Vaginal microbiome profiles in young women at risk for HIV infection

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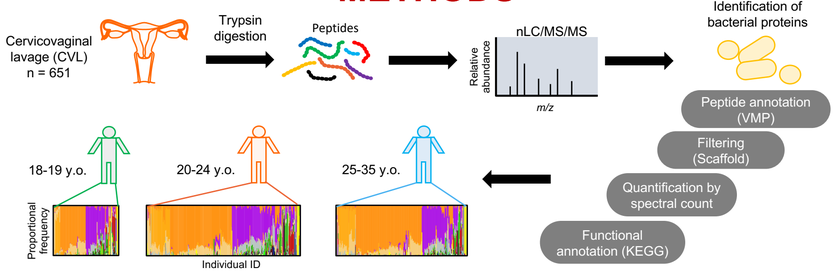
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BACKGROUND

- Adolescent girls and young women (15-24 years old (y.o.)) in sub-Saharan Africa are disproportionally at risk of HIV infection[1]
- Beyond behavioral factors, biological differences between younger and adult women may be at play
- Vaginal microbial dysbiosis and depletion of *Lactobacillus* spp. has been linked with increased HIV susceptibility in women[2, 3]
- Here we examined associations between the vaginal microbiome and age in South African women at high risk of HIV acquisition from the CAPRISA 004 trial.

METHODS

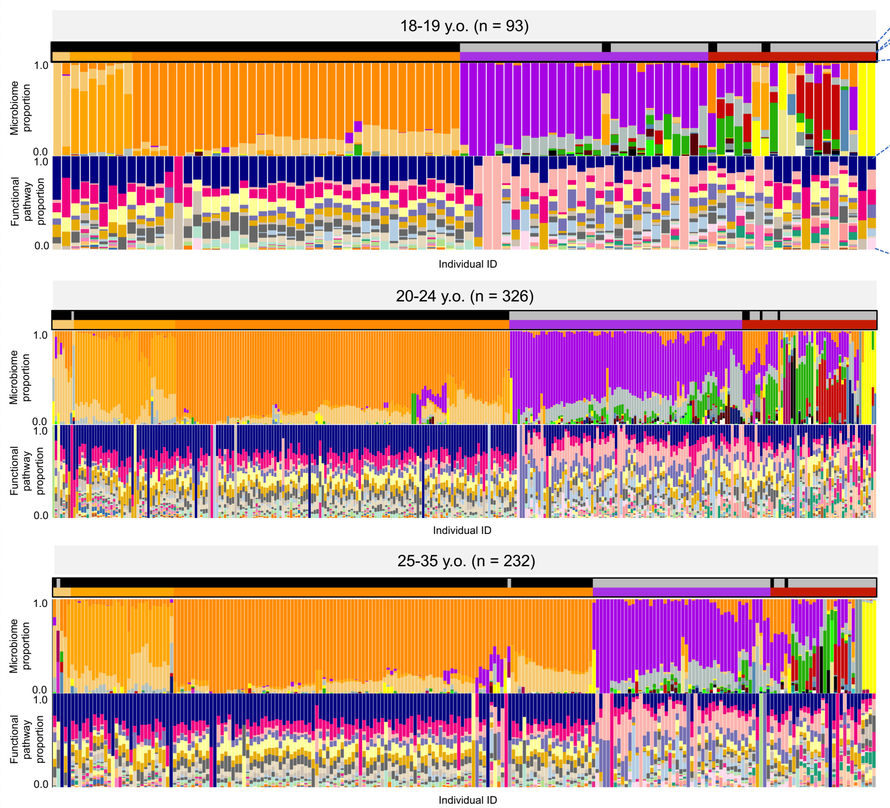


COHORT

Variable	Overall	18-19 y.o.	20-24 y.o.	25-35 y.o.	P value
Baseline Demographics	651	93 (14.3%)	326 (50.1%)	232 (35.6%)	
Age at visit (Mean ± SD; range)	23.7 ± 4.2; 18-35	18.7 ± 0.5; 18-19	21.7 ± 1.3; 20-24	28.4 ± 3.0; 25-35	
HIV seroconverters (n, %)	59 (9.1)	8 (8.6)	35 (10.7)	16 (6.9)	0.293
Years in trial (Mean ± SD; range)	1.6 ± 0.5; 0.2-2.4	1.5 ± 0.4; 0.2-2.3	1.6 ± 0.5; 0.3-2.4	1.6 ± 0.5; 0.3-2.4	**0.0499**
TFV arm (n, %)	325 (49.9)	42 (45.2)	163 (50.0)	120 (51.7)	0.564
Rural (n, %)	482 (74.0)	80 (86.0)	246 (75.5)	156 (67.2)	**0.00161**
Given Birth (n, %)	510 (78.3)	61 (65.6)	241 (73.9)	208 (89.7)	**2.83E-7**
Age at sexual debut (Mean ± SD; range)	17.4 ± 2.0; 12-26	16.3 ± 1.4; 13-19	17.3 ± 1.7; 12-22	18.0 ± 2.4; 12-26	**6.67E-12**
Total lifetime sex partners (Mean ± SD; range)	2.8 ± 8.2; 1-202	1.8 ± 1.2; 1-6	2.3 ± 2.2; 1-21	3.9 ± 13.4; 1-202	**6.94E-10**
Any STI reported in trial (n, %)	129 (19.8)	25 (26.9)	62 (19.0)	42 (18.1)	0.084
HSV-2					
Baseline HSV-2 seroprevalence (n, %)	319 (49.3)	29 (31.2)	129 (39.9)	161 (69.8)	**7.3E-14**
HSV-2 incidence during trial (n, %)	66 (10.1)	16 (17.2)	37 (11.3)	13 (5.6)	0.486
Vaginal insertion ever reported in trial (n, %)	112 (17.2)	9 (9.7)	53 (16.3)	50 (21.6)	**3.05E-2**
Condom Use (n, %)					0.346
Always	187 (28.7)	25 (26.9)	98 (30.1)	64 (27.6)	
Most times	120 (18.4)	15 (16.1)	65 (19.9)	40 (17.2)	
Occasionally	239 (36.7)	33 (35.5)	122 (37.4)	84 (36.2)	
Never	105 (16.1)	20 (21.5)	41 (12.6)	44 (19.0)	
Demographics at visit of sample collection					
Lactobacillus Dominant (n, %)	386 (59.3)	49 (52.7)	185 (56.7)	152 (65.5)	**0.0433**
Contraception use (n, %)					**0.00753**
DMPA	430 (66.1)	70 (75.3)	217 (66.6)	143 (61.6)	
NET-EN	116 (17.8)	16 (17.2)	63 (18.4)	37 (15.9)	
COC	90 (13.8)	6 (6.5)	40 (12.3)	44 (19.0)	
Non-Hormonal Contraceptive	12 (1.8)	0 (0.0)	4 (1.2)	8 (3.4)	
Vaginal discharge (n, %)	72 (11.1)	10 (10.8)	40 (12.3)	22 (9.5)	0.523
Any cervical ectopy (n, %)	47 (7.2)	3 (3.2)	29 (8.9)	15 (6.5)	0.127
Vaginal insertion at visit (n, %)	33 (5.1)	2 (2.2)	20 (6.1)	11 (4.7)	0.291
Antibiotic use in past 30 days (n, %)	52 (8.0)	8 (8.6)	23 (7.1)	21 (9.05)	0.673
Sex acts in past 30 days (Mean ± SD; range)	5.6 ± 5.1; 0-42	6.1 ± 5.6; 0-28	5.1 ± 4.5; 0-22	6.0 ± 5.7; 0-42	0.405
Median adherence during trial >50% (n, %)	390 (59.9)	45 (48.4)	194 (59.5)	151 (65.1)	**0.0207**

RESULTS

Differences observed in microbial composition across age groups.



**Megasphaera* (a bacterial vaginosis (BV) associated bacteria) was significantly more prevalent in the 18-19 y.o. group compared to the 25-35 y.o. group (adjusted $p = 0.026$, log2 fold difference (L2FD) = 1.74).

***Bacterial pathway of **butanoate metabolism** (linked to inflammatory metabolites) was also significantly more prevalent in the 18-19 y.o. group compared to the 25-35 y.o. group (adjusted $p = 0.019$, L2FD = 1.45)

Age is a primary risk factor for non-*Lactobacillus* dominant and polymicrobial microbiome

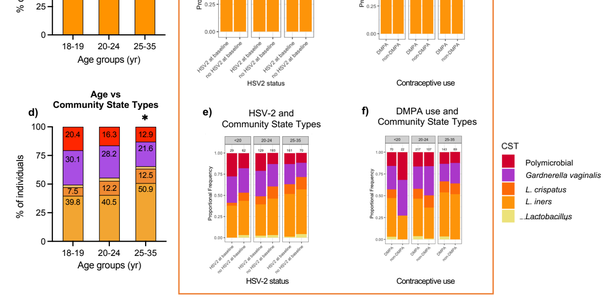


Figure 1. Vaginal microbiome profiles (top) and functional pathway profiles (bottom) are shown for each age group with annotation for microbiome types. Four distinct vaginal microbiome types were identified including those with lower diversity *L. crispatus* (11.7%) or *L. iners* dominant (44.1%) microbiome, and those with anaerobic species containing *G. vaginalis* (26.1%) or a polymicrobial microbiome (15.7%). While all four microbiome types are preserved in each age group, a trend of increasing *L. iners*-dominant and decreasing polymicrobial microbiome can be observed with increasing age.

Figure 2. a) Compared to 25-35 y.o. women, 18-19 y.o. and 20-24 y.o. women were more likely to have a non-*Lactobacillus*-dominant microbiome (OR: 1.67, CI: 1.02-2.75, P=0.026; OR: 1.45, CI: 1.03-2.06, P=0.023, respectively). Within each age group, no significant differences in *Lactobacillus*-dominant (LD) status were found between those with HSV-2 at baseline and those without (b) or between those who used DMPA and those who did not (c). d) 18-19 y.o. women were more likely to have a polymicrobial microbiome group (OR: 2.62, CI: 1.00-6.63, P=0.046). Within each age group, no significant differences in community state types (CSTs) were found between those with HSV-2 at baseline and those without (e) or between those who used DMPA and those who did not (f).

CONCLUSION

- Compared to 25-35 y.o. women, 18-19 y.o. young adults were more likely to have
  - Non-*Lactobacillus* dominant microbiome
  - Diverse, polymicrobial microbiome
  - Increased abundance of BV-associated bacteria, *Megasphaera*
  - Expression of bacterial metabolic pathway linked to inflammatory metabolites
- Differences in the vaginal microbiome may be a contributing factor to increased HIV-1 susceptibility in young women
- Strategies to promote vaginal *Lactobacillus* and reduce BV-associated bacteria in young women may help reduce the burden of new HIV infections in young women.

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