Appendix Supplement A. Bayesian EH Model Building (Models 1, 2 and 3)

Bayesian EH Model Building

The modeling process progressed using two main approaches, each of which utilized a Bayesian framework. In the first approach, EH was modeled as the outcome and was formulated in three ways. The first formulation modeled EH as binary on the individual level. This collapsed the information on EH, which was originally scored for six regions for two teeth for each child, to a single value describing whether or not the child was scored as having EH on any region. More specifically, a child was considered negative for EH if the child had complete data and there were no positive scores for EH for all six regions. The child was scored positive for EH if any of the six regions were scored positive for EH, even if there were missing data for one or more regions. A child's EH status was considered missing if there were missing data for that child and the non-missing observations were all scored negative for EH. Logistic regression was then utilized to estimate the effects of covariates on EH (model 1).

$$y_i^{EH} \sim Bern(p_i);$$
$$\text{logit}(p_i) = x_i^t\beta + R_i \qquad \text{Model (1)}$$

with $\beta \sim N(0, \tau_\beta^{-1})$ and R_i consists of chosen random effects for the *i* th child.

The second outcome formulation maintained the EH information at the region level. We then used the binary data for a single region (incisal, middle, or cervical) as the outcome and again utilized logistic regression. For longitudinal covariates in this approach, we modeled specific 4 week time frames (the study visits) in an attempt to identify temporal factors that may be associated with EH development at specific tooth regions.

$$y_i^{EH} \sim Bern(p_i);$$
$$\text{logit}(p_i) = x_i^t\beta + R_i \qquad \text{Model (2)}$$

where y_i is the EH status for a single region for the *i* th child.

In the third outcome formulation for the first approach we summed the number of regions that were scored positive for EH to create an EH extent score. This score ranged from 0 to 6, although the highest score observed was 4. If any of the regions had missing values, the total EH score for that child was considered missing, as the sum of regions scored positive could not be calculated. This introduced 5 additional missing EH scores. Using these total EH scores, we utilized truncated Poisson regression with the distribution truncated at 7 to prevent any invalid scores.

$$y_i^{sc} \sim TPois(\mu_i; 7)$$
$$log(\mu_i) = x_i^t\beta + R_i \qquad \text{Model (3)}$$

Upon generating our outcomes of interest, we began exploratory analyses in which we assessed the associations of covariates with EH one at a time using two models: one with no other model terms, and another

with an uncorrelated subject-level random effect. The covariates included in these analyses fell into two general categories, longitudinal maternal covariates (iPTH, Ca, P, 25(OH)D and $1,25(OH)_2D$) and counts of infections; and time invariant covariates (maternal age, maternal race/ethnicity, and child cord blood iPTH, Ca, P, 25(OH)D and $1,25(OH)_2D$). Within the longitudinal maternal covariates, there were both continuous covariates and binary covariates. For continuous longitudinal covariates, such as 25(OH)D, iPTH, and Ca, we considered various summary methods that included the mean, median, change value for multiple time frames, change + baseline, maximum, and maximum + baseline. For binary longitudinal covariates, such as indicators for acid reflux and infections at each visit, we considered summarizing the data as either indicators over the course of the study or counts of the event in question. Apart from longitudinal maternal covariates, we had a number of time invariant covariates that did not require further summation.

With the parent study an RCT of vitamin D_3 we were particularly interested in the association of EH with vitamin D_3, both the substrate and active forms. While the RCT for which the data were gathered focused on the effect of vitamin D_3 supplementation, we focused on the vitamin D related biological factors involved in EH development. For that reason, we assessed the relationship between EH and vitamin D_3 using not only by treatment assignments for vitamin D_3 supplementation, but also for the serum circulating 25(OH)D and $1,25(OH)_2D$ concentrations.

Following exploratory analyses, we decided to use model 3 for further investigation and generated a full model that included covariates with demonstrated associations at the 0.05 level and others (maternal age, race/ethnicity, maternal median 25(OH)D status, and body mass index (BMI) at 12 weeks) that we decided *a priori* required adjustment. In addition to these covariates, an uncorrelated subject-level random effect was included to account for unmeasured heterogeneity among the study population. We then performed backwards model selection in which covariates with small coefficient values and large 95% credible intervals were removed one at a time. At each stage of selection, the deviance information criterion (DIC) (Spiegelhalter et al. 2014) was calculated. Model selection stopped when the only model terms remaining were those with significant associations with the outcome and those that required adjustment. A final model (Table 3, Model 3) was then chosen using DIC as a primary criterion and parsimony as a secondary criterion.