

The salivary microbiota is altered in cervical dysplasia patients and influenced by conization

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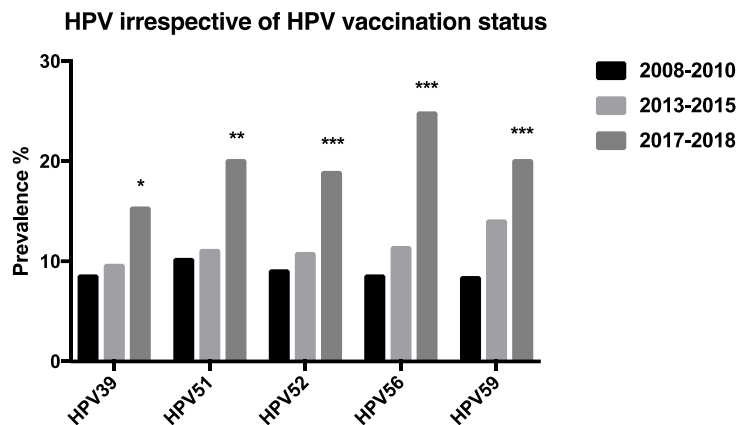
† In memoriam of Dr. Sonia Andersson (1934-2022).



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Introduction

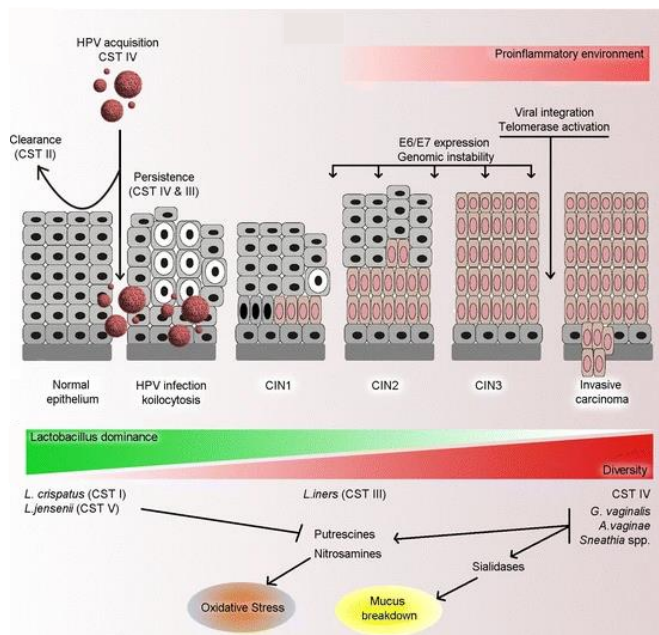


World Health Organization launched a global strategy to accelerate the elimination of cervical cancer.

Known risk factors for cervical cancer include Human Papillomavirus (HPV) infection, immunodeficiency virus (HIV) infection, smoking, and increased parity.

The current vaccines do not cover all oncogenic HPV types, and HPV types that not covered in current vaccines had increased.

Emerging evidence supports that vaginal microbiota is associated to HPV infection and dysplasia.

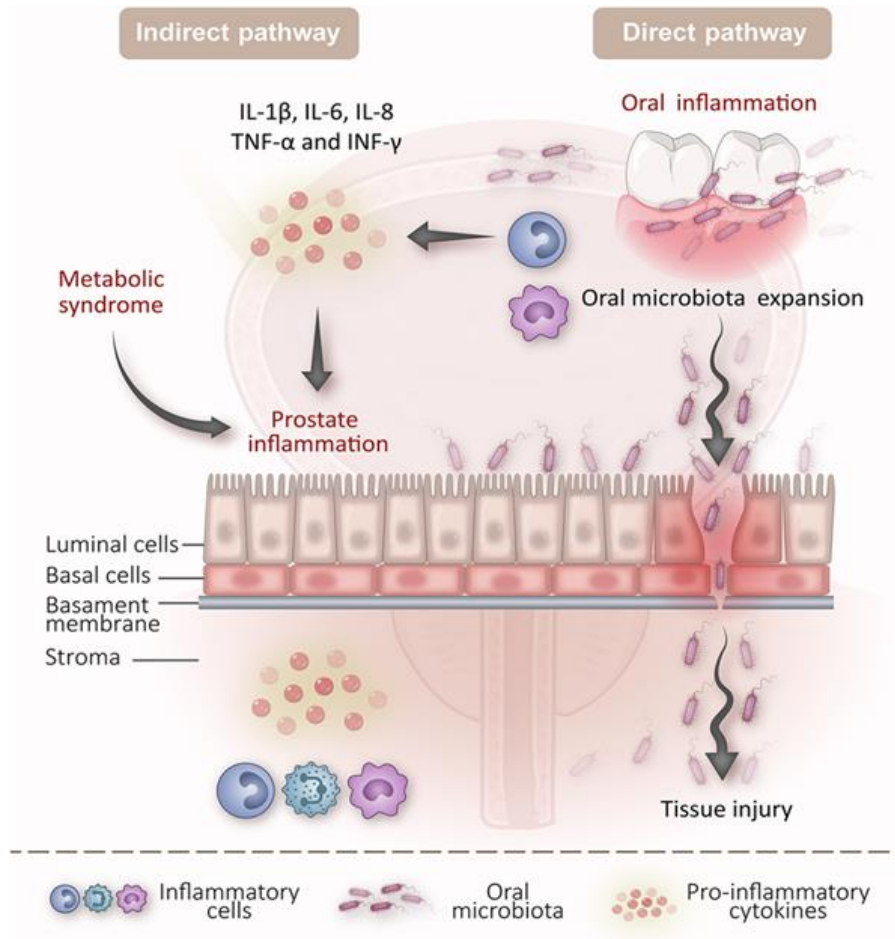


Ährlund-Richter Andreas, et al. *Frontiers in cellular and infection microbiology* 9 (2019): 59.

Anita Mitra, et al. *Microbiome* 4 (2016): 58 .



Introduction



Poor oral hygiene and tooth loss are associated with an increased risk of oral squamous cell cancer.

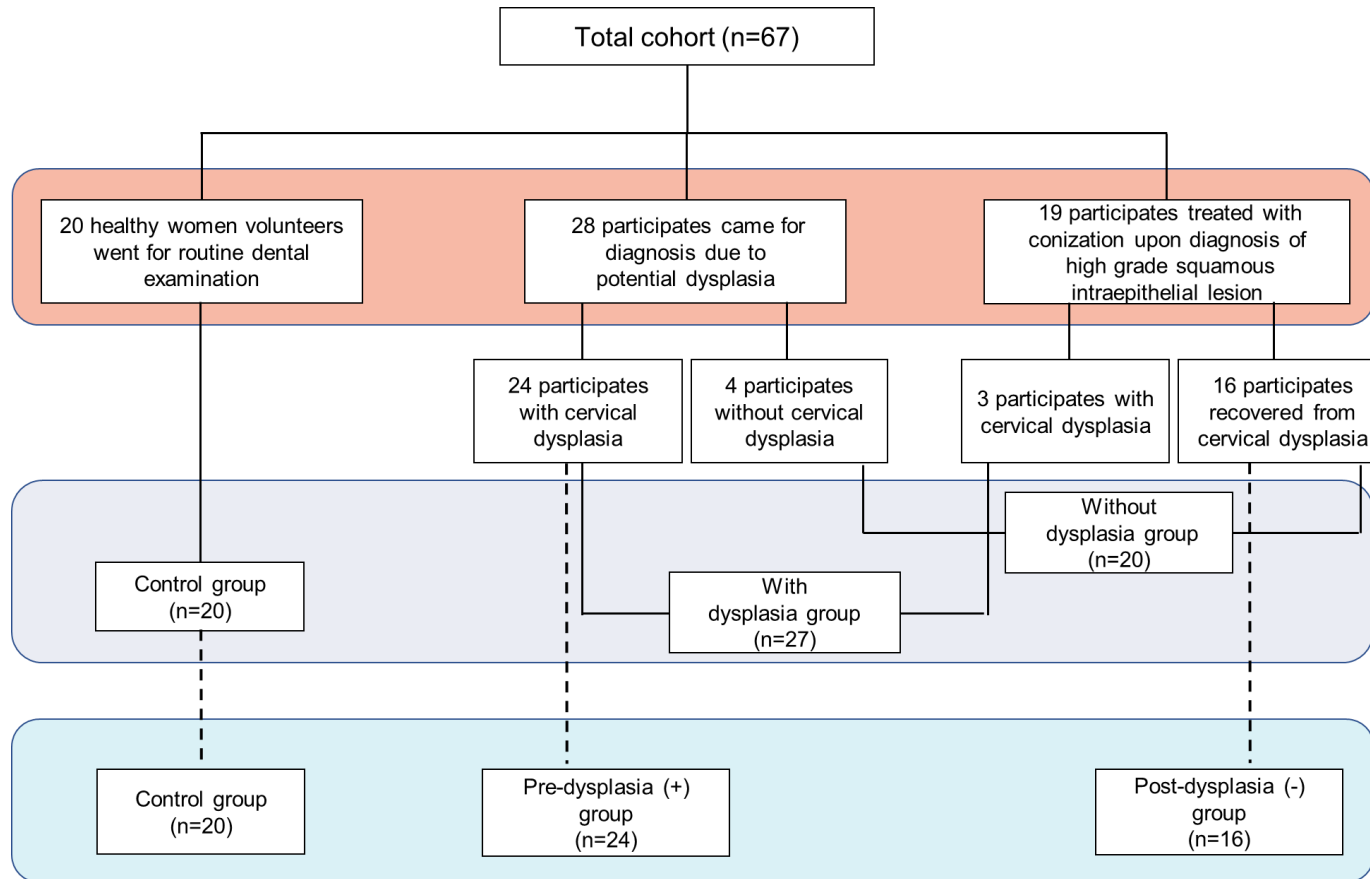
Several oral bacterial pathogens, including *Fusobacterium*, *Campylobacter*, *Prevotella* et al, are correlated with different cancers.

Numerous studies have shown that smoking is a significant risk factor for developing cervical abnormalities, including cervical dysplasia and cervical cancer.

Data related to oral or salivary microbiota and cervical dysplasia are still limited.



Methods

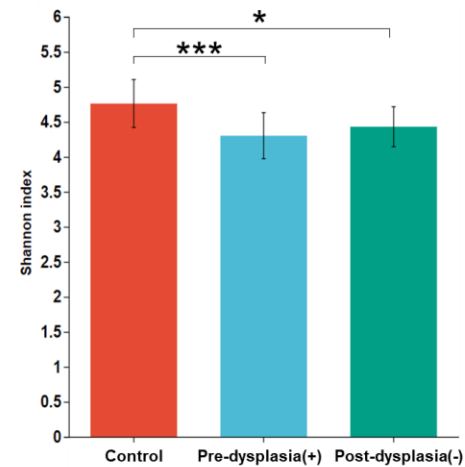
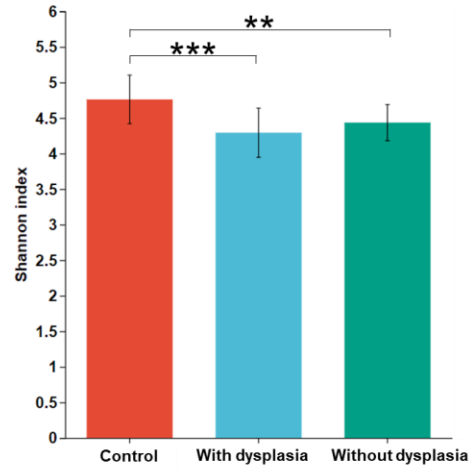


DNA were extracted from all 67 saliva samples and tested for 27 HPV subtypes with the MAGPIX luminex instrument.

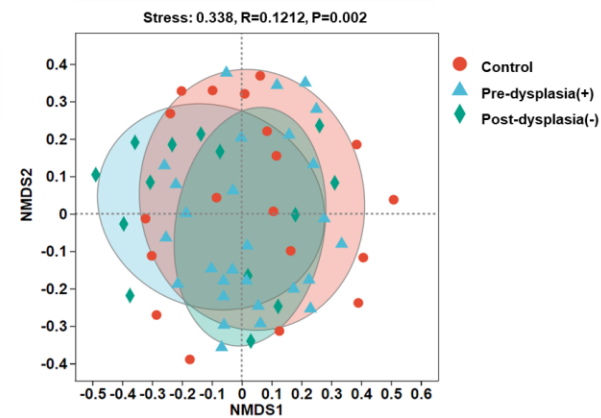
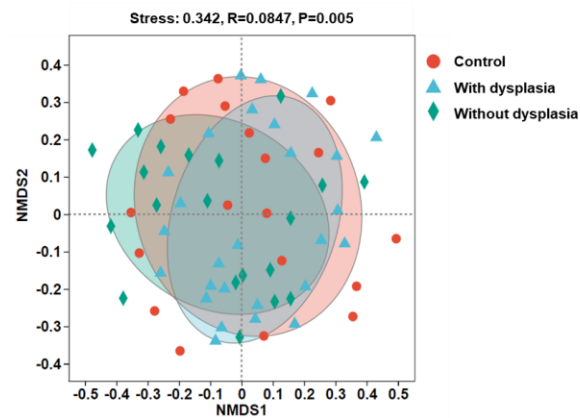
The V3–V4 regions of the 16S rRNA genes were amplified using Illumina sequencing index-binding primer pairs 341F/805R and sequenced on an Illumina MiSeq sequencing platform.



Results I



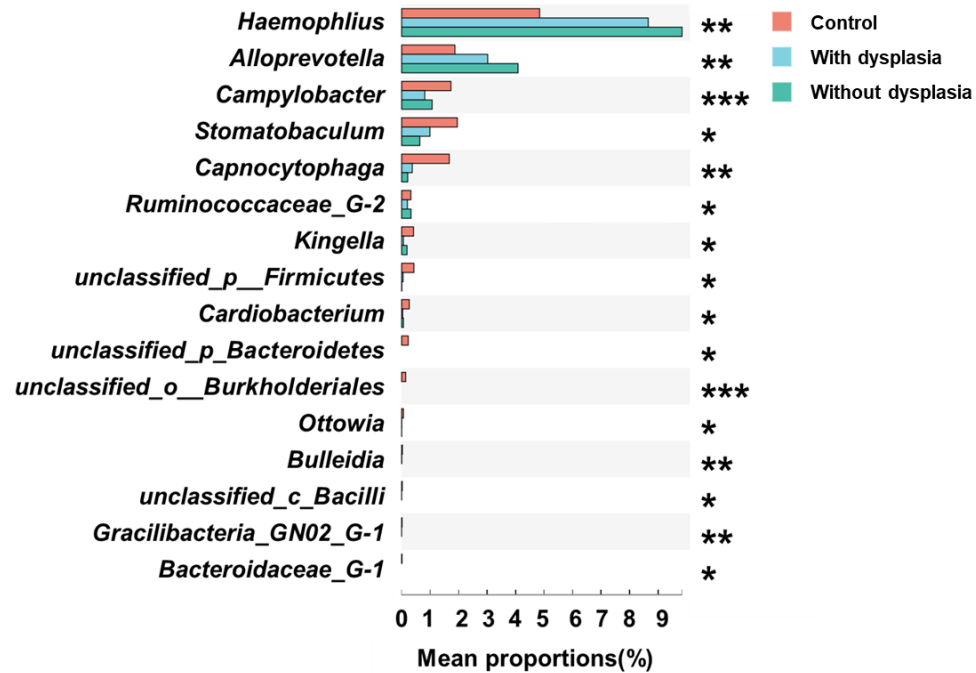
Significantly decreased microbial community richness, diversity, and significant dissimilarity were observed in participants with and without dysplasia when compared to the control group.



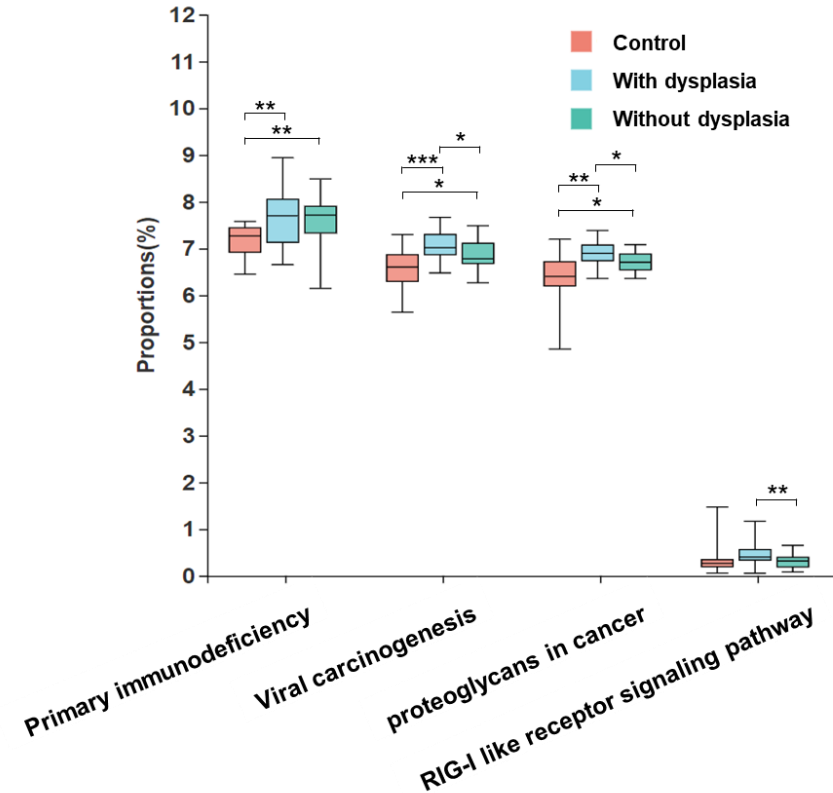
Similar trends were observed in participants of the pre-dysplasia (+) and post-dysplasia (-) groups and in participants from different histological groups compared to the control group.



Results II



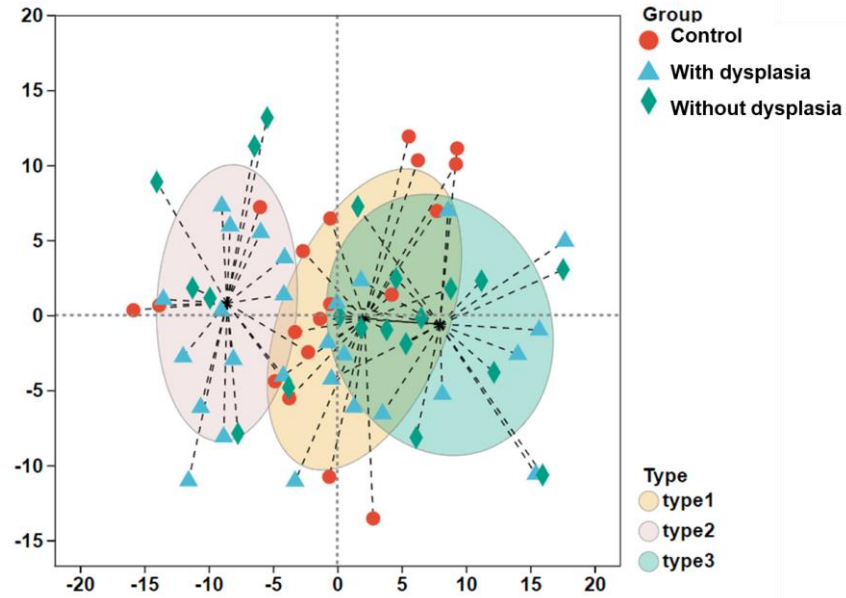
The relative abundance of *Haemophilus* and *Alloprevotella* were significantly increased among saliva samples from vaginal examination participants than the healthy participants.



The pathways of primary immunodeficiency, viral carcinogenesis, proteoglycans in cancer, and retinoic acid-inducible gene I (RIG-I)-like receptor signaling pathways were significantly changed.

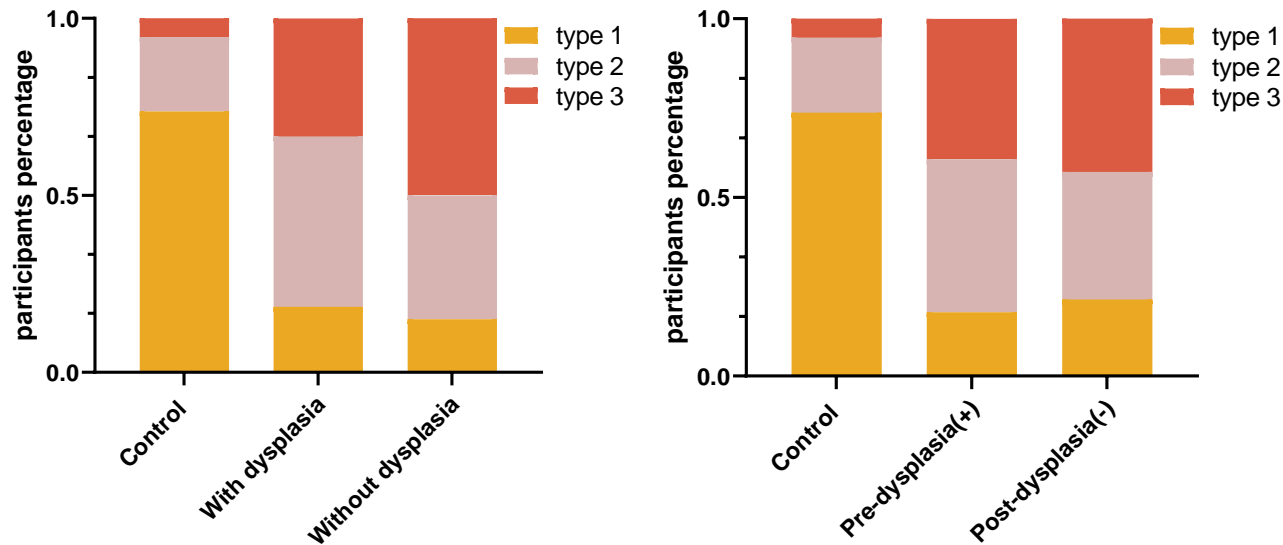


Results III



Based on the similarities in the genera identified from different samples, three different salivary microbial types were generated.

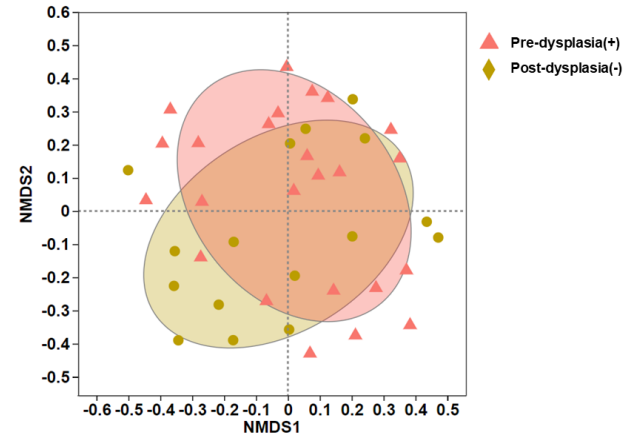
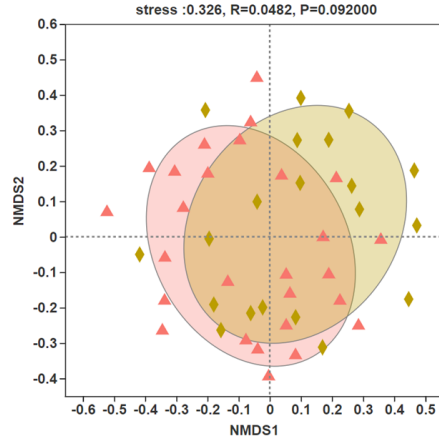
Participants in the groups with and without dysplasia had higher percentages of type 2 and type 3 than the participants in the control group.



A similar trend was observed when comparing pre-dysplasia (+) and post-dysplasia (-) groups with the control group.



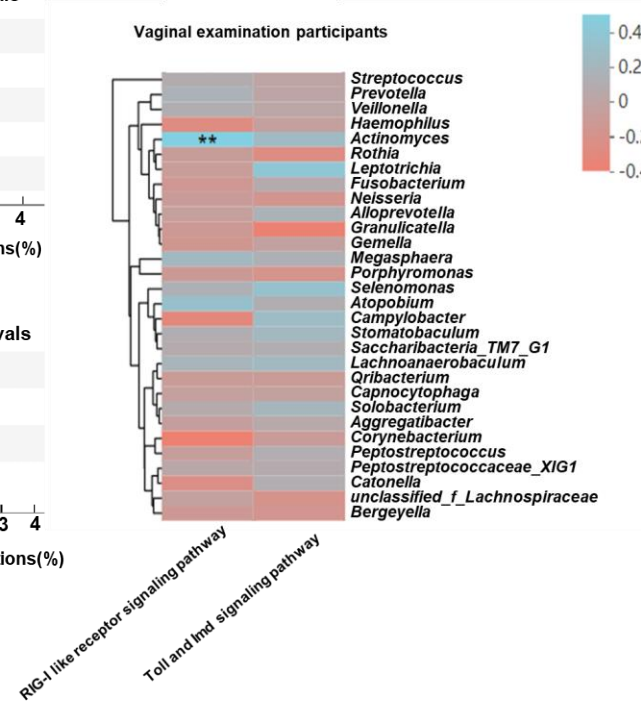
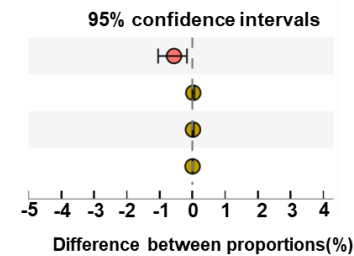
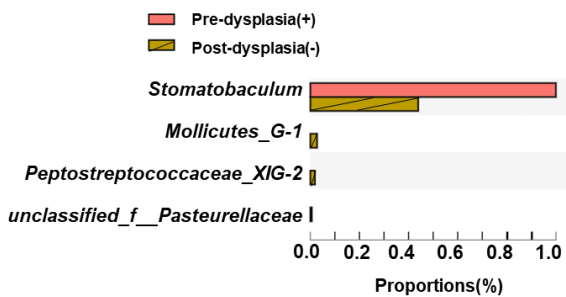
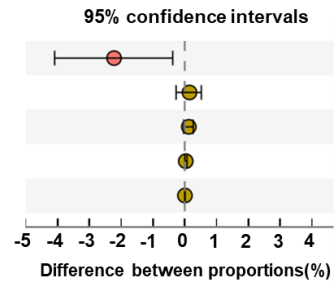
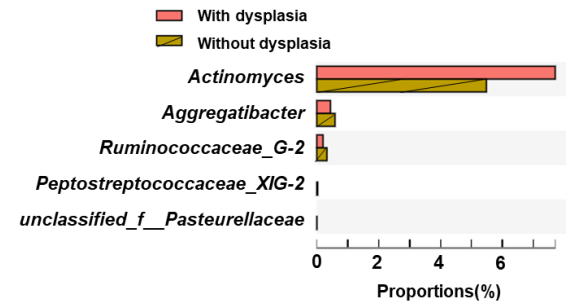
Results IV



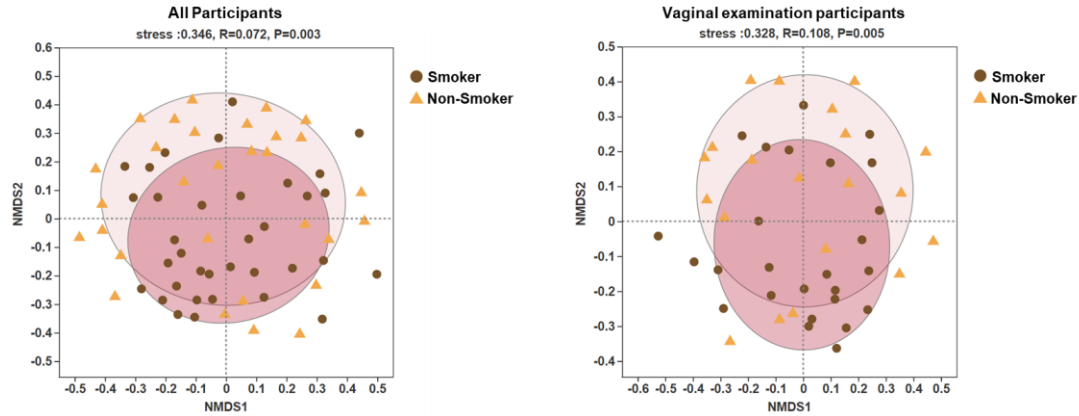
Microbiota beta diversity between the pre-dysplasia (+) and post-dysplasia (-) participants was significantly altered.

Actinomyces was significantly increased in the dysplasia group.

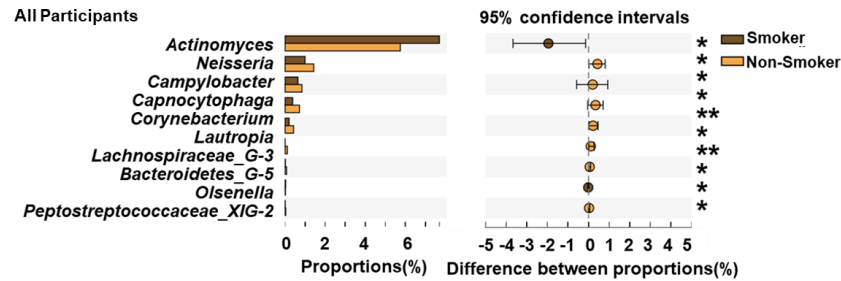
Actinomyces was found to be correlated with increased RIG-I-like receptor signaling, which is elevated in patients with dysplasia.



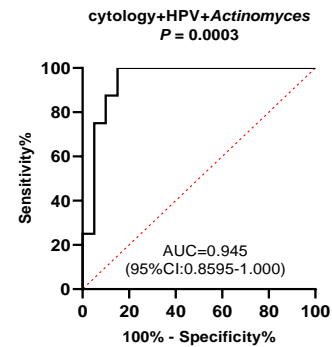
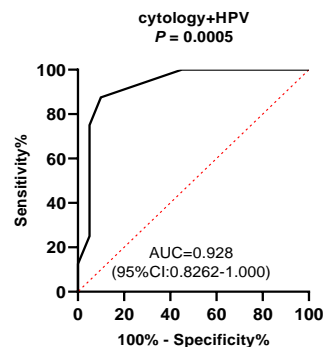
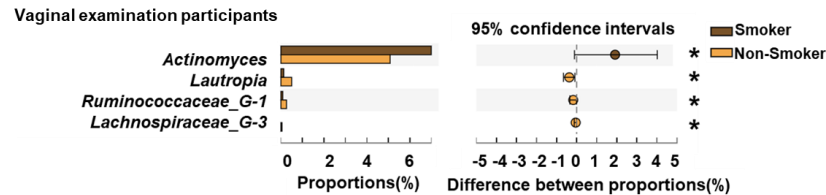
Results V



The smokers had significantly altered salivary microbiota beta diversity when compared with participants who never smoked.



Actinomyces was once again significantly increased among smokers compared to non-smokers.



Combining cytology and HPV infection testing with the oral *Actinomyces* abundance, the diagnostic ability improved to the classification of AUC = 0.945.

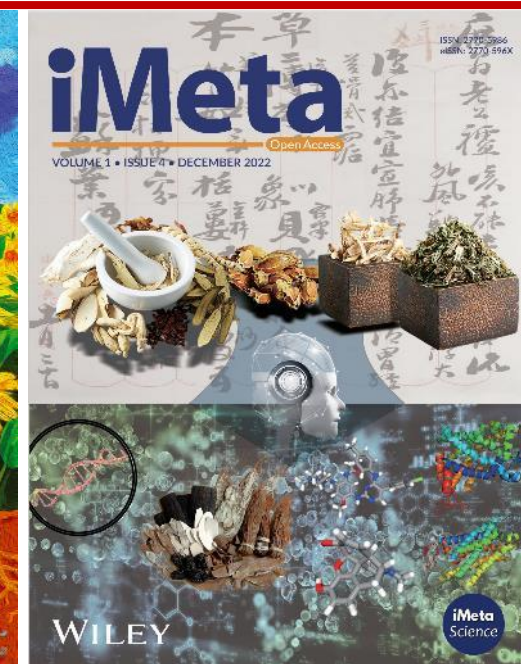


Summary

- The salivary microbiota diversity and richness were significantly decreased among the participants who underwent dysplasia screening.
- Significantly reduced salivary *Haemophilus* and *Alloprevotella*, as well as increased *Actinomyces*, demonstrated high specificity in identifying cervical dysplasia.
- Three salivary microbiota types were identified, with type 2 (higher abundance of *Prevotella* and *Actinomyces*) and type 3 (higher abundance of *Haemophilus*) mainly found in the pre- and post-dysplasia groups.
- Smoking affects the salivary microbiota and is associated with an increased risk of cervical dysplasia.

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