

Characterizing the FRT-GIT microbiome in infertility: insights from 16S rRNA analysis



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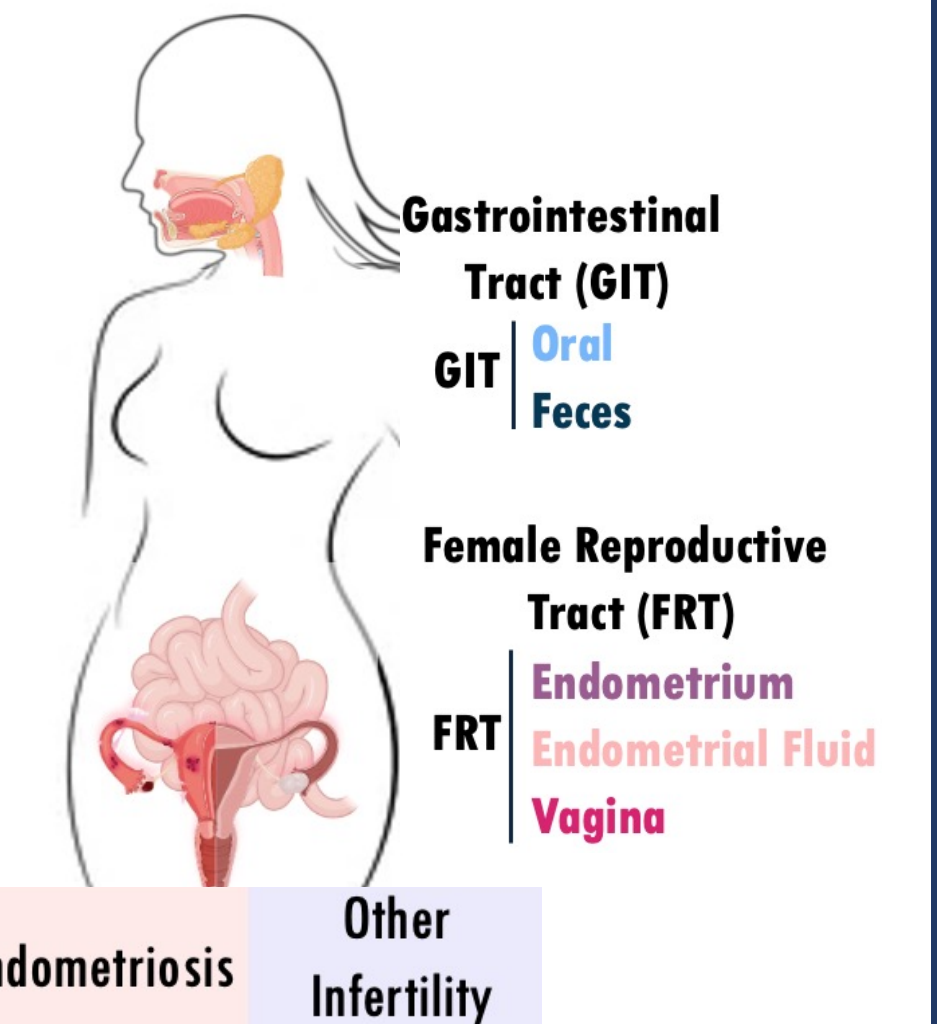
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Background

Sex hormone fluctuations throughout life influence host-microbial interaction and are associated with several diseases. Infertility-related conditions affect the female reproductive tract (FRT) and its resident microbiota. However, disruption of homeostasis could affect FRT and other distal body sites, such as the gastrointestinal tract (GIT). The microbiota plays a vital role in communication and systemic health by releasing metabolites, thus implying that modulation of the microbiota could be crucial in the development of gynecological diseases and infertility. The **purpose of the study is to determine the homeostasis in the FRT-GIT microbiome and its impact on female reproductive function in infertile patients undergoing reproductive therapy.**

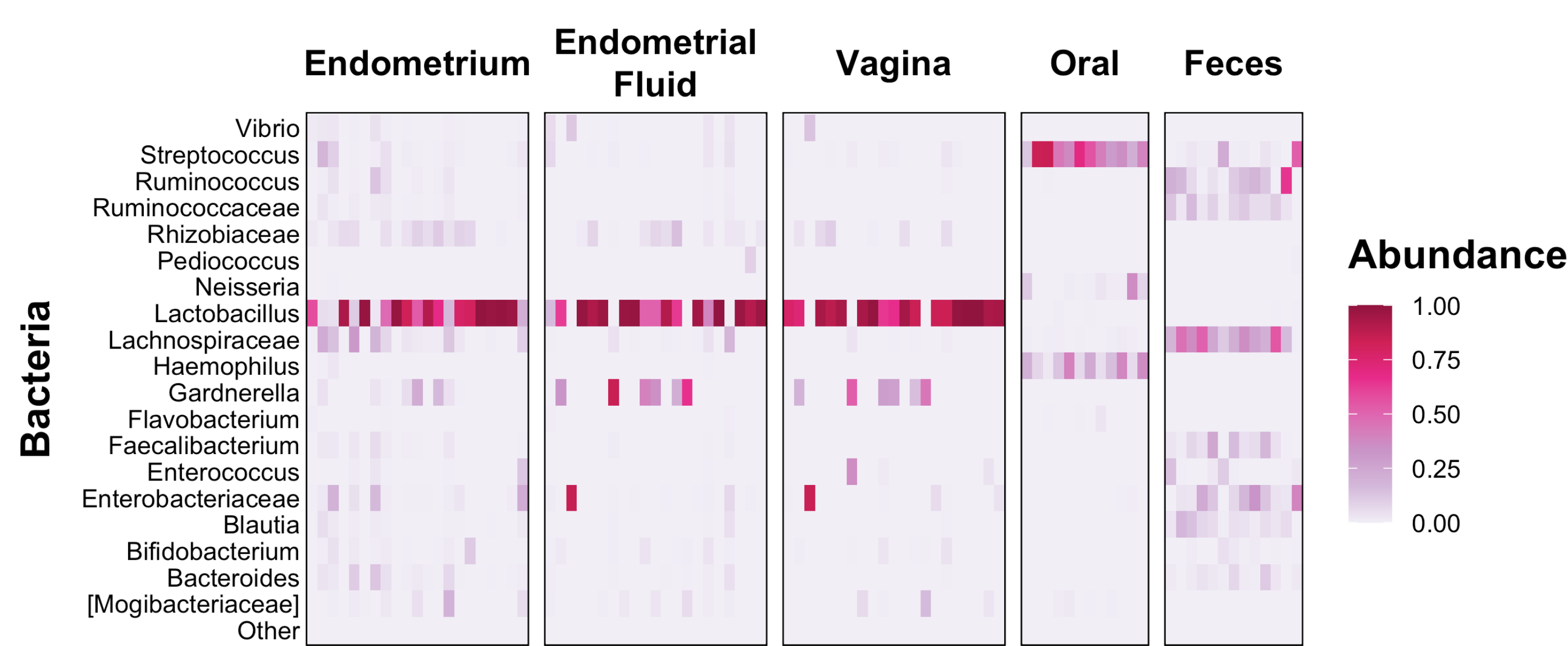
Material & Methods

We collected clinical profiles and five samples from 21 patients with infertility-associated diseases. Using the QIIME2 bioinformatics platform, we processed 16S rRNA gene sequencing data to analyze the bacterial composition and calculate diversity metrics. To assess differences in diversity and potential associations with infertility conditions, we conducted statistical analyses, including the Wilcoxon Rank-Sum Test and PERMANOVA. Additionally, we performed a Nestedness test to explore interrelationships within microbial communities in the context of infertility.

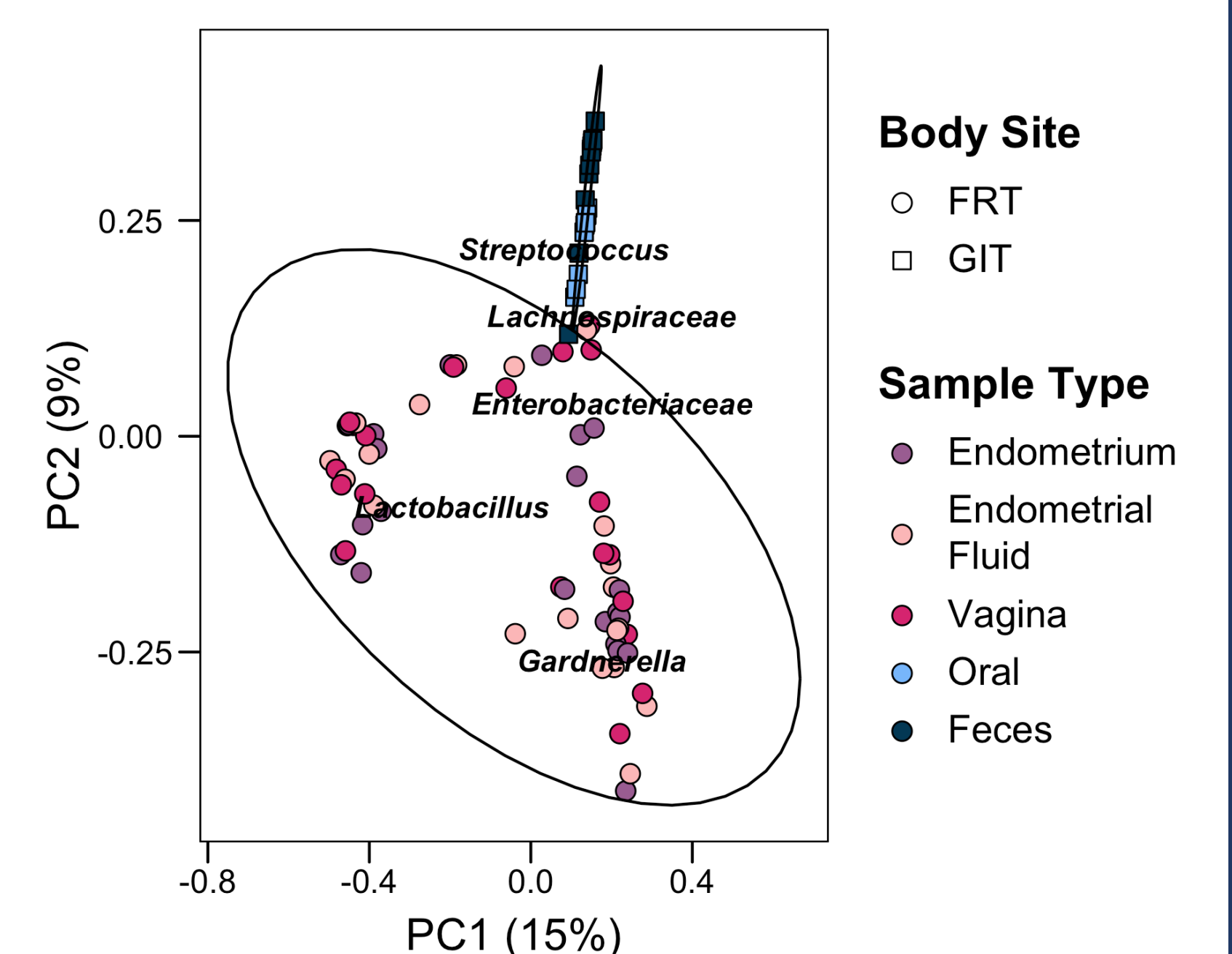


Results

Female gastrointestinal and reproductive microbial profile

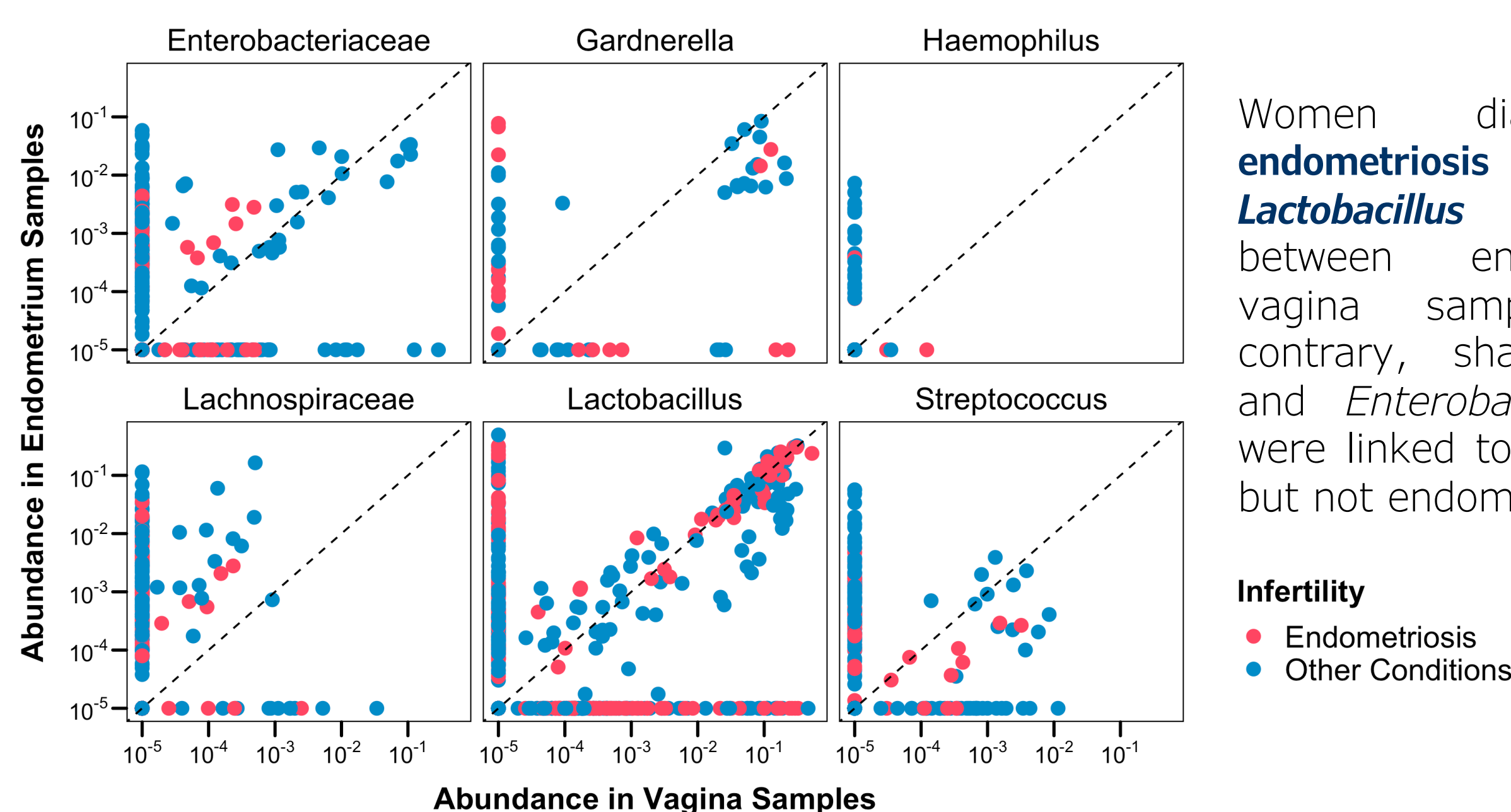


The **FRT** samples exhibited high similarity in genera, mainly dominated by *Lactobacillus*. In contrast, the **oral** bacterial population differed significantly, highlighting the presence of *Streptococcus* and *Haemophilus*. The **fecal** microbiota displayed greater diversity, with notable abundance of *Lachnospiraceae* (left figure).

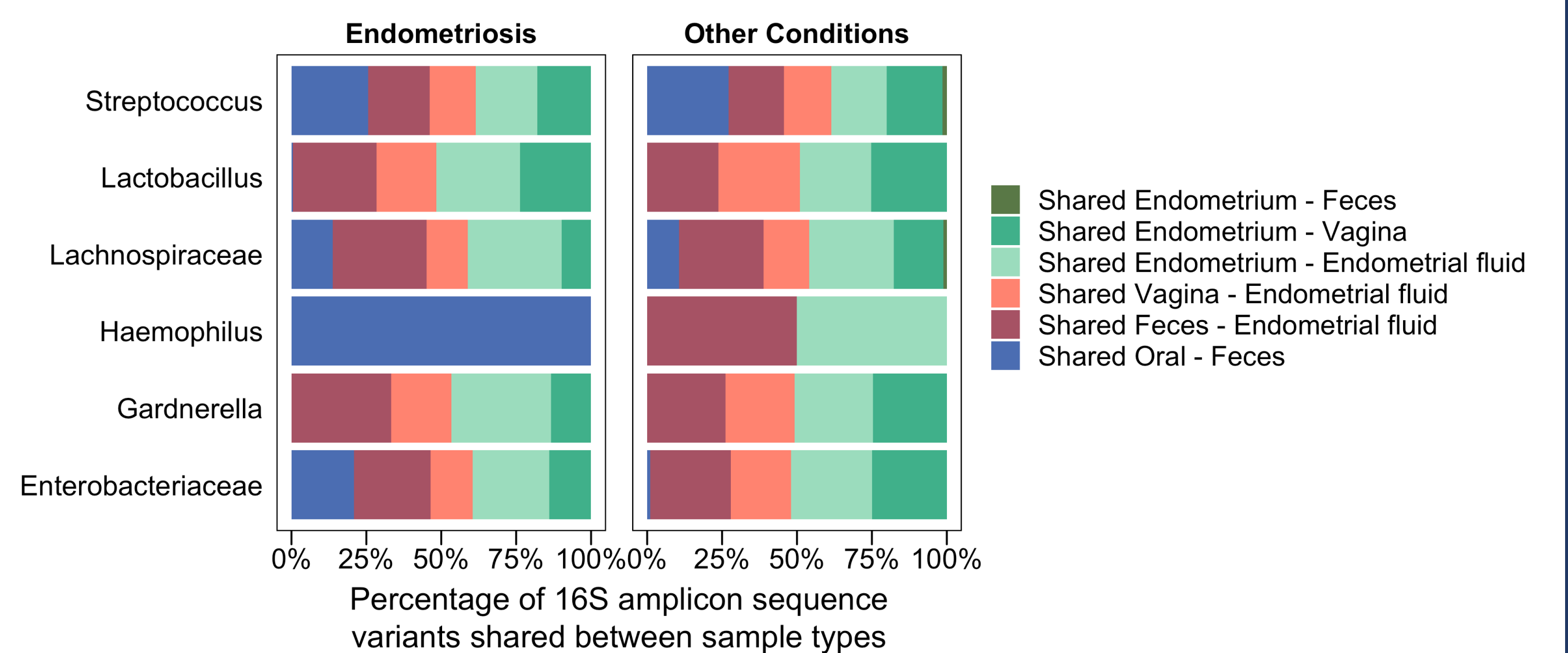


The Bray-Curtis index showed significant **dissimilarity** ($P = 0.001$) between **GIT** and **FRT** samples. **FRT** samples formed **two groups** based on *Lactobacillus* or *Gardnerella* dominance (right figure).

FRT-GIT microbiome connection in fertility through Nestedness



Women diagnosed with **endometriosis** had **higher shared Lactobacillus ASVs** between endometrial and vagina samples. On the contrary, shared *Gardnerella* and *Enterobacteriaceae* ASVs were linked to other conditions but not endometriosis.

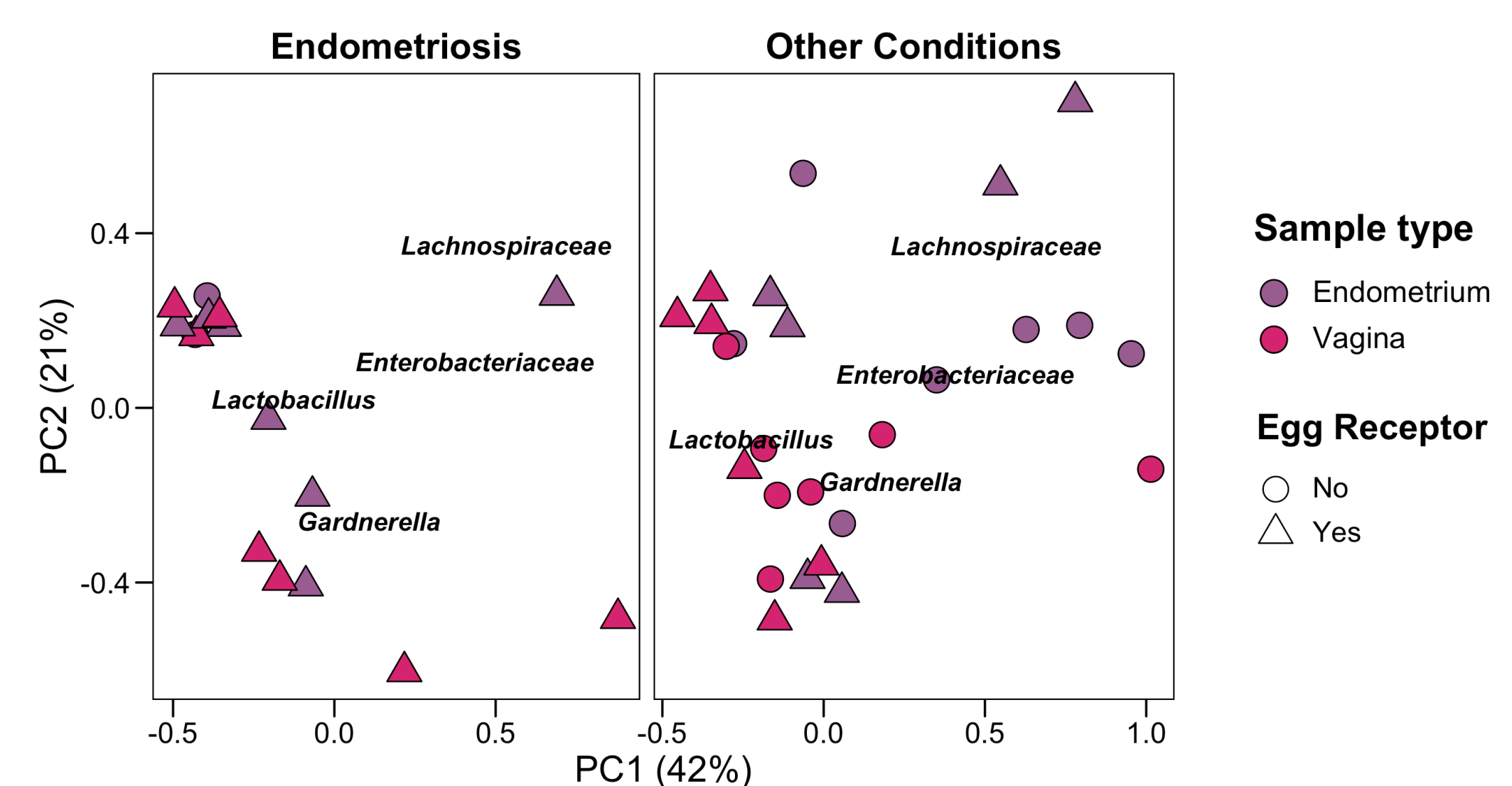
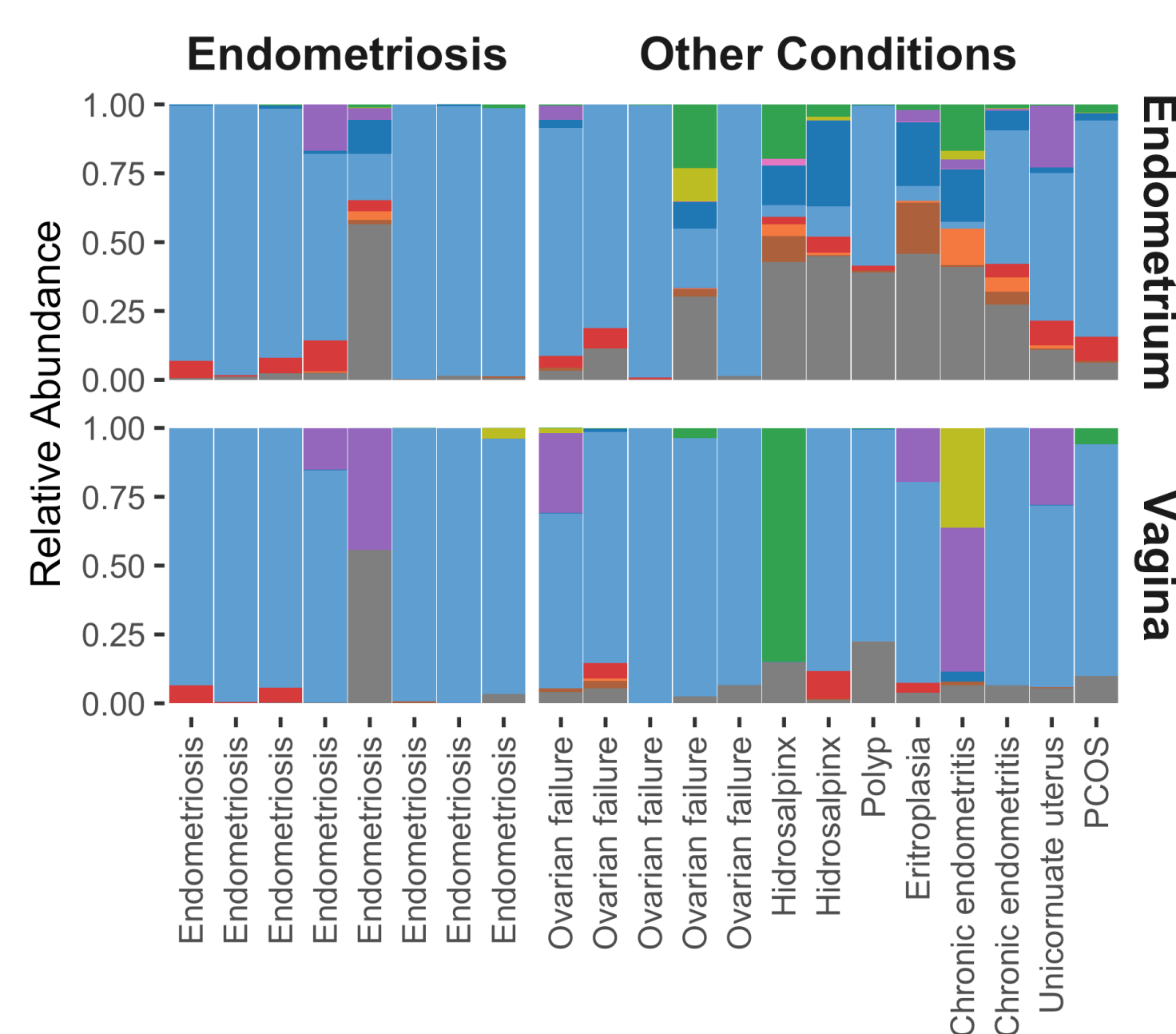


Gardnerella was shared in the **endometrial-vaginal** samples but did not appear in the **GIT** samples. Remarkably, *Haemophilus* was a specific **GIT-shared** taxa in endometriosis.

Female reproductive tract microbiome associated with fertility

We observed a high level of homogeneity among samples from women with **endometriosis** and a striking **similarity** between the **endometrial** and **vaginal** microbiomes. The **low species diversity** observed in these samples, along with the predominance of *Lactobacillus*, suggests a distinctive **microbial profile associated with endometriosis**.

The variability among samples from women with other conditions suggests that FRT microbiome composition may be related to specific gynecological conditions.



Notably, the majority of **women with endometriosis required egg donation** for successful pregnancy. Distinctively, among women with other conditions, only those with pathologies affecting ovarian function or ovulation required egg donation.

Conclusions

- Lachnospiraceae*, related to the intestinal niche, was found in the endometrium when *Lactobacillus* declined, suggesting that microorganisms from distant body sites might be connected.
- Haemophilus* ASVs were shared in oral-feces for endometriosis. This finding might explain the ability of *Haemophilus* to adapt to the endometriosis environment compared to other infertility conditions.
- Pathologies compromising ovarian function and ovulation might impact the fertility-related microbiota in the reproductive tract, potentially leading to difficulties in achieving pregnancy.

Acknowledgements

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