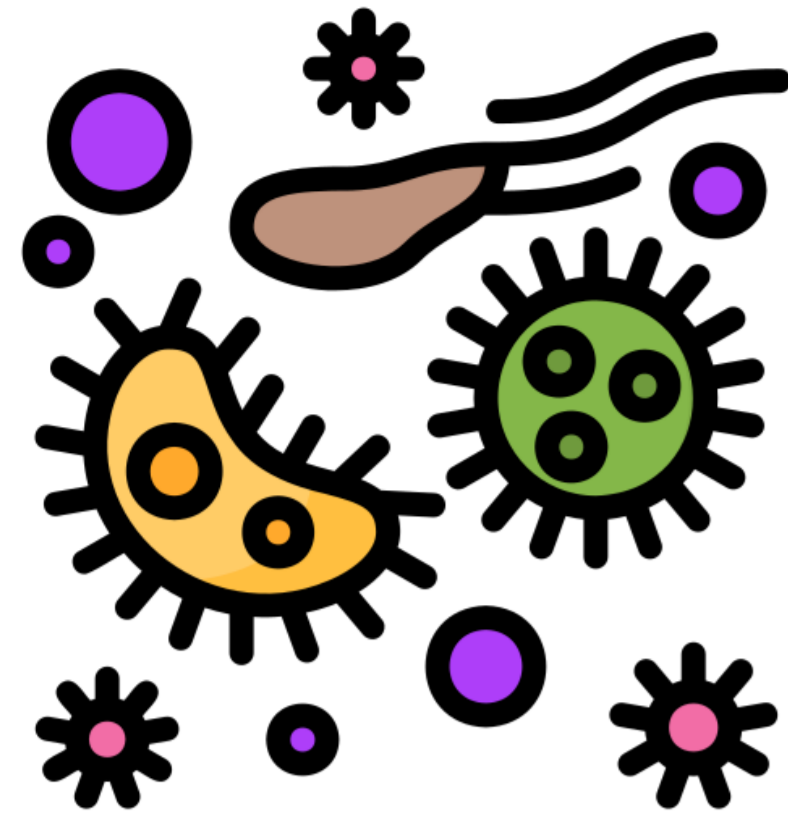# Childhood HIV Infection and Exposure Impacts Temporal and Spatial Assembly of the Supragingival Plaque Microbiome

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Introduction

The oral microbiome is composed of distinct microbial communities that colonize diverse ecological niches across the oral cavity. Unlike other densely populated human-associated microbial ecosystems, the oral microbiome is regularly exposed to the external environment and is thus thought to be less stable over time. Cross-sectional studies of the oral microbiome capture a glimpse of this temporal dynamism, yet a full appreciation of the relative stability, robusticity, and spatial structure of the oral environment is necessary to understand the role of microbial communities in promoting health or disease.

In this study we investigate the temporal and spatial stability of the oral microbiome in the context of tooth decay and HIV infection and exposure.
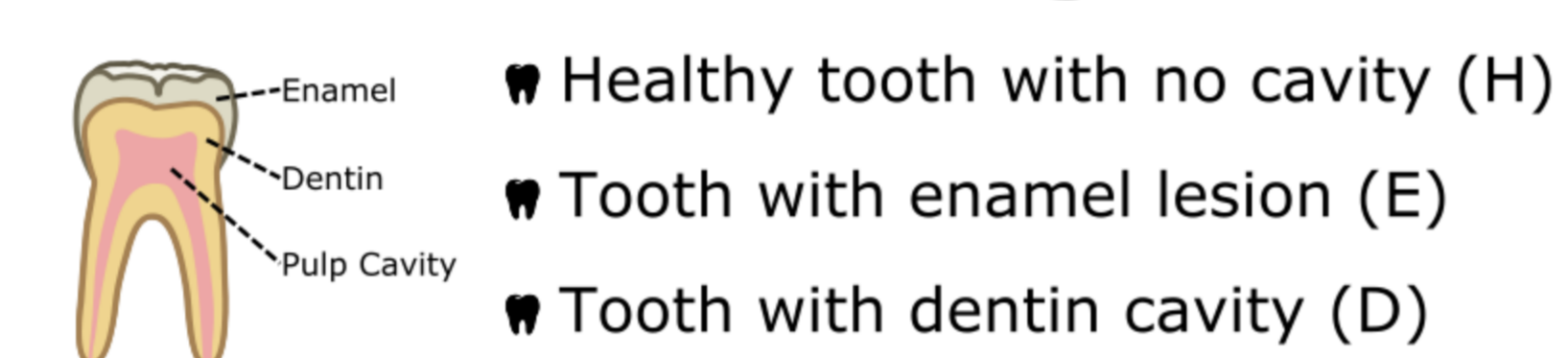
Methods

1,960 Supragingival Plaque Samples
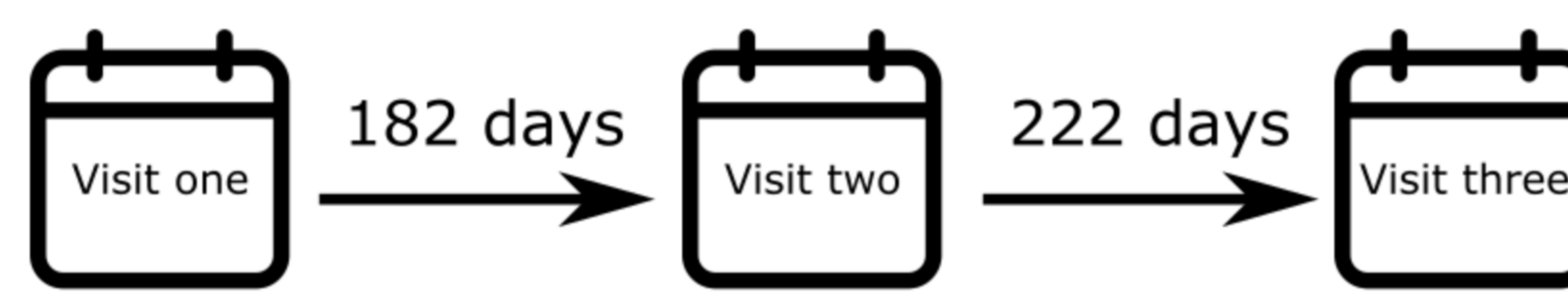
Three HIV Exposure Groups

Children living with HIV (HI)   Exposed but uninfected children (HEU)   Unexposed and uninfected children (HUU)

Three Tooth Health Categories

Enamel — Dentin — Pulp Cavity

- Healthy tooth with no cavity (H)
- Tooth with enamel lesion (E)
- Tooth with dentin cavity (D)

Three Clinical Visits

Visit one — 182 days → Visit two — 222 days → Visit three

HIV Infection Homogenizes the Oral Microbiome Across The Anterior and Posterior Dentition

- **The anterior and posterior teeth are inhabited by distinct microbial communities**

- **This distinction is clear in HUU and HEU children, but not among HI children**

- **Children living with HIV have reduced salivary flow and lower saliva pH which may homogenize the oral microbiome across the dentition**
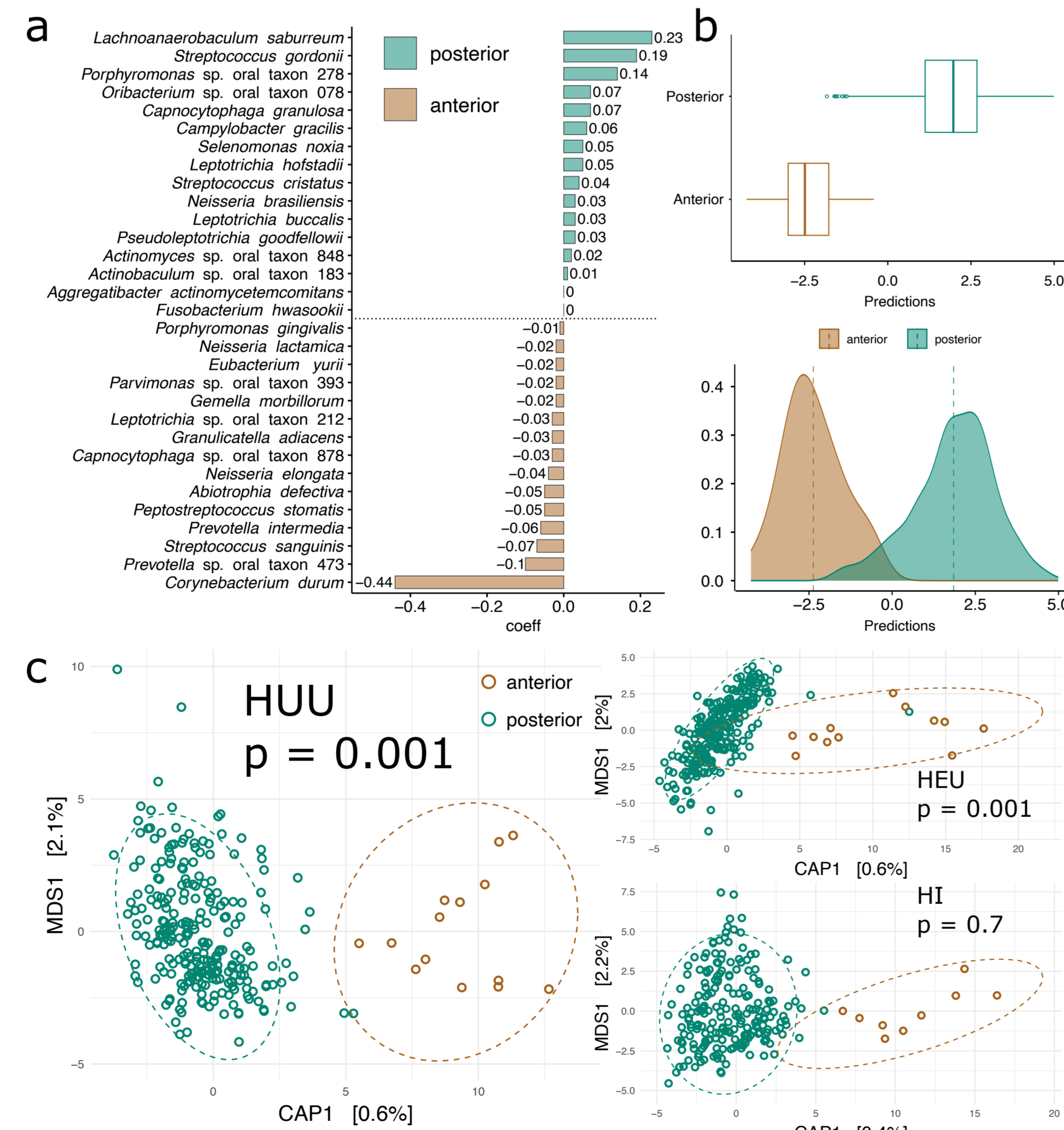

Figure 2: Community stratification of the anterior and posterior dentition is clear among HUU and HEU children, but is dismantled in HI children. (a) Microbial signature of the anterior and posterior teeth among all individuals independent of HIV status. The relative weight of each taxon is listed as its coefficient value (y axis). (b) Prediction box and density plots of the microbial signature model for anterior and posterior teeth driven by the balance of taxa listed in subplot a. (c) Capscale plots depicting the Aitchison distance of anterior and posterior teeth in HUU, HEU, and HI children. Significance between groups determined by PERMANOVA analysis and listed as Bonferroni adjusted p values. Only adult H-CF teeth were included in this analysis.
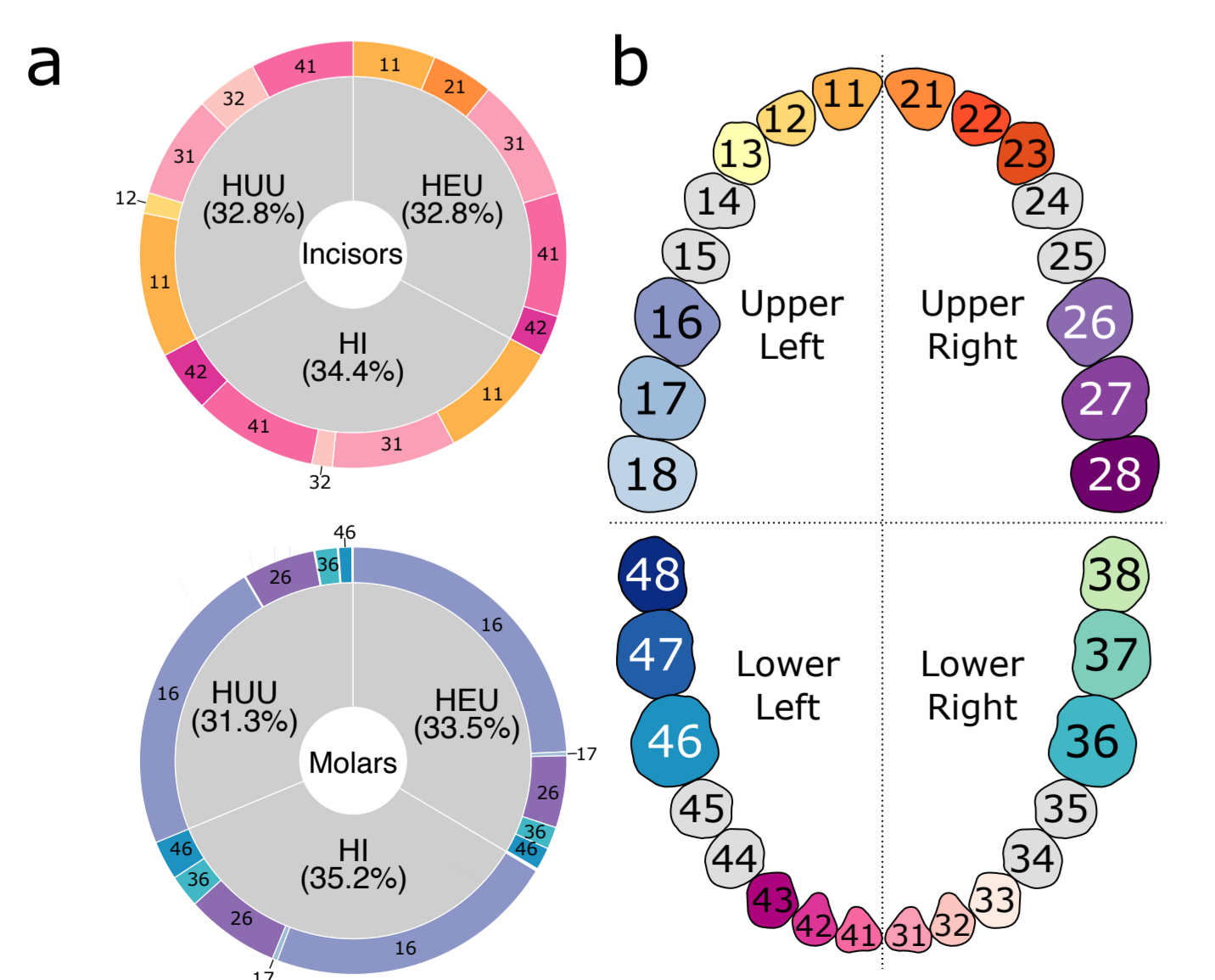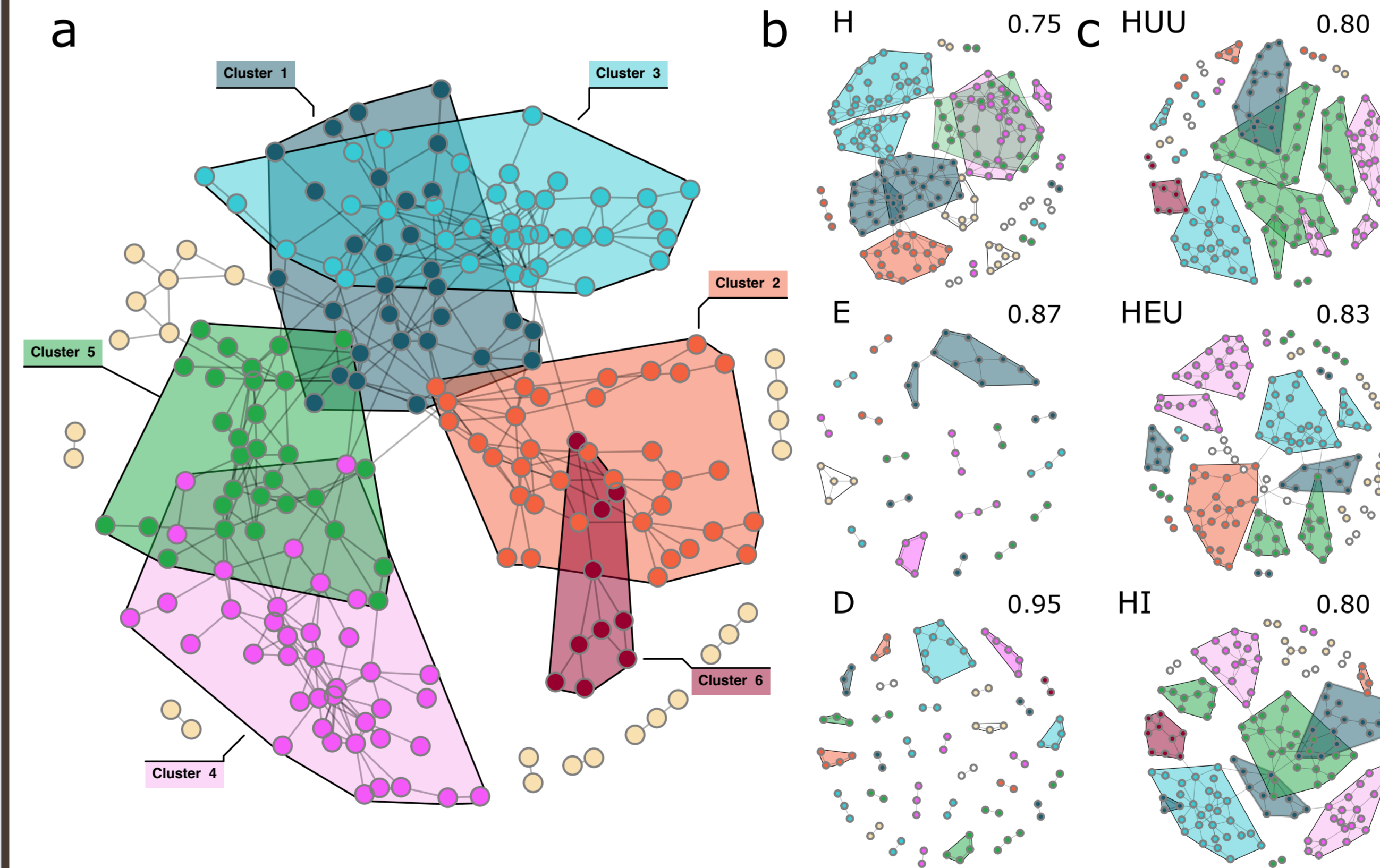

Figure 1: Sampling of each tooth across the dentition. (a) Proportion of each tooth by HIV group. Warm colors indicate anterior teeth, cool colors are posterior teeth.

HIV Infection and Exposure Characterized by Low Community Dynamism Over Time

- **The oral microbiome on a tooth from an HUU child on average changes more than the microbiome from HI or HEU children (Fig 3a & 3b)**

- **Community dynamics in HI children largely driven by changes in tooth health status (i.e., healthy   disease or vice versa)**

- **Low community dynamism in HI children associated with bacteria that cause cavities (i.e., Streptococcus mutans) (Fig 3d)**
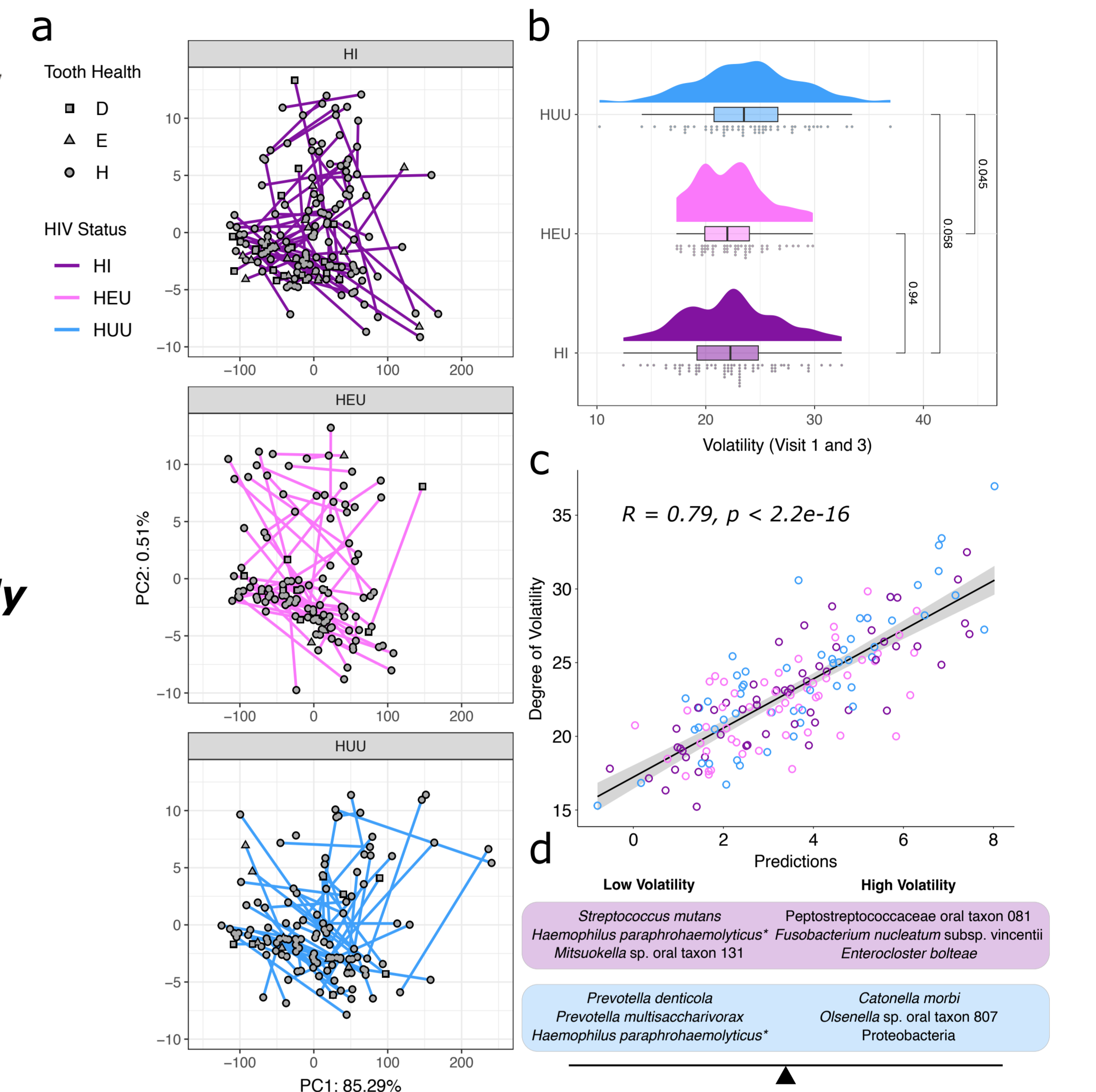
Figure 3: Community dynamism is higher in HUU as compared to HEU and HI children. (a) Principal coordinate plot of individual teeth collected from visit one and visit three for each of the three HIV status groups. Lines connect plaque samples collected from the same tooth and same individual. Point shapes indicate tooth health at time of sampling. (d) Distribution of community dynamism scores for each of the three groups at visit one versus visit three. (c) Predictions plot of the microbial signature model generated using all teeth with more than one sampling point. (d) The top three weighted taxa in the microbial signature model for high or low community dynamism for HI children (purple) and HUU children (blue). No significant taxa were identified for HEU children.

- **Despite having high community variability over time, all HIV status groups have modules of taxa that are shared consistently over all three visits (Fig 4c)**

- **High community modularity is strongly associated with later-stage caries disease (Fig 4b)**

- **While individual HUU and HI networks are similar in structure and modularity, HEU lacks cluster six and instead has robust representation of cluster 2**

Figure 4: Core association networks (CAN) highlighting modules of oral species that are consistently co-associated over all three visits. (a) Global core association network of all samples included in this study irrespective of HIV status or tooth health. Highlighted are six major clusters of co-associated taxa that are consistently co-associated across all three clinical visits. Clusters one, three, four, and five include a variety of commensal taxa while cluster six and two include potential and actual pathogenic taxa. Cluster six is composed almost entirely with cariogenic taxa while cluster two includes several important periodontal pathogens. (b) CANs of individual tooth health status groups. Increasing modularity scores indicate a loss of community cohesion as caries disease progresses. Clusters and individual nodes are colored according to their membership in the global CAN. (c) CANs of individual HIV status groups across all three visits. Clusters and individual nodes are colored according to their membership in the global CAN.