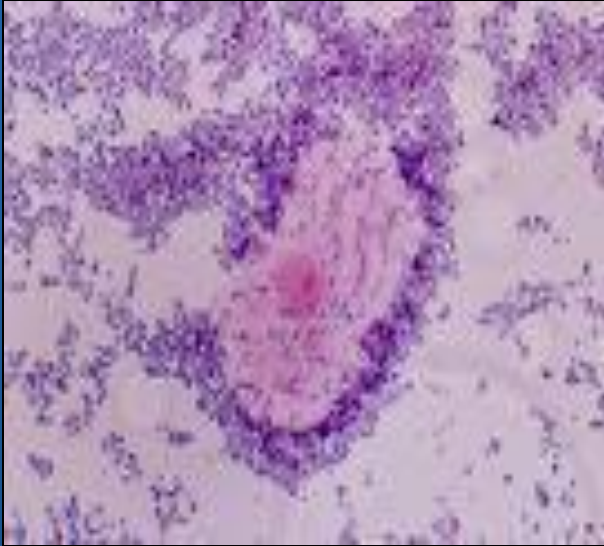
# Treatment and Prevention of BV

## Current CDC Recommendations

- **MTZ 500mg po bid X7d**
- **MTZ 0.75% gel daily X5d**
- **Clinda 2% cream daily X7d**
- TDZ 2g orally daily X2d
- TDZ 1g orally daily X5d
- Clinda 300mg orally bid X7d
- Clinda 100mg ovules daily X3d
- Suppression for women with frequent recurrences
  - MTZ 0.75% gel twice weekly for 4-6 months



# Treatment and Prevention of BV



## New approaches to control BV

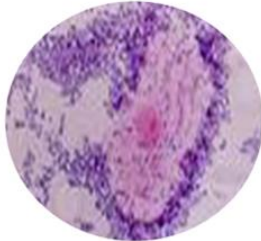
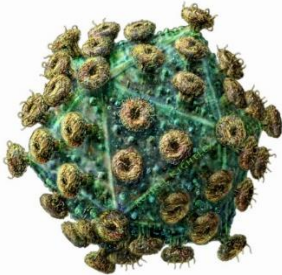
- Alternative drug regimens
- Bio-therapeutic Products
- Biofilm disruptors
- Risk factor modification
  - Intravaginal practices
- Periodic presumptive treatment



# Summary

- Vaginal bacterial communities and presence of specific bacterial taxa may influence HIV risk through recruitment of activated CD4+ T cells and other inflammatory and non-inflammatory mechanisms
- Interventions can reduce BV for extended periods
- Effect of these interventions on vaginal microbial communities and taxa have not been well characterized in molecular studies
- Interventions that eliminate high-risk vaginal bacterial communities or taxa could reduce women's susceptibility to infection with HIV

Thank you!



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