

Network analysis reveals a complex relationship between the cervicovaginal environment, body mass index (BMI), and spontaneous preterm birth (SPTB)



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Introduction

Studies report an association between vaginal health (*Lactobacillus crispatus* dominance) with term pregnancy, and a diverse microbiome or *L. iners* with SPTB [1-7]. However, some women who deliver at term (often those reporting African ancestry) present with a diverse microbiota/*L. iners* dominance regardless of pregnancy outcome. A more in-depth investigation of the vaginal environment and clinical phenotyping is needed. We interrogated the complex relationship between the cervico-vaginal fluid (CVF) metagenome, metabolome, inflammatory markers, BMI, and SPTB using network analysis. We undertook a validation study of our metabolite-based biomarker test for prediction of SPTB [1].

Socio-demographics

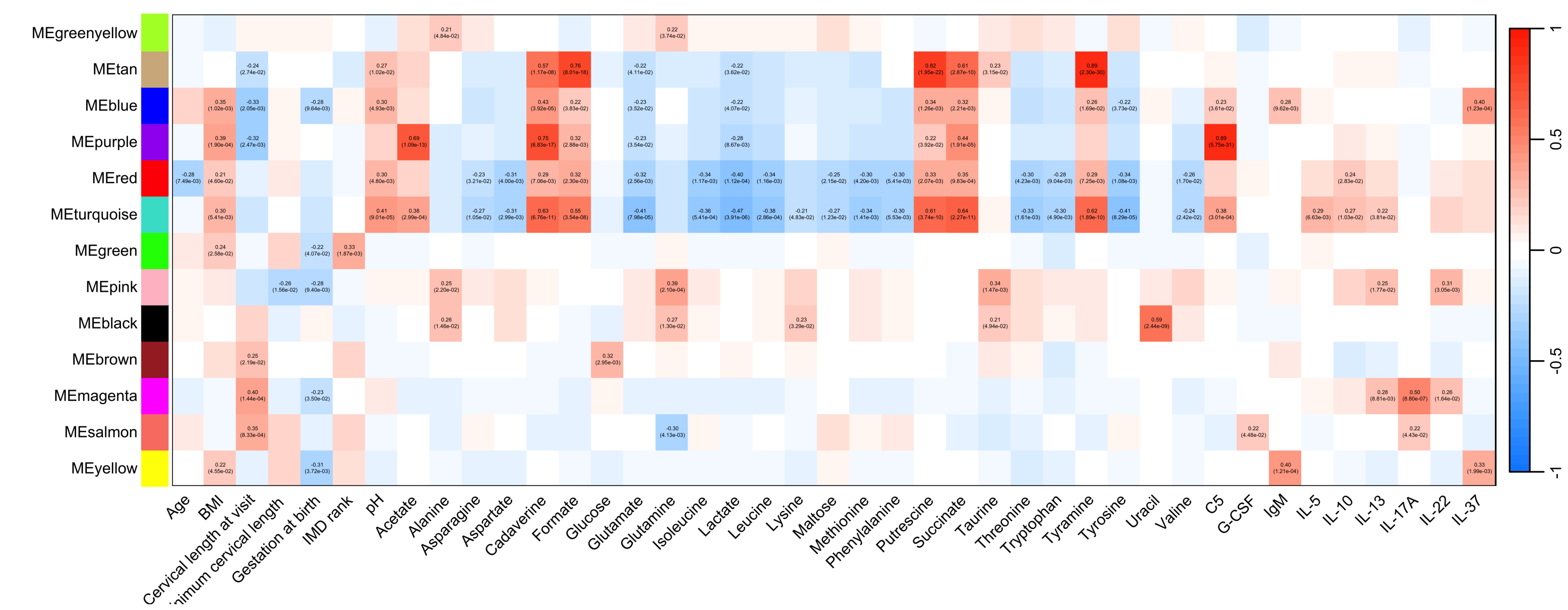
	Term (n=59)	sPTB (n=28)	Total (n=87)	P value by outcome
Maternal age (mean ± stdev)	30.85 ± 5.93 (n=59)	30.86 ± 6.19 (n=28)	30.85 ± 5.98 (n=87)	0.953
BMI (mean ± stdev)	27.37 ± 5.84	32.44 ± 5.50	28.96 ± 6.18 (n=86)	0.000149
IMD rank (mean ± stdev)	9911 ± 5098 (n=58)	11041 ± 6604 (n=28)	10279 ± 5618 (n=86)	0.678
Risk status at enrolment				
High risk	0 (0%)	24 (85.71%)	24 (27.59%)	
Low risk	59 (100%)	4 (14.29%)	63 (72.41%)	

A subset of 87 women self-reporting African ancestry (with clinical data and 10-15⁺ week CVF samples) were identified from the INSIGHT cohort [8]

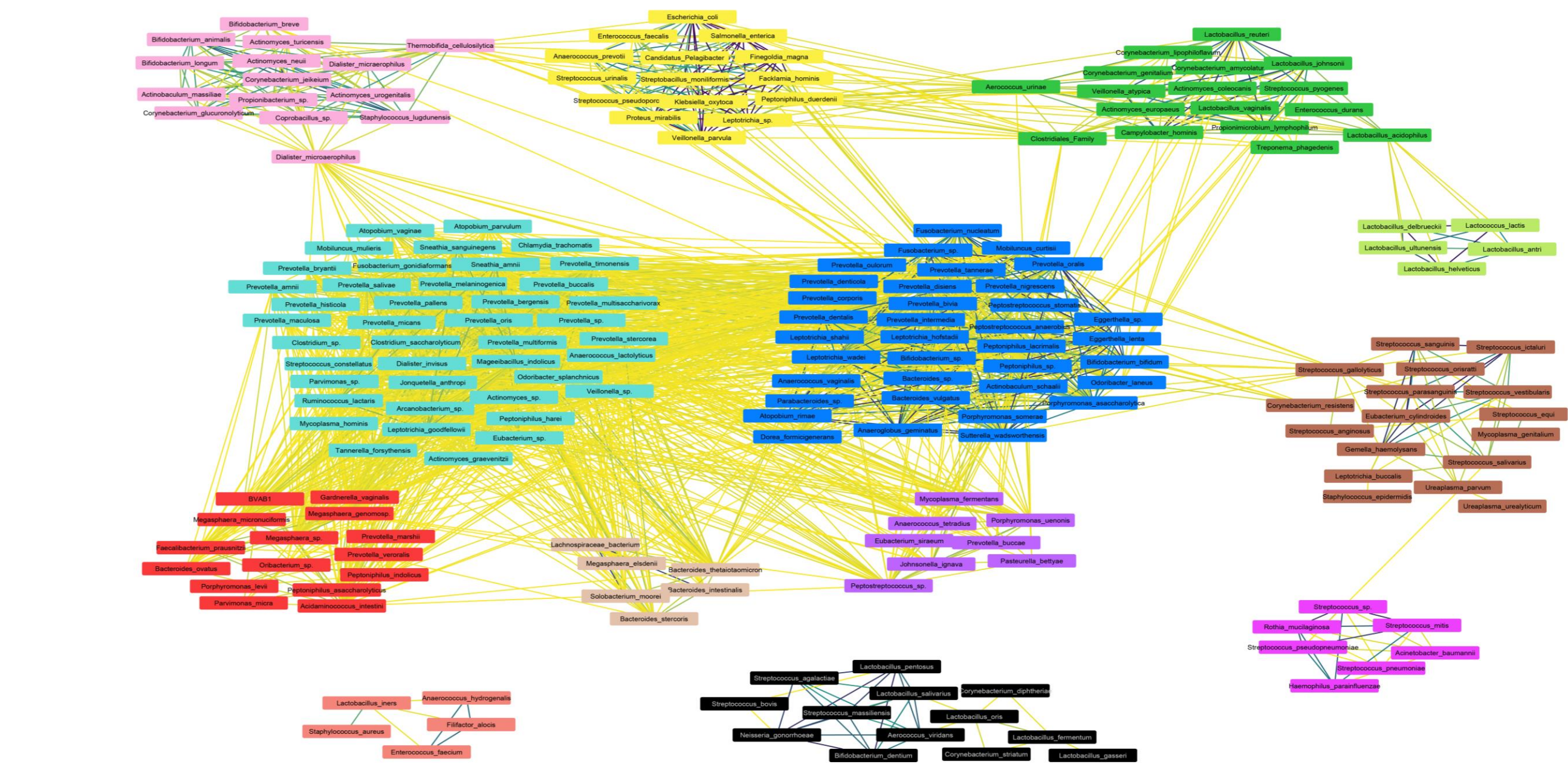
Acknowledgements and references

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[1] Flaviani et al., 2021 [2] DiGiulio DB, et al. 2015 [3] MacIntyre DA et al. 2015 [4] Stafford GP, et al. 2017 [5] Elovitz et al, 2019 [6] Fettweis JM, et al. 2019 [7] Serrano MG, et al. 2019 [8] Hezelgrave et al. 2020 [9] Mohd-Zaki et al. 2022 [10] Chandiramani et al.2012.

Network analyses

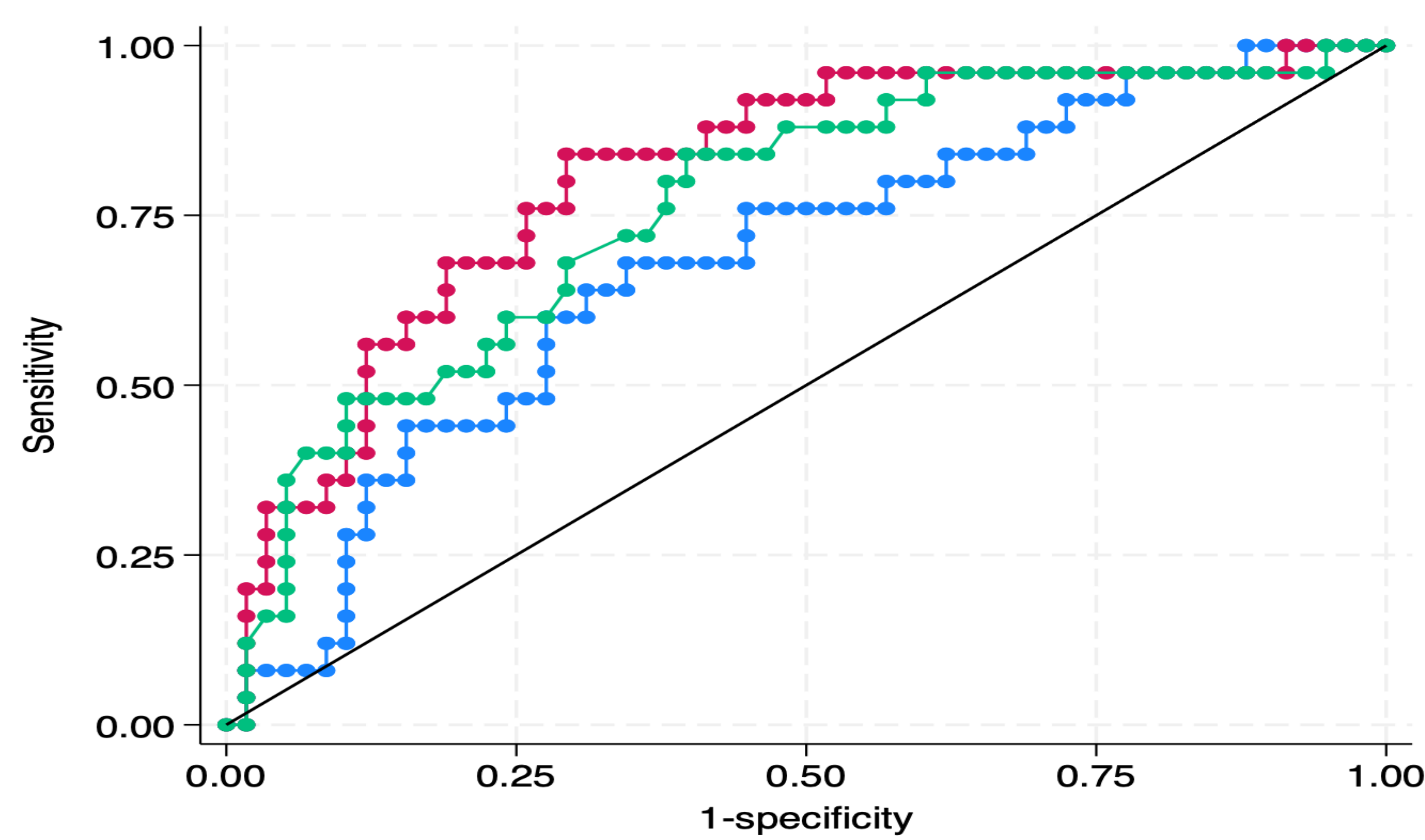


B.



Weighted gene correlation network analysis (WGCNA, 9) was performed to investigate patterns of co-occurrence and inter-relationships among cervicovaginal microbial species (A and B). Distinct modules of highly correlated species identified (A and B) and their associations with clinical factors such as, birth outcome, BMI, and features of the vaginal environment (NMR metabolome [1], cytokines and other inflammatory markers measured using multiplex ELISA [10]).

Model validation – SPTB prediction



In this cohort, BMI alone has a modest performance (ROC area 0.76 (95% CI 0.65-0.88). Validation of our previous composite-metabolite model showed moderate performance (ROC area 0.68 (95% CI 0.56-0.81)) that was improved with the inclusion of BMI (ROC area 0.81 (95% CI 0.71-0.91).

Conclusions

WGCN analysis provides insight into how bacterial networks shape the cervico-vaginal environment and influence cervical length and gestation at birth. This work highlights the influence of BMI on the vaginal environment (bacterial species and inflammation) and hence the contribution of BMI to increased SPTB risk.

