

Background

- Spontaneous preterm birth (sPTB) is a multi-factorial syndrome where infection and inflammation are implicated as causative factors¹.
- Colonisation of the vagina by *Lactobacillus* species, in particular *L. crispatus*, is protective against sPTB and mid-trimester loss (MTL)². Mechanisms underpinning microbial colonisation and host responses remain poorly defined.
- Microbiota composition and disease risk are associated with histo-blood group antigens³.

Objective

- To evaluate whether blood-group antigens are associated with microbiota compositions and sPTB risk

Methods

- Women attending preterm birth prevention clinics at four hospitals in the UK were included in the study (n=1935). A subset had vaginal swabs collected at timepoint A: 12-16 and B: 20-24 weeks.
- Bacterial DNA was extracted and the composition assessed using 16S rRNA gene sequencing surveying the V1-V2 region (n=238). Cytokine immunoassays were performed on matched supernatant (n=103).
- Results were analysed according to ABO blood group status and risk factor for sPTB. Analyses were performed using R Studio and GraphPad Prism 8 software.
- χ -squared tests were used to compare discrete outcome variables, continuous with Kruskal-Wallis tests

Results

- Women with blood group O were at increased risk of second trimester cervical shortening (RR 1.414, 95% CI 1.125 to 1.783, p=0.001) and sPTB <34 weeks (RR 1.343 (0.9508-1.901), p=0.043) when compared to those of blood group A.
- These relationships applied to women with previous MTL/sPTB but not previous excisional cervical treatment (large-loop excision of the transformation zone – LLETZ)(fig 1).

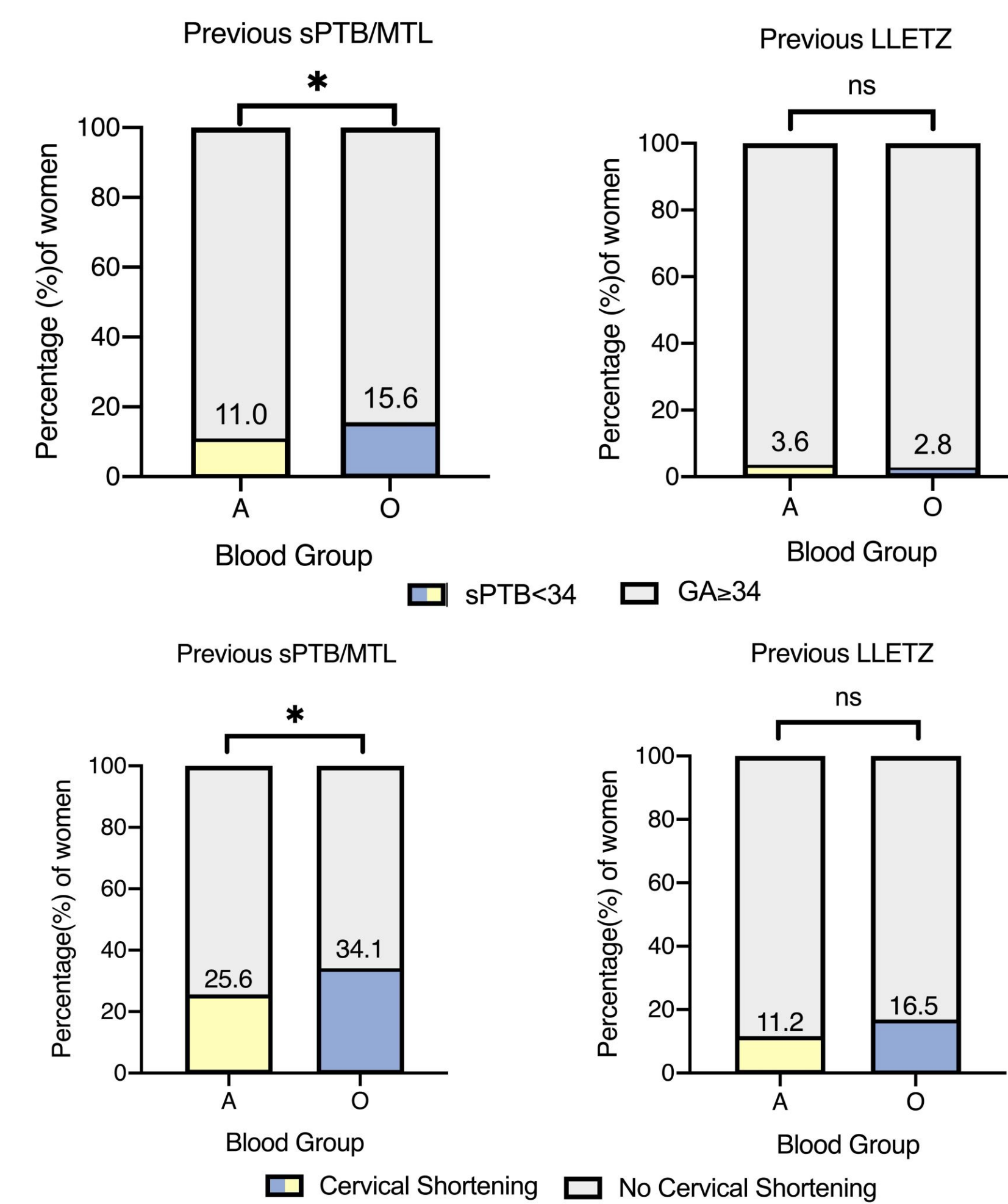


Figure 1: Pregnancy outcomes for blood groups A and O according to risk factor for sPTB.

- Blood group O women with sPTB <34 weeks were significantly less likely to be colonised with *L. crispatus* in the early and late second trimester than those who delivered at term (RR 0.29 (0.018-0.82), p=0.016, RR 0.39 (0.17-0.79), p=0.006). These relationships were not seen with blood group A (fig 2)
- For women with sPTB <34 and <37 weeks, blood group O participants were significantly less likely to be colonised with *L. crispatus* than those of blood group A (fig 2).

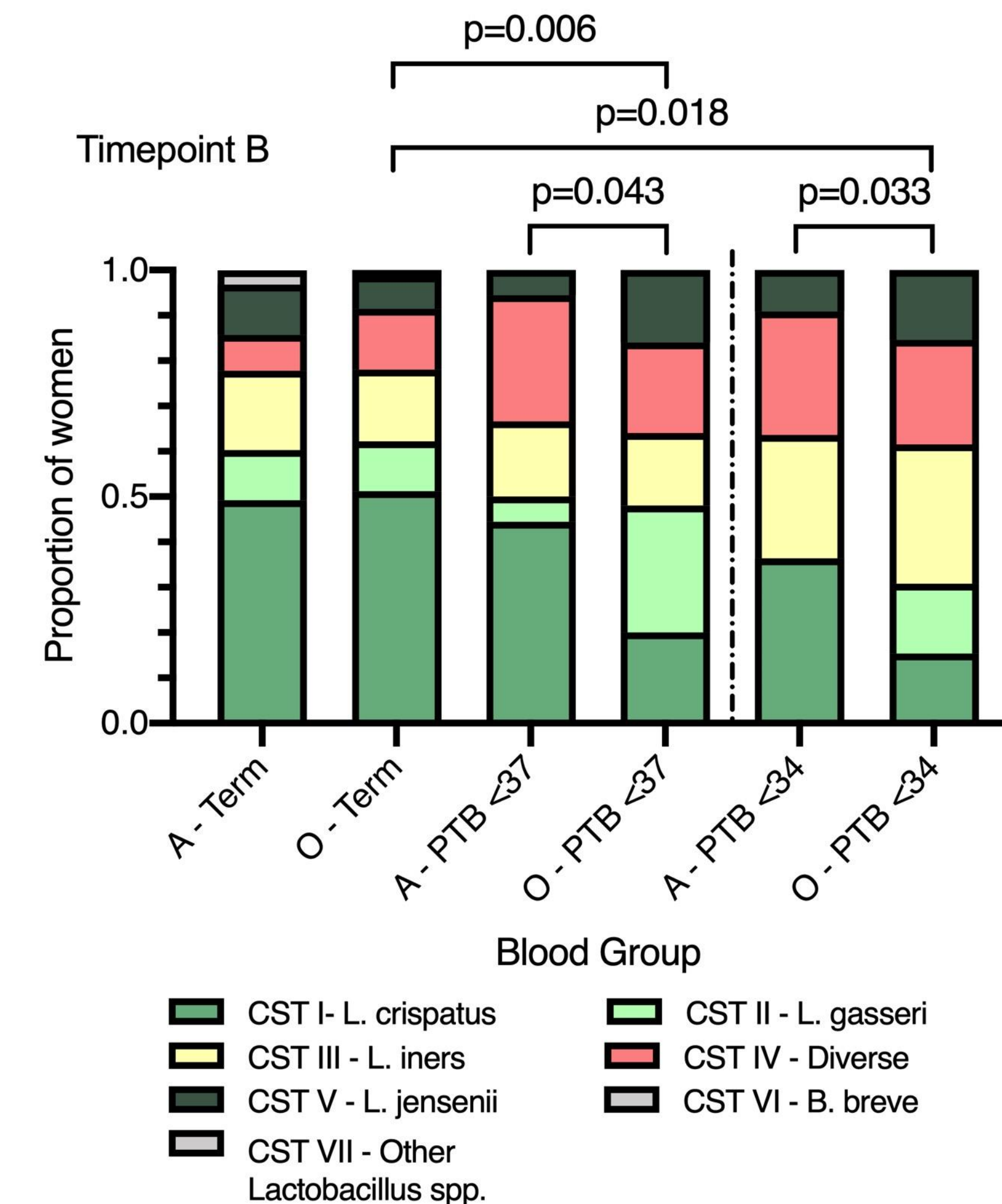


Figure 2: Relationship between the vaginal microbiome, blood group and pregnancy outcome (n=198)

- Inflammatory cytokines IL-8, IL-6 and IL-1 β were highly correlated with *L. iners* and bacterial vaginosis-associated taxa (e.g. *G. vaginalis*) in women of blood group O, and negatively correlated with *L. crispatus*. In blood group A women, there was poor correlation between cytokines and bacterial taxa.
- A significant relationship between *L. crispatus* proportion (dominant or deplete (80% relative abundance cut-off)) and CVF IL-8 was seen only in women with blood group O (Dunn's multiple comparison's test, p=0.007, Fig 3).

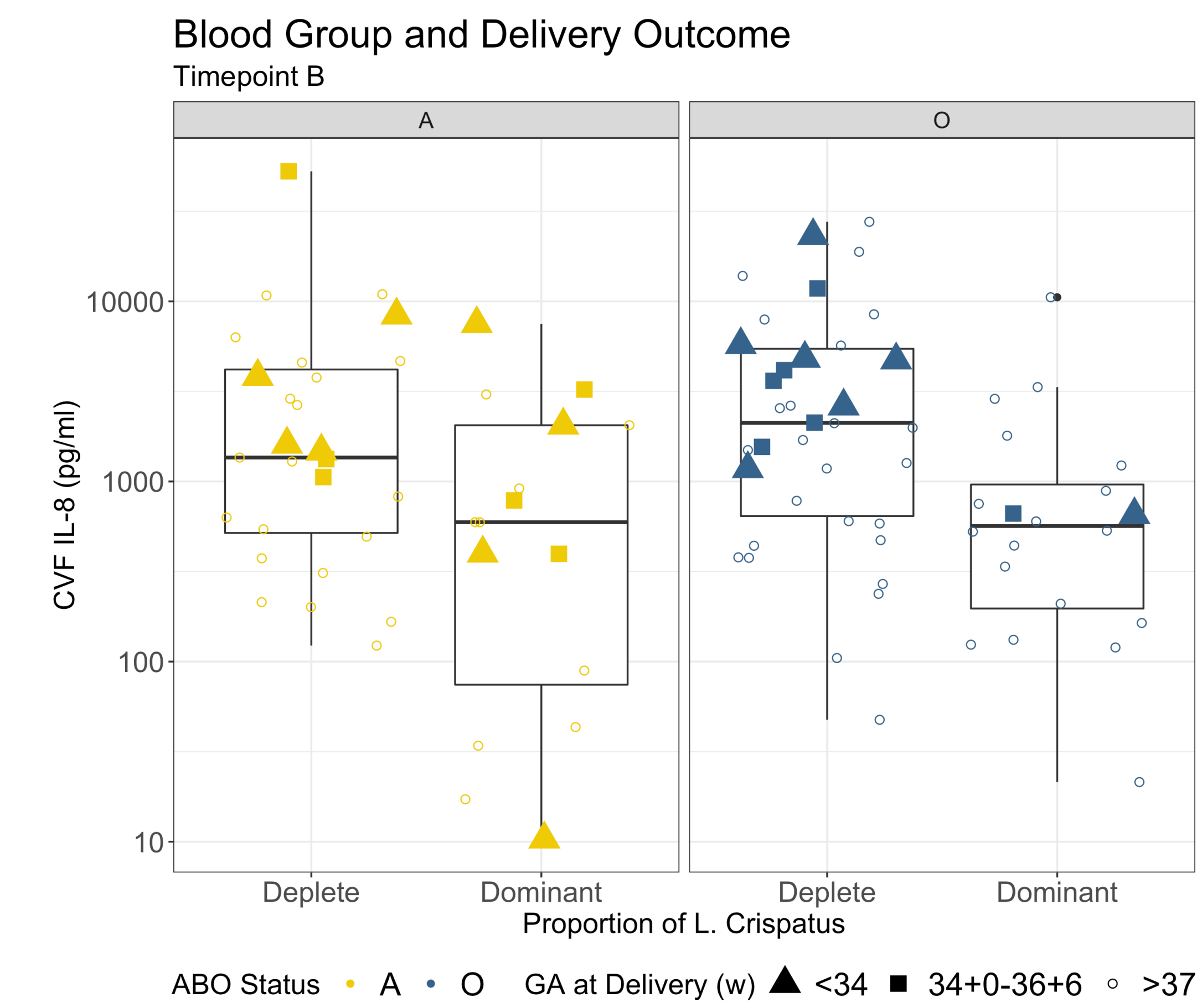


Figure 3: Relationship between blood group, *L. crispatus* proportion in vaginal samples, CVF-IL-8 concentration and pregnancy outcome (n=103)

Key Findings

In women at risk of preterm birth, blood group O is associated with higher rates of cervical shortening and early preterm birth.

Women with blood group O are less likely to be colonised with *L. crispatus* and more likely to have local inflammation than women with blood group A.

We conclude that cervicovaginal blood group antigens are involved in microbial driven preterm birth

References

- Goldenberg, R.L., et al., *Epidemiology and causes of preterm birth*. The Lancet, 2008. **371**(9606): p. 75-84.
- Bayar, E., et al., *The pregnancy microbiome and preterm birth*. Semin Immunopathol, 2020. **42**(4): p. 487-499.
- Cooling, L., *Blood Groups in Infection and Host Susceptibility*. Clin Microbiol Rev, 2015. **28**(3): p. 801-70.