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Prediction of Early Childhood Caries Onset and Oral Microbiota

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Early childhood caries (ECC) is a chronic and destructive oral disease that disproportionately afflicts children living in poverty and with limited access to dental care (Casamassimo et al. 2009). The disease is multifactorial, with onset influenced by interactions between a cariogenic microbiota and host genetics, immunity and diet (Bowen et al. 2018; Pitts et al. 2017; Simon-Soro and Mira 2015). ECC has a significant impact on young children's quality of life and is difficult to treat effectively (Dye et al. 2007). Recent national data indicate that the prevalence of ECC in US preschool children is 24%, but ranges from 11% to 72% depending on household income, ethnicity, and demographic factors (Dye et al. 2015; Ismail et al. 2008; Kopycka-Kedzierawski et al. 2008; Phipps et al. 2012; Schroth et al. 2005).

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Competing interests

The authors declare that they have no competing interests.

Caries risk assessment (CRA) is an important component of dental caries management whereby clinicians assess the likelihood of future dental caries onset to inform preventive intervention measures (Fontana 2015; Twetman and Fontana 2009). A broad range of environmental, behavioral, and biological factors are associated with ECC risk, including diet, saliva composition, dental caries history, genetics, and socioeconomic status (Fontana 2015; Mejare et al. 2014). Combinations of these factors have been incorporated into numerous tools for CRA in dental practice. However, the causal impact and predictive accuracy of these risks remain uncertain, and none is considered adequate for clinical practice (Fontana 2015; Tellez et al. 2013).

Molecular and microbial biomarkers represent an additional source of dental caries risk assessment. Next generation sequencing technology has made it feasible to profile the composition of the oral microbiota, and advances in laboratory technologies have led to an increased understanding of the likely microbial contributions to the etiology and microbial ecology of ECC (Hajishengallis et al. 2017; Jiang et al. 2016; Luo et al. 2012). Previous work using these methods has identified an association of ECC with *S. mutans*, *Lactobacillus, Viellonella,* and *Prevotella* along with an increase in ECC severity due to co-infection of *S. mutans* and *Candida albicans* (Xiao et al. 2018). Although these cariogenic bacteria have been associated with ECC, they have not been demonstrated to be necessary or sufficient to cause the disease (Simon-Soro and Mira 2015).

We conducted a study (Grier et al. 2020) to identify oral microbiota taxa that are causal for ECC and to develop predictive models of ECC risk and prevention. Sequencing of 16S rRNA amplicons was employed for microbiome analysis of saliva samples that were collected at six-month intervals for 24 months from 56 initially caries-free children aged 1-3 years over the 2-year study period. Thirty-six children became caries-active and 20 remained caries-free over the study period. Taxonomic analysis determined that the top 12 most abundant genera accounted for 94.2% of the overall composition across all samples; *Streptococcus* was the most abundant (61.7% overall abundance), followed by *Veillonella* (9.2%), *Neisseria* (4.1%), *Granulicatella* (3.7%), and an unnamed genus of *Gemellaceae* (3.7%). ECC onset is thought to be the result of a progressive process, with increasingly cariogenic microbiota developing from healthy to pre-caries to caries-active states. We included all three states in our analysis model and used the caries-free state as the comparison. Using univariate tests of each species-level taxonomic unit and mixed-effects models that account for repeated sampling and the progressive nature of ECC, we identified five taxa – *Corynebacterium sp.*, *Selenomonas sp.*, *Kingella sp., Veillonella parvula*, and unclassified *Pseudomonas* –as differentially abundant between caries states by all our descriptive tests. Four of these taxa—*Corynebacterium sp.*, *Selenomonas sp.*, unclassified *Pseudomonas*, and *Veillonella parvula* – were detected in both the baseline-visit and all time point univariate tests as differing between pre-caries and healthy. Of these, all but *Selenomonas sp.* were also differentially abundant between caries-active and healthy, suggesting that they may be early and persistent biomarkers of an oral environment developing towards a cariogenic state.

We next developed machine learning models to predict ECC risks that are generalizable and sensitive up to two years prior to ECC onset, and become increasingly selective as the risk of

ECC onset becomes imminent. Two common machine learning models were used, random forest and gradient boosting classifiers, both capable of capturing interactions between features and non-linear relationships. Both models demonstrated significant predictive power based on either the enrollment visit or last visit prior to caries diagnosis, and were able to distinguish between those children with ECC onset during the 24 months following the initial visit and those who remained caries-free. Optimal performance was achieved with the random forest model when based on the last visit prior to caries, achieving an AUC (area under the curve, or concordance statistic) of 0.89 ($p < 0.001$) with an accuracy of 85.5% at the optimal threshold (sensitivity = 0.857 and specificity = 0.850). Three taxa were consistently predicted as important in these models, *Streptococcus sp., Rothia mucilaginosa*, and *Veillonella parvula*. Of these three taxa, the *Streptococcus sp.* and *Veillonella parvula* have long been associated with dental caries (Burne 2018; Cross et al. 2016; Simon-Soro and Mira 2015). The presence of these three robust bacterial biomarkers of ECC, with metabolic and ecological interdependence suggest a mutualistic community and ecological framework that promotes a caries-active state. More importantly, these findings demonstrate the oral microbiota signatures can serve as accurate and robust predictors of ECC risk in caries-free children.

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References

Bowen WH, Burne RA, Wu H, Koo H. 2018. Oral biofilms: Pathogens, matrix, and polymicrobial interactions in microenvironments. Trends Microbiol. 26(3):229–242. [PubMed: 29097091]

Burne RA. 2018. Getting to know “the known unknowns”: Heterogeneity in the oral microbiome. Adv Dent Res. 29(1):66–70. [PubMed: 29355408]

Casamassimo PS, Thikkurissy S, Edelstein BL, Maiorini E. 2009. Beyond the dmft: The human and economic cost of early childhood caries. J Am Dent Assoc. 140(6):650–657. [PubMed: 19491160]

Cross B, Faustoferri RC, Quivey RG Jr.2016. What are we learning and what can we learn from the human oral microbiome project?Curr Oral Health Rep. 3(1):56–63. [PubMed: 27152251]

Dye BA, Thornton-Evans G, Li X, Iafolla TJ. 2015. Dental caries and sealant prevalence in children and adolescents in the united states, 2011-2012. NCHS Data Brief. (191):1–8.

Fontana M2015. The clinical, environmental, and behavioral factors that foster early childhood caries: Evidence for caries risk assessment. Pediatr Dent. 37(3):217–225. [PubMed: 26063551]

Grier A, Myers JA, O’Connor TG, Quivey RG, Gill SR, Kopycka-Kedzierawski DT. 2020. Oral microbiota composition predicts early childhood caries onset. J Dent Res.22034520979926.

Hajishengallis E, Parsaei Y, Klein MI, Koo H. 2017. Advances in the microbial etiology and pathogenesis of early childhood caries. Mol Oral Microbiol. 32(1):24–34. [PubMed: 26714612]

Ismail AI, Lim S, Sohn W, Willem JM. 2008. Determinants of early childhood caries in low-income african american young children. Pediatr Dent. 30(4):289–296. [PubMed: 18767507]

Jiang S, Gao X, Jin L, Lo EC. 2016. Salivary microbiome diversity in caries-free and caries-affected children. Int J Mol Sci. 17(12).

Kopycka-Kedzierawski DT, Bell CH, Billings RJ. 2008. Prevalence of dental caries in early head start children as diagnosed using teledentistry. Pediatr Dent. 30(4):329–333. [PubMed: 18767513]

Luo AH, Yang DQ, Xin BC, Paster BJ, Qin J. 2012. Microbial profiles in saliva from children with and without caries in mixed dentition. Oral Dis. 18(6):595–601. [PubMed: 22458262]

Mejare I, Axelsson S, Dahlen G, Espelid I, Norlund A, Tranaeus S, Twetman S. 2014. Caries risk assessment. A systematic review. Acta Odontol Scand. 72(2):81–91. [PubMed: 23998481]

Phipps KR, Ricks TL, Manz MC, Blahut P. 2012. Prevalence and severity of dental caries among american indian and alaska native preschool children. J Public Health Dent. 72(3):208–215. [PubMed: 22515656]

Pitts NB, Zero DT, Marsh PD, Ekstrand K, Weintraub JA, Ramos-Gomez F, Tagami J, Twetman S, Tsakos G, Ismail A. 2017. Dental caries. Nat Rev Dis Primers. 3:17030. [PubMed: 28540937]

Schroth RJ, Smith PJ, Whalen JC, Lekic C, Moffatt ME. 2005. Prevalence of caries among preschool-aged children in a northern manitoba community. J Can Dent Assoc. 71(1):27. [PubMed: 15649337]

Simon-Soro A, Mira A. 2015. Solving the etiology of dental caries. Trends Microbiol. 23(2):76–82. [PubMed: 25435135]

Tellez M, Gomez J, Pretty I, Ellwood R, Ismail AI. 2013. Evidence on existing caries risk assessment systems: Are they predictive of future caries?Community Dent Oral Epidemiol. 41(1):67–78. [PubMed: 22978796]

Twetman S, Fontana M. 2009. Patient caries risk assessment. In: Pitts N, editor. Detection, assessment, diagnosis and monitoring of caries. Karger Publishers. p. 91–101.

Xiao J, Grier A, Faustoferri RC, Alzoubi S, Gill AL, Feng C, Liu Y, Quivey RG, Kopycka-Kedzierawski DT, Koo Het al.2018. Association between oral candida and bacteriome in children with severe ecc. J Dent Res. 97(13):1468–1476. [PubMed: 30049240]