

RECOVERY OF VAGINAL MICROBIOTA AFTER STANDARD TREATMENT FOR BACTERIAL VAGINOSIS INFECTION: AN OBSERVATIONAL STUDY

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INTRODUCTION:

Dysbiosis of vaginal microbiota and Bacterial Vaginosis (BV) has been linked to negative reproductive health, e.g. decreased fertility and adverse pregnancy outcomes. Although BV can be treated with antibiotics, the recurrence rates remain significant. Understanding changes in vaginal microbiota composition in BV during and after antibiotic treatment would aid in making more accurate decisions on the treatment regimen and avoid unnecessary use of antibiotics.

OBJECTIVES:

To investigate vaginal microbiota and Nugent score changes after 5-day metronidazole treatment of BV and compare the results with healthy women.

MATERIALS & METHODS:

This clinical trial was conducted in 30 women with symptomatic BV (Group 2) and in 30 asymptomatic healthy women (Group 1) in Scotland, UK. Vaginal microbiota was assessed via Nugent score and by sequencing the V4 region of 16S ribosomal (rRNA) gene in swabs collected on baseline Day 1, on Day 8 and 15 after cessation of metronidazole. Sequencing data were analyzed using QIIME. Taxonomy was assigned to aligned amplicon sequence variants using 'q2-feature-classifier' trained on the Greengenes v. 13.8 database using 515F/806R 99% OTUs. Vaginal microbiota composition was grouped into community state types (CSTs) by hierarchical clustering.

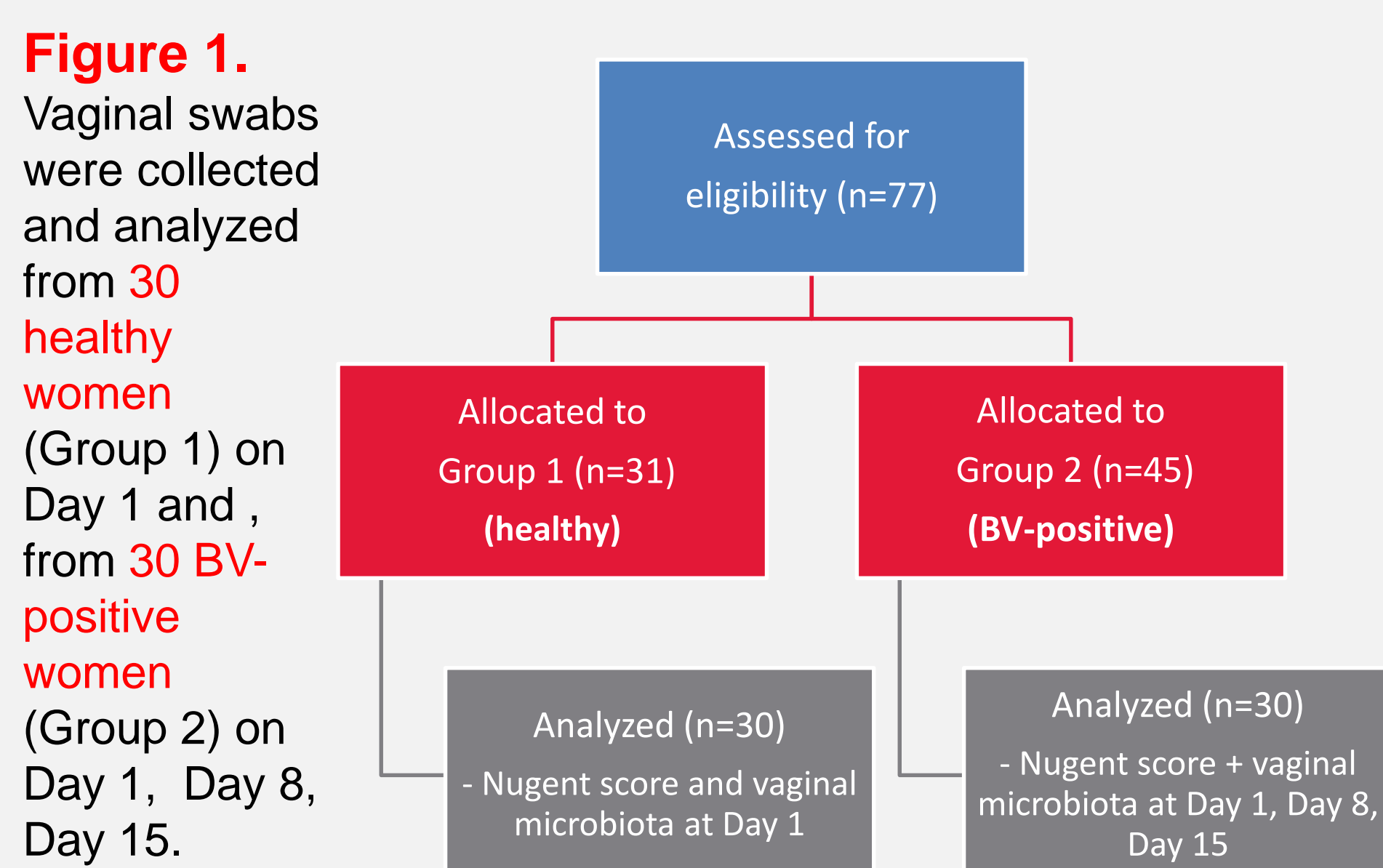


Table 1. On Day 1, prior metronidazole, Nugent score differed significantly between groups. In Group 2, 50% of women had Nugent score <7, regardless of being symptomatic for BV. There were no differences between study groups on Day 8, or Day 15 indicating recovery time 3 days after metronidazole cessation.

Nugent score	Group 1		Group 2	
	Day 1	Day 1	Day 8	Day 15
0-3	21	11	25	20
4-6	6	4	2	4
>7	3	15	3	6

Figure 2. On Day 1, most abundant species in Group 1 were *L. iners* (37.5%) and *L. crispatus/acidophilus* (19.2%). In Group 2, most abundant species were *L. iners* (25.8%), *Prevotella timonensis/bivia* (18.0%), and *G. vaginalis* (14.6%). After metronidazole on Days 8 and 15, microbiota was dominated by *L. iners*, and on Day 8 its abundance was significantly higher in Group 2 vs. Group 1 (67.8% vs. 37.5%, $P=0.049$). On Day 15, the relative abundance of microbial taxa was similar between the groups (FDR $P>0.05$) indicating recovery of 10 days after metronidazole cessation.

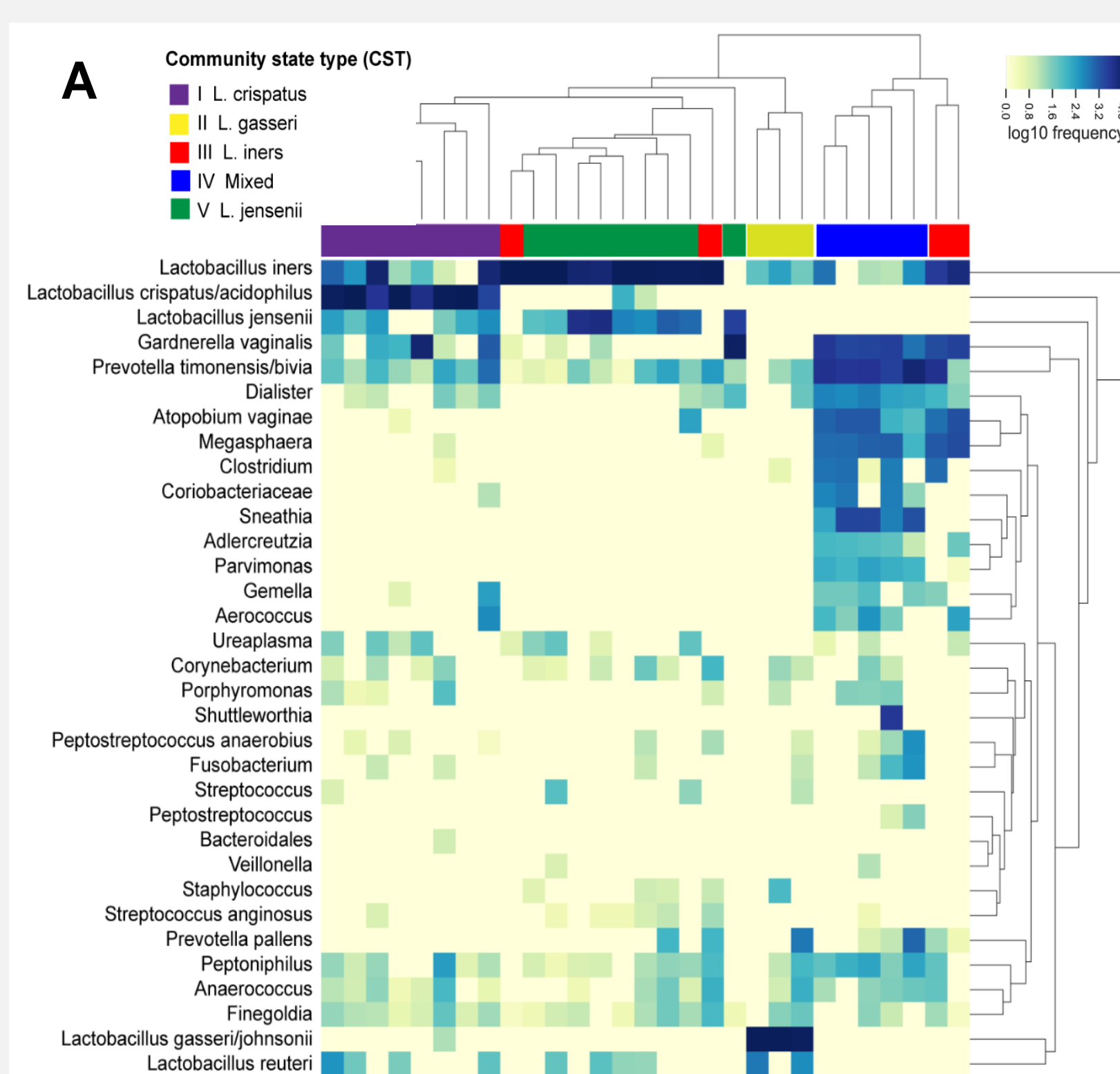
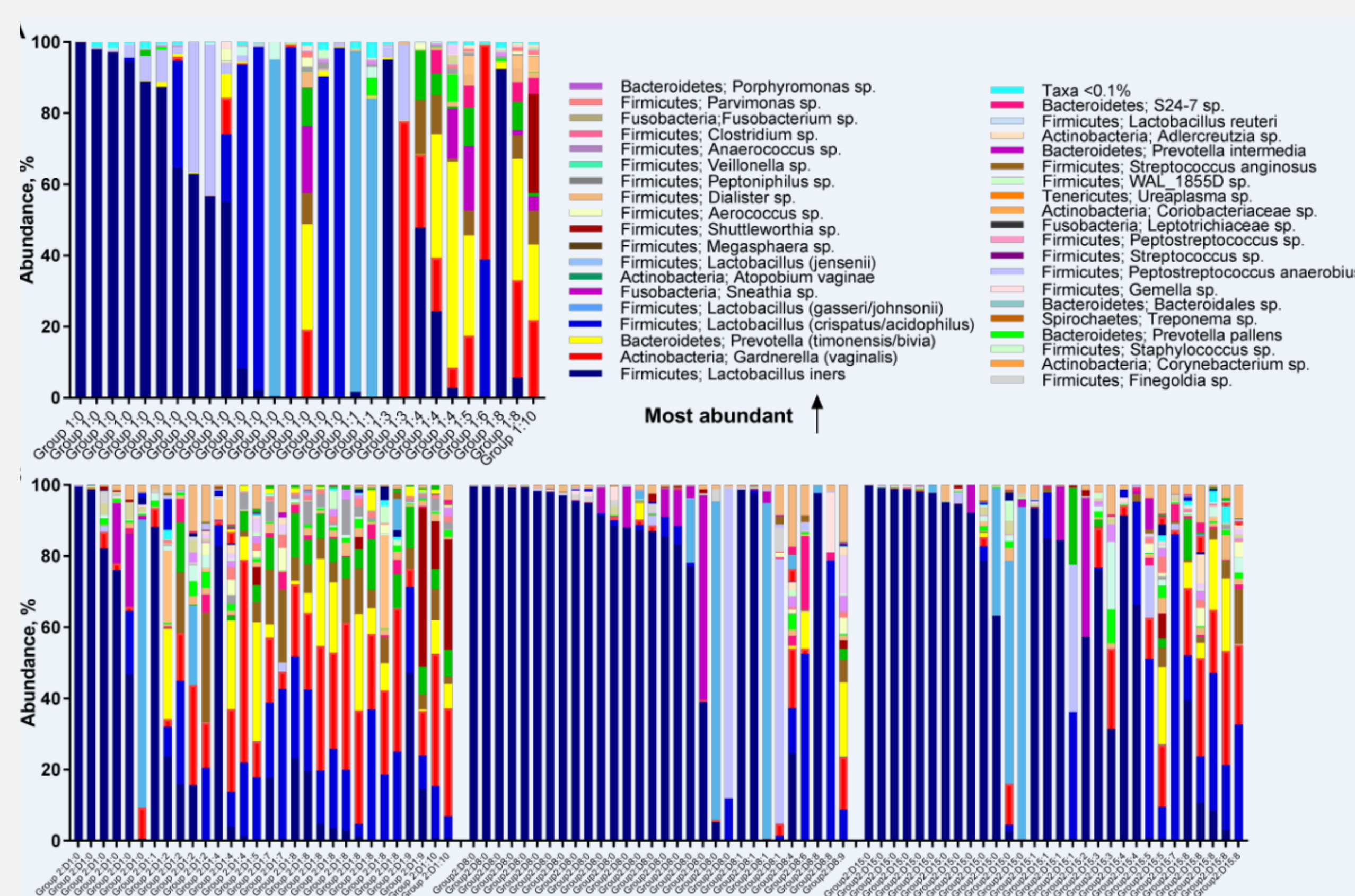
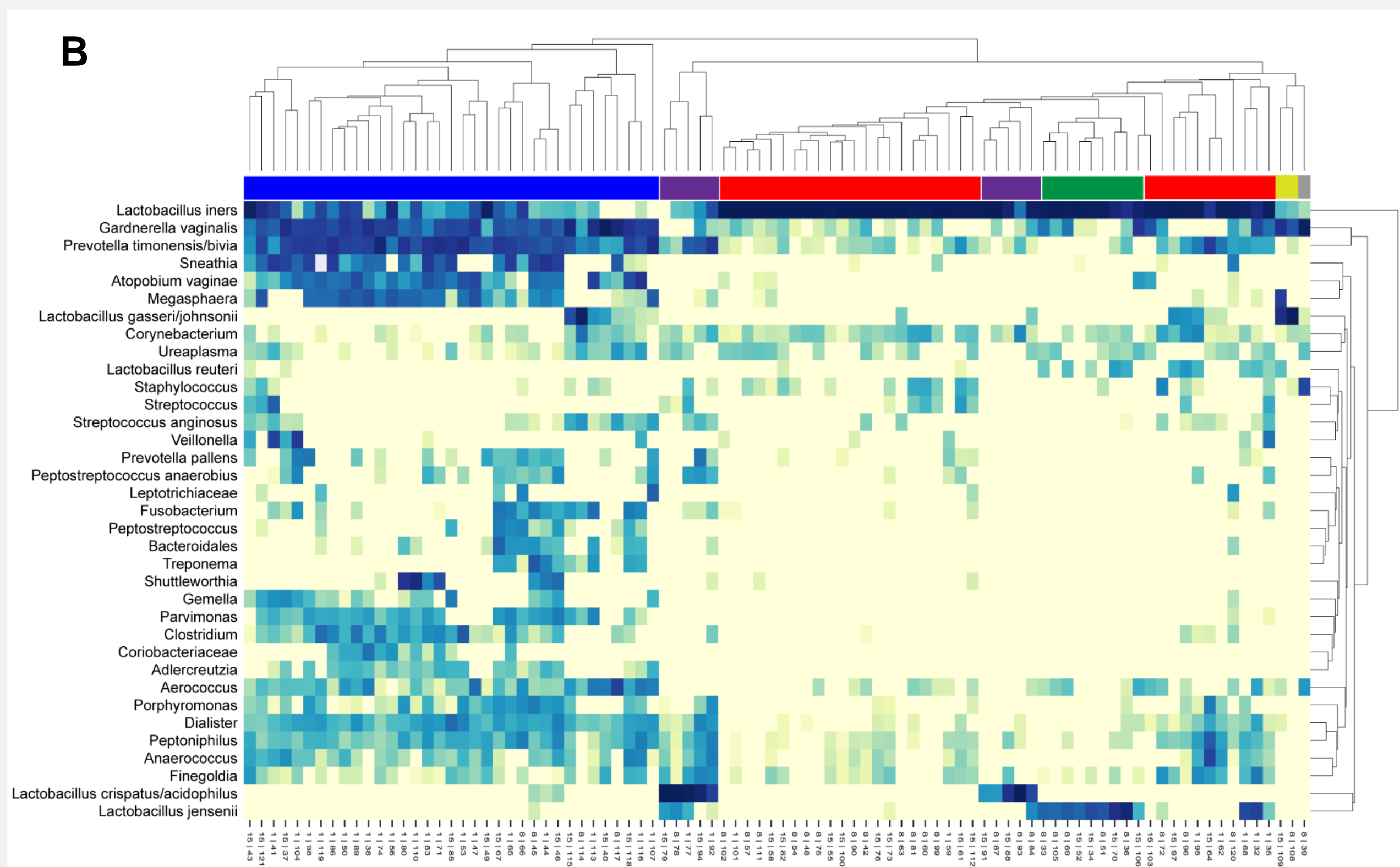


Figure 3. All five CSTs were identified in both groups. **A)** Group 1 was mostly represented with CST I (*L. crispatus*) and CST V (*L. jensenii*). **B)** In contrast, Group 2 at Day 1 were mostly represented with CST IV (mixed) or CST III (*L. iners*). After antibiotic treatment at Day 8 and Day 15, communities were markedly changed with increased dominance of CST III (*L. iners*). At Day 15, there was an increase with CST IV (mixed) when compared with Day 1 and Day 8. Notably in both groups, *L. iners* was present in all CST clusters with relatively high abundance.



CONCLUSIONS:

Metronidazole treatment of women with symptoms of BV shifted the vaginal microbiota to resemble that of healthy controls after completion of antibiotic treatment. Inclusion of sequencing analysis into BV diagnostics provides more in-depth understanding of changes in vaginal microbiota composition in health and disease.



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