Appendix

Toward preventing enamel hypoplasia: Modeling maternal and neonatal biomarkers of human calcium homeostasis

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Appendix Table 1. Week-level values of maternal covariates for calcium homeostasis by maternal treatment group, median 25(OH)D status and child EH and extent

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Treatment Group | | | Median 25(OH)D Status | | Child EH Status | | Child EH Extent Group | | |
| Variable | All | 400 IU  (n=55) | 2000 IU  (n=51) | 4000 IU  (n=55) | Deficient/  Insufficient  (n=58) | Sufficient/  Optimal  (n=103) | No EH (n=85) | EH (n=60) | No EH (n=85) | EH=1 (n=23) | EH>1 (n=32) |
|
| 25(OH)D |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 34.5 | 30.4 | 34.1 | 39.0 | 22.5 | 41.1 | 34.1 | 36.4 | 34.1 | 39.5 | 34.7 |
| (14.7) | (13.7) | (13.7) | (15.3) | (9.3) | (12.7) | (14.7) | (14.9) | (14.7) | (14.9) | (14.2) |
| Week 12 | 22.3 | 24.3 | 20.5 | 22.0 | 15.5 | 26.1 | 21.8 | 23.7 | 21.8 | 27.8 | 21.8 |
| (10.2) | (12.8) | (8.0) | (8.9) | (6.0) | (10.1) | (9.7) | (11.3) | (9.7) | (13.1) | (9.4) |
| Week 16 | 32.0 | 31.1 | 31.5 | 33.5 | 21.9 | 37.7 | 31.9 | 34.3 | 31.9 | 36.1 | 33.0 |
| (11.3) | (12.3) | (10.1) | (11.3) | (8.3) | (8.4) | (11.2) | (11.1) | (11.2) | (13.0) | (9.7) |
| Week 20 | 35.0 | 32.4 | 33.2 | 39.1 | 23.8 | 40.9 | 34.3 | 37.3 | 34.3 | 41.5 | 35.7 |
| (12.8) | (14.0) | (10.4) | (12.8) | (9.2) | (10.3) | (11.9) | (14.1) | (11.9) | (14.0) | (13.0) |
| Week 24 | 36.6 | 30.6 | 36.3 | 42.7 | 22.6 | 44.2 | 36.5 | 38.4 | 36.5 | 39.7 | 37.3 |
| (13.9) | (13.2) | (12.2) | (13.7) | (8.5) | (9.8) | (14.7) | (12.9) | (14.7) | (12.0) | (13.4) |
| Week 28 | 37.5 | 30.8 | 38.0 | 43.7 | 24.0 | 44.8 | 36.6 | 39.6 | 36.6 | 42.6 | 37.8 |
| (14.3) | (12.3) | (13.5) | (14.4) | (8.8) | (11.1) | (14.2) | (15.0) | (14.2) | (15.5) | (14.5) |
| Week 32 | 40.1 | 33.0 | 40.2 | 46.9 | 25.3 | 48.6 | 39.5 | 41.8 | 39.5 | 45.4 | 39.7 |
| (15.7) | (16.0) | (14.2) | (13.9) | (10.8) | (11.2) | (16.3) | (15.5) | (16.3) | (15.4) | (14.4) |
| Week 36 | 39.1 | 31.1 | 40.0 | 46.0 | 24.7 | 46.9 | 39.3 | 41.1 | 39.3 | 44.2 | 38.8 |
| (16.0) | (13.6) | (16.1) | (14.9) | (9.8) | (13.1) | (15.9) | (16.3) | (15.9) | (15.0) | (17.0) |
| 1,25(OH)2D |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 102.0 | 93.3 | 105.6 | 107.3 | 90.6 | 108.2 | 101.0 | 104.6 | 101.0 | 111.1 | 100.8 |
| (40.5) | (33.4) | (43.8) | (42.3) | (32.6) | (43.0) | (40.1) | (41.8) | (40.1) | (49.3) | (35.3) |
| Week 12 | 73.2 | 75.6 | 73.9 | 70.2 | 69.5 | 75.3 | 73.2 | 73.5 | 73.2 | 74.3 | 75.2 |
| (23.6) | (24.3) | (23.4) | (23.3) | (22.0) | (24.3) | (26.8) | (20.7) | (26.8) | (19.9) | (21.6) |
| Week 16 | 89.7 | 85.7 | 87.0 | 96.5 | 83.1 | 93.5 | 88.3 | 94.0 | 88.3 | 95.1 | 94.2 |
| (30.3) | (28.6) | (31.7) | (30.0) | (31.3) | (29.2) | (30.9) | (31.2) | (30.9) | (33.9) | (30.8) |
| Week 20 | 100.8 | 93.2 | 100.8 | 108.4 | 90.7 | 106.2 | 97.8 | 107.2 | 97.8 | 119.4 | 99.3 |
| (35.3) | (31.3) | (35.4) | (37.9) | (30.4) | (36.7) | (31.8) | (39.0) | (31.8) | (48.0) | (29.8) |
| Week 24 | 102.5 | 92.3 | 108.3 | 107.2 | 89.0 | 110.1 | 103.2 | 101.5 | 103.2 | 106.0 | 96.3 |
| (34.9) | (31.6) | (36.5) | (34.9) | (28.6) | (36.0) | (31.8) | (39.6) | (31.8) | (44.8) | (34.6) |
| Week 28 | 114.6 | 103.7 | 120.9 | 119.5 | 101.4 | 121.8 | 113.7 | 118.1 | 113.7 | 132.6 | 108.5 |
| (45.5) | (40.1) | (44.6) | (50.4) | (36.3) | (48.5) | (43.2) | (48.1) | (43.2) | (66.5) | (30.8) |
| Week 32 | 118.0 | 99.6 | 127.3 | 127.7 | 98.4 | 129.4 | 115.5 | 122.3 | 115.5 | 128.0 | 118.3 |
| (46.4) | (32.2) | (57.2) | (42.6) | (28.9) | (50.8) | (50.4) | (43.3) | (50.4) | (48.6) | (39.1) |
| Week 36 | 117.4 | 104.6 | 124.0 | 124.1 | 104.7 | 124.2 | 116.4 | 120.0 | 116.4 | 127.2 | 117.8 |
| (41.7) | (35.7) | (43.1) | (43.9) | (36.5) | (43.0) | (40.5) | (44.7) | (40.5) | (50.5) | (41.0) |
| iPTH |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 18.5 | 18.9 | 18.2 | 18.3 | 21.5 | 16.9 | 17.8 | 19.7 | 17.8 | 18.7 | 20.9 |
| (10.5) | (10.8) | (10.5) | (10.3) | (10.9) | (10.0) | (10.7) | (10.9) | (10.7) | (9.0) | (12.2) |
| Week 12 | 18.8 | 18.1 | 18.3 | 20.0 | 20.0 | 18.1 | 18.8 | 19.0 | 18.8 | 19.7 | 17.8 |
| (10.6) | (10.0) | (9.1) | (12.3) | (9.6) | (11.0) | (12.0) | (9.3) | (12.0) | (10.8) | (7.9) |
| Week 16 | 16.5 | 15.7 | 17.5 | 16.5 | 18.5 | 15.4 | 16.7 | 16.5 | 16.7 | 16.0 | 17.8 |
| (9.2) | (8.2) | (11.1) | (8.3) | (7.4) | (9.9) | (10.0) | (8.7) | (10.0) | (8.1) | (9.2) |
| Week 20 | 16.8 | 17.0 | 15.5 | 17.9 | 19.2 | 15.6 | 15.2 | 18.7 | 15.2 | 19.6 | 18.4 |
| (9.2) | (8.4) | (8.8) | (10.4) | (8.2) | (9.5) | (8.5) | (9.7) | (8.5) | (10.1) | (9.9) |
| Week 24 | 18.0 | 17.9 | 18.5 | 17.8 | 21.2 | 16.3 | 17.6 | 19.4 | 17.6 | 17.3 | 21.6 |
| (10.3) | (9.0) | (12.3) | (9.5) | (12.1) | (8.8) | (9.2) | (12.5) | (9.2) | (8.5) | (15.3) |
| Week 28 | 20.3 | 22.0 | 19.5 | 19.3 | 24.7 | 18.0 | 19.0 | 22.4 | 19.0 | 20.2 | 25.3 |
| (11.4) | (11.0) | (11.4) | (11.9) | (11.2) | (10.9) | (10.2) | (13.7) | (10.2) | (9.0) | (15.9) |
| Week 32 | 18.7 | 20.5 | 17.5 | 18.0 | 22.2 | 16.7 | 17.0 | 21.5 | 17.0 | 19.3 | 23.8 |
| (9.5) | (10.7) | (8.2) | (9.4) | (9.6) | (8.9) | (9.2) | (10.1) | (9.2) | (6.2) | (12.1) |
| Week 36 | 20.5 | 21.5 | 21.3 | 18.6 | 25.0 | 18.0 | 20.5 | 20.5 | 20.5 | 18.4 | 22.7 |
| (12.7) | (16.0) | (11.5) | (9.5) | (15.2) | (10.3) | (14.2) | (11.5) | (14.2) | (9.9) | (12.7) |
| Serum Calcium |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 9.0 | 9.0 | 8.9 | 9.0 | 8.9 | 9.0 | 9.0 | 8.9 | 9.0 | 8.9 | 9.0 |
| (0.3) | (0.3) | (0.4) | (0.4) | (0.3) | (0.4) | (0.3) | (0.4) | (0.3) | (0.3) | (0.4) |
| Week 12 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 | 9.2 |
| (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.4) |
| Week 16 | 9.1 | 9.1 | 9.0 | 9.1 | 9.1 | 9.0 | 9.0 | 9.1 | 9.0 | 9.1 | 9.1 |
| (0.3) | (0.3) | (0.3) | (0.4) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.4) |
| Week 20 | 9.0 | 9.0 | 9.0 | 9.0 | 9.0 | 9.0 | 9.0 | 8.9 | 9.0 | 8.9 | 9.0 |
| (0.4) | (0.4) | (0.4) | (0.3) | (0.4) | (0.3) | (0.4) | (0.3) | (0.4) | (0.2) | (0.4) |
| Week 24 | 8.9 | 8.9 | 8.9 | 9.0 | 8.8 | 8.9 | 8.9 | 8.9 | 8.9 | 8.8 | 9.0 |
| (0.3) | (0.3) | (0.4) | (0.3) | (0.3) | (0.3) | (0.3) | (0.4) | (0.3) | (0.2) | (0.4) |
| Week 28 | 8.8 | 8.8 | 8.8 | 8.8 | 8.8 | 8.8 | 8.9 | 8.8 | 8.9 | 8.8 | 8.8 |
| (0.4) | (0.3) | (0.3) | (0.4) | (0.3) | (0.4) | (0.3) | (0.4) | (0.3) | (0.3) | (0.5) |
| Week 32 | 8.9 | 8.9 | 8.8 | 9.0 | 8.8 | 8.9 | 8.9 | 8.8 | 8.9 | 8.9 | 8.8 |
| (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.3) | (0.2) | (0.4) |
| Week 36 | 8.9 | 8.9 | 8.9 | 9.0 | 8.8 | 8.9 | 8.9 | 8.9 | 8.9 | 8.9 | 8.9 |
| (0.3) | (0.3) | (0.3) | (0.4) | (0.3) | (0.4) | (0.3) | (0.3) | (0.3) | (0.4) | (0.3) |
| Serum Phosphorus |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 3.9 | 3.9 | 4.0 | 3.9 | 3.9 | 4.0 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 |
| (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.5) | (0.6) | (0.6) | (0.5) |
| Week 12 | 4.0 | 4.0 | 4.0 | 3.9 | 3.9 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 |
| (0.5) | (0.5) | (0.5) | (0.6) | (0.5) | (0.5) | (0.6) | (0.5) | (0.6) | (0.4) | (0.5) |
| Week 16 | 4.0 | 4.0 | 4.1 | 3.9 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 3.9 | 4.0 |
| (0.6) | (0.6) | (0.6) | (0.5) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.5) | (0.6) |
| Week 20 | 3.9 | 4.0 | 3.9 | 3.8 | 3.9 | 3.9 | 4.0 | 3.8 | 4.0 | 3.7 | 3.9 |
| (0.5) | (0.5) | (0.5) | (0.6) | (0.5) | (0.5) | (0.6) | (0.5) | (0.6) | (0.6) | (0.5) |
| Week 24 | 3.9 | 3.9 | 3.8 | 4.0 | 3.8 | 4.0 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 |
| (0.5) | (0.5) | (0.6) | (0.5) | (0.5) | (0.6) | (0.5) | (0.6) | (0.5) | (0.6) | (0.5) |
| Week 28 | 3.7 | 3.7 | 3.9 | 3.7 | 3.7 | 3.8 | 3.7 | 3.8 | 3.7 | 3.7 | 3.7 |
| (0.6) | (0.5) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.6) | (0.5) |
| Week 32 | 3.9 | 3.9 | 4.0 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 |
| (0.5) | (0.6) | (0.5) | (0.5) | (0.5) | (0.5) | (0.5) | (0.5) | (0.5) | (0.6) | (0.5) |
| Week 36 | 4.0 | 4.0 | 4.1 | 4.0 | 3.9 | 4.1 | 4.0 | 4.1 | 4.0 | 4.1 | 4.2 |
| (0.7) | (0.7) | (0.8) | (0.5) | (0.7) | (0.6) | (0.7) | (0.5) | (0.7) | (0.6) | (0.52) |

Appendix Table 2. Week-level longitudinal maternal medication use by maternal treatment group, median 25(OH)D status and child EH and extent

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Treatment Group | | | Median 25(OH)D Status | | Child EH Status | | Child EH Extent Group | | |
| Variable | All | 400 IU  (n=55) | 2000 IU  (n=51) | 4000 IU  (n=55) | Deficient/  Insufficient  (n=58) | Sufficient/  Optimal  (n=103) | No EH (n=85) | EH (n=60) | No EH (n=85) | EH=1 (n=23) | EH>1 (n=32) |
|
| Reflux Meds |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 93 | 32 | 27 | 34 | 32 | 61 | 53 | 30 | 53 | 10 | 18 |
| (57.8) | (58.2) | (52.9) | (61.8) | (55.2) | (59.2) | (62.4) | (50.0) | (62.4) | (43.5) | (56.3) |
| Week 12 | 22 | 7 | 7 | 8 | 9 | 13 | 12 | 7 | 12 | 3 | 4 |
| (13.7) | (12.7) | (13.7) | (14.5) | (15.5) | (12.6) | (14.1) | (11.7) | (14.1) | (13.0) | (12.5) |
| Week 16 | 36 | 10 | 12 | 14 | 12 | 24 | 23 | 10 | 23 | 3 | 6 |
| (22.4) | (18.2) | (23.5) | (25.5) | (20.7) | (23.3) | (27.1) | (16.7) | (27.1) | (13.0) | (18.8) |
| Week 20 | 33 | 14 | 8 | 11 | 7 | 26 | 21 | 11 | 21 | 4 | 6 |
| (20.5) | (25.5) | (15.7) | (20.0) | (12.1) | (25.2) | (24.7) | (18.3) | (24.7) | (17.4) | (18.8) |
| Week 24 | 42 | 15 | 11 | 16 | 8 | 34 | 27 | 14 | 27 | 5 | 7 |
| (26.1) | (27.3) | (21.6) | (29.1) | (13.8) | (33.0) | (31.8) | (23.3) | (31.8) | (21.7) | (21.9) |
| Week 28 | 49 | 19 | 11 | 19 | 14 | 35 | 29 | 16 | 29 | 5 | 10 |
| (30.4) | (34.5) | (21.6) | (34.5) | (24.1) | (34.0) | (34.1) | (26.7) | (34.1) | (21.7) | (31.3) |
| Week 32 | 50 | 17 | 14 | 19 | 15 | 35 | 30 | 19 | 30 | 6 | 12 |
| (31.1) | (30.9) | (27.5) | (34.5) | (25.9) | (34.0) | (35.3) | (31.7) | (35.3) | (26.1) | (37.5) |
| Week 36 | 55 | 17 | 19 | 19 | 15 | 40 | 33 | 19 | 33 | 7 | 12 |
| (34.2) | (30.9) | (37.3) | (34.5) | (25.9) | (38.8) | (38.8) | (31.7) | (38.8) | (30.4) | (37.5) |
| Antacids |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 84 | 26 | 26 | 32 | 26 | 58 | 47 | 29 | 47 | 9 | 18 |
| (52.2) | (47.3) | (51.0) | (58.2) | (44.8) | (56.3) | (55.3) | (48.3) | (55.3) | (39.1) | (56.3) |
| Week 12 | 16 | 4 | 6 | 6 | 7 | 9 | 10 | 4 | 10 | 1 | 3 |
| (9.9) | (7.3) | (11.8) | (10.9) | (12.1) | (8.7) | (11.8) | (6.7) | (11.8) | (4.3) | (9.4) |
| Week 16 | 32 | 10 | 12 | 10 | 10 | 22 | 20 | 9 | 20 | 3 | 5 |
| (19.9) | (18.2) | (23.5) | (18.2) | (17.2) | (21.4) | (23.5) | (15.0) | (23.5) | (13.0) | (15.6) |
| Week 20 | 27 | 11 | 7 | 9 | 7 | 20 | 18 | 8 | 18 | 3 | 4 |
| (16.8) | (20.0) | (13.7) | (16.4) | (12.1) | (19.4) | (21.2) | (13.3) | (21.2) | (13.0) | (12.5) |
| Week 24 | 37 | 12 | 11 | 14 | 7 | 30 | 25 | 11 | 25 | 4 | 5 |
| (23.0) | (21.8) | (21.6) | (25.5) | (12.1) | (29.1) | (29.4) | (18.3) | (29.4) | (17.4) | (15.6) |
| Week 28 | 40 | 13 | 9 | 18 | 10 | 30 | 24 | 13 | 24 | 4 | 8 |
| (24.8) | (23.6) | (17.6) | (32.7) | (17.2) | (29.1) | (28.2) | (21.7) | (28.2) | (17.4) | (25.0) |
| Week 32 | 38 | 12 | 10 | 16 | 12 | 26 | 25 | 12 | 25 | 5 | 7 |
| (23.6) | (21.8) | (19.6) | (29.1) | (20.7) | (25.2) | (29.4) | (20.0) | (29.4) | (21.7) | (21.9) |
| Week 36 | 49 | 14 | 17 | 18 | 13 | 36 | 31 | 15 | 31 | 6 | 9 |
| (30.4) | (25.5) | (33.3) | (32.7) | (22.4) | (35.0) | (36.5) | (25.0) | (36.5) | (26.1) | (28.1) |
| H2 Blocker |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 13 | 4 | 4 | 5 | 3 | 10 | 7 | 5 | 7 | 1 | 4 |
| (8.1) | (7.3) | (7.8) | (9.1) | (5.2) | (9.7) | (8.2) | (8.3) | (8.2) | (4.3) | (12.5) |
| Week 12 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 |
| (0.6) | (0.0) | (0.0) | (1.8) | (0.0) | (1.0) | (1.2) | (0.0) | (1.2) | (0.0) | (0.0) |
| Week 16 | 3 | 1 | 0 | 2 | 1 | 2 | 3 | 0 | 3 | 0 | 0 |
| (1.9) | (1.8) | (0.0) | (3.6) | (1.7) | (1.9) | (3.5) | (0.0) | (3.5) | (0.0) | (0.0) |
| Week 20 | 4 | 2 | 1 | 1 | 0 | 4 | 2 | 2 | 2 | 1 | 1 |
| (2.5) | (3.6) | (2.0) | (1.8) | (0.0) | (3.9) | (2.4) | (3.3) | (2.4) | (4.3) | (3.1) |
| Week 24 | 3 | 2 | 1 | 0 | 0 | 3 | 2 | 1 | 2 | 1 | 0 |
| (1.9) | (3.6) | (2.0) | (0.0) | (0.0) | (2.9) | (2.4) | (1.7) | (2.4) | (4.3) | (0.0) |
| Week 28 | 7 | 4 | 2 | 1 | 2 | 5 | 4 | 2 | 4 | 1 | 1 |
| (4.3) | (7.3) | (3.9) | (1.8) | (3.4) | (4.9) | (4.7) | (3.3) | (4.7) | (4.3) | (3.1) |
| Week 32 | 9 | 3 | 4 | 2 | 1 | 8 | 5 | 4 | 5 | 1 | 3 |
| (5.6) | (5.5) | (7.8) | (3.6) | (1.7) | (7.8) | (5.9) | (6.7) | (5.9) | (4.3) | (9.4) |
| Week 36 | 7 | 2 | 4 | 1 | 0 | 7 | 5 | 2 | 5 | 1 | 1 |
| (4.3) | (3.6) | (7.8) | (1.8) | (0.0) | (6.8) | (5.9) | (3.3) | (5.9) | (4.3) | (3.1) |
| Proton Pump Inhibitor |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 7 | 1 | 1 | 5 | 0 | 7 | 4 | 3 | 4 | 0 | 3 |
| (4.3) | (1.8) | (2.0) | (9.1) | (0.0) | (6.8) | (4.7) | (5.0) | (4.7) | (0.0) | (9.4) |
| Week 12 | 2 | 0 | 0 | 2 | 0 | 2 | 1 | 1 | 1 | 0 | 1 |
| (1.2) | (0.0) | (0.0) | (3.6) | (0.0) | (1.9) | (1.2) | (1.7) | (1.2) | (0.0) | (3.1) |
| Week 16 | 3 | 1 | 0 | 2 | 0 | 3 | 2 | 1 | 2 | 0 | 1 |
| (1.9) | (1.8) | (0.0) | (3.6) | (0.0) | (2.9) | (2.4) | (1.7) | (2.4) | (0.0) | (3.1) |
| Week 20 | 3 | 1 | 1 | 1 | 0 | 3 | 2 | 1 | 2 | 0 | 1 |
| (1.9) | (1.8) | (2.0) | (1.8) | (0.0) | (2.9) | (2.4) | (1.7) | (2.4) | (0.0) | (3.1) |
| Week 24 | 4 | 1 | 1 | 2 | 0 | 4 | 2 | 2 | 2 | 0 | 2 |
| (2.5) | (1.8) | (2.0) | (3.6) | (0.0) | (3.9) | (2.4) | (3.3) | (2.4) | (0.0) | (6.3) |
| Week 28 | 6 | 1 | 1 | 4 | 0 | 6 | 3 | 3 | 3 | 0 | 3 |
| (3.7) | (1.8) | (2.0) | (7.3) | (0.0) | (5.8) | (3.5) | (5.0) | (3.5) | (0.0) | (9.4) |
| Week 32 | 6 | 1 | 1 | 4 | 0 | 6 | 4 | 2 | 4 | 0 | 2 |
| (3.7) | (1.8) | (2.0) | (7.3) | (0.0) | (5.8) | (4.7) | (3.3) | (4.7) | (0.0) | (6.3) |
| Week 36 | 5 | 1 | 1 | 3 | 0 | 5 | 3 | 2 | 3 | 0 | 2 |
| (3.1) | (1.8) | (2.0) | (5.5) | (0.0) | (4.9) | (3.5) | (3.3) | (3.5) | (0.0) | (6.3) |
| Antibiotics |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 46 | 15 | 16 | 15 | 25 | 19 | 27 | 13 | 27 | 6 | 6 |
| (28.6) | (27.3) | (31.4) | (27.3) | (43.1) | (18.4) | (31.8) | (21.7) | (31.8) | (26.1) | (18.8) |
| Week 12 | 16 | 4 | 6 | 6 | 12 | 4 | 8 | 4 | 8 | 1 | 3 |
| (9.9) | (7.3) | (11.8) | (10.9) | (20.7) | (3.9) | (9.4) | (6.7) | (9.4) | (4.3) | (9.4) |
| Week 16 | 16 | 5 | 6 | 5 | 6 | 10 | 10 | 6 | 10 | 3 | 2 |
| (9.9) | (9.1) | (11.8) | (9.1) | (10.3) | (9.7) | (11.8) | (10.0) | (11.8) | (13.0) | (6.3) |
| Week 20 | 4 | 2 | 1 | 1 | 3 | 1 | 3 | 1 | 3 | 0 | 0 |
| (2.5) | (3.6) | (2.0) | (1.8) | (5.2) | (1.0) | (3.5) | (1.7) | (3.5) | (0.0) | (0.0) |
| Week 24 | 5 | 3 | 1 | 1 | 2 | 3 | 3 | 2 | 3 | 1 | 1 |
| (3.1) | (5.5) | (2.0) | (1.8) | (3.4) | (2.9) | (3.5) | (3.3) | (3.5) | (4.3) | (3.1) |
| Week 28 | 6 | 3 | 1 | 2 | 2 | 4 | 5 | 1 | 5 | 1 | 0 |
| (3.7) | (5.5) | (2.0) | (3.6) | (3.4) | (3.9) | (5.9) | (1.7) | (5.9) | (4.3) | (0.0) |
| Week 32 | 6 | 4 | 1 | 1 | 6 | 0 | 5 | 1 | 5 | 0 | 0 |
| (3.7) | (7.3) | (2.0) | (1.8) | (10.3) | (0.0) | (5.9) | (1.7) | (5.9) | (0.0) | (0.0) |
| Week 36 | 7 | 3 | 2 | 2 | 4 | 2 | 4 | 3 | 4 | 2 | 1 |
| (4.3) | (5.5) | (3.9) | (3.6) | (6.9) | (2.9) | (4.7) | (5.0) | (4.7) | (8.7) | (3.1) |
| Antifungals |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 27 | 8 | 8 | 11 | 7 | 17 | 17 | 5 | 17 | 2 | 2 |
| (16.8) | (14.5) | (15.7) | (20.0) | (12.1) | (16.5) | (20.0) | (8.3) | (20.0) | (8.7) | (6.3) |
| Week 12 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| (0.6) | (0.0) | (2.0) | (0.0) | (0.0) | (1.0) | (0.0) | (1.7) | (0.0) | (0.0) | (3.1) |
| Week 16 | 5 | 1 | 0 | 4 | 3 | 2 | 2 | 2 | 2 | 0 | 1 |
| (3.1) | (1.8) | (0.0) | (7.3) | (5.2) | (1.9) | (2.4) | (3.3) | (2.4) | (0.0) | (3.1) |
| Week 20 | 7 | 5 | 1 | 1 | 3 | 4 | 6 | 1 | 6 | 0 | 1 |
| (4.3) | (9.1) | (2.0) | (1.8) | (5.2) | (3.9) | (7.1) | (1.7) | (7.1) | (0.0) | (3.1) |
| Week 24 | 6 | 1 | 2 | 3 | 2 | 4 | 5 | 1 | 5 | 0 | 0 |
| (3.7) | (1.8) | (3.9) | (5.5) | (3.4) | (3.9) | (5.9) | (1.7) | (5.9) | (0.0) | (0.0) |
| Week 28 | 4 | 2 | 1 | 1 | 0 | 4 | 3 | 1 | 3 | 1 | 0 |
| (2.5) | (3.6) | (2.0) | (1.8) | (0.0) | (3.9) | (3.5) | (1.7) | (3.5) | (4.3) | (0.0) |
| Week 32 | 6 | 3 | 2 | 1 | 2 | 4 | 5 | 1 | 5 | 1 | 0 |
| (3.7) | (5.5) | (3.9) | (1.8) | (3.4) | (3.9) | (5.9) | (1.7) | (5.9) | (4.3) | (0.0) |
| Week 36 | 5 | 2 | 3 | 0 | 2 | 3 | 4 | 0 | 4 | 0 | 0 |
| (3.1) | (3.6) | (5.9) | (0.0) | (3.4) | (2.9) | (4.7) | (0.0) | (4.7) | (0.0) | (0.0) |
| Fluconazole |  |  |  |  |  |  |  |  |  |  |  |
| Weeks 12-36 | 13 | 5 | 3 | 5 | 4 | 5 | 8 | 1 | 8 | 0 | 1 |
| (8.1) | (9.1) | (5.9) | (9.1) | (6.9) | (4.9) | (9.4) | (1.7) | (9.4) | (0.0) | (3.1) |
| Week 12 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| (0.6) | (0.0) | (2.0) | (0.0) | (0.0) | (1.0) | (0.0) | (1.7) | (0.0) | (0.0) | (3.1) |
| Week 16 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| (0.6) | (0.0) | (0.0) | (1.8) | (1.7) | (0.0) | (1.2) | (0.0) | (1.2) | (0.0) | (0.0) |
| Week 20 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| (0.6) | (1.8) | (0.0) | (0.0) | (1.7) | (0.0) | (1.2) | (0.0) | (1.2) | (0.0) | (0.0) |
| Week 24 | 2 | 1 | 1 | 0 | 1 | 1 | 2 | 0 | 2 | 0 | 0 |
| (1.2) | (1.8) | (2.0) | (0.0) | (1.7) | (1.0) | (2.4) | (0.0) | (2.4) | (0.0) | (0.0) |
| Week 28 | 2 | 2 | 0 | 0 | 0 | 2 | 2 | 0 | 2 | 0 | 0 |
| (1.2) | (3.6) | (0.0) | (0.0) | (0.0) | (1.9) | (2.4) | (0.0) | (2.4) | (0.0) | (0.0) |
| Week 32 | 5 | 3 | 2 | 0 | 2 | 3 | 5 | 0 | 5 | 0 | 0 |
| (3.1) | (5.5) | (3.9) | (0.0) | (3.4) | (2.9) | (5.9) | (0.0) | (5.9) | (0.0) | (0.0) |
| Week 36 | 2 | 2 | 0 | 0 | 1 | 1 | 2 | 0 | 2 | 0 | 0 |
| (1.2) | (3.6) | (0.0) | (0.0) | (1.7) | (1.0) | (2.4) | (0.0) | (2.4) | (0.0) | (0.0) |

Appendix Table 3. Model selection with maternal median 25(OH)D status using truncated Poisson regression to model counts of positive EH scores (EH extent)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Model Selection Stage | | | | | | | | | | | | | |
|  | 1 | |  | 2 | |  | 3 | |  | 4 | |  | 5 | |
| Model Term | β | exp(β) |  | β | exp(β) |  | β | exp(β) |  | β | exp(β) |  | β | exp(β) |
| Maternal suff/opt 25(OH)D status | 0.39 | 1.48 |  | 0.32 | 1.38 |  | -0.01 | 0.99 |  | -0.05 | 0.95 |  | -0.09 | 0.91 |
| (-1.39, 2.29) | (0.25, 9.87) |  | (-1.24, 2.21) | (0.29, 9.12) |  | (-0.59, 0.58) | (0.55, 1.79) |  | (-0.61, 0.53) | (0.54, 1.70) |  | (-0.68, 0.47) | (0.51, 1.60) |
| Child at birth iPTH | -0.06 | 0.94 |  | -0.06 | 0.94 |  | -0.06 | 0.94 |  | -0.05 | 0.95 |  | -0.06 | 0.94 |
| (-0.14, 0.00) | (0.87, 1.00) |  | (-0.11, -0.01) | (0.90, 0.99) |  | (-0.11, -0.01) | (0.90, 0.99) |  | (-0.11, 0.00) | (0.90, 1.00) |  | (-0.11, -0.01) | (0.90, 0.99) |
| Child at birth 1,25/10 | 0.33 | 1.39 |  | 0.32 | 1.38 |  | 0.26 | 1.30 |  | 0.26 | 1.30 |  | 0.25 | 1.28 |
| (-0.02, 0.70) | (0.98, 2.01) |  | (-0.01, 0.67) | (0.99, 1.95) |  | (0.05, 0.45) | (1.05, 1.57) |  | (0.05, 0.44) | (1.05, 1.55) |  | (0.03, 0.44) | (1.03, 1.55) |
| Suff/opt\* Child at birth iPTH | 0.00 | 1.00 |  | - | - |  | - | - |  | - | - |  | - | - |
| (-0.10, 0.10) | (0.90, 1.11) |  |  |  |  |
| Suff/opt\* Child at birth 1,25/10 | -0.10 | 0.90 |  | -0.08 | 0.92 |  | - | - |  | - | - |  | - | - |
| (-0.51, 0.28) | (0.60, 1.32) |  | (-0.50, 0.28) | (0.61, 1.32) |  |  |  |
| Antacid count | -0.11 | 0.90 |  | -0.11 | 0.90 |  | -0.11 | 0.90 |  | -0.11 | 0.90 |  | - | - |
| (-0.25, 0.03) | (0.78, 1.03) |  | (-0.25, 0.02) | (0.78, 1.02) |  | (-0.25, 0.02) | (0.78, 1.02) |  | (-0.26, 0.01) | (0.77, 1.01) |  |
| Gestational age/10 | -0.03 | 0.97 |  | -0.03 | 0.97 |  | -0.04 | 0.96 |  | - | - |  | - | - |
| (-0.13, 0.05) | (0.88, 1.05) |  | (-0.12, 0.04) | (0.89, 1.04) |  | (-0.12, 0.04) | (0.89, 1.04) |  |  |
| Maternal age | 0.16 | 1.17 |  | 0.16 | 1.17 |  | 0.13 | 1.14 |  | 0.12 | 1.13 |  | 0.13 | 1.14 |
| (-0.31, 0.65) | (0.73, 1.92) |  | (-0.33, 0.68) | (0.72, 1.97) |  | (-0.35, 0.65) | (0.70, 1.92) |  | (-0.34, 0.63) | (0.71, 1.88) |  | (-0.35, 0.16) | (0.70, 1.17) |
| Log(maternal BMI) | -0.41 | 0.66 |  | -0.33 | 0.72 |  | -0.25 | 0.78 |  | -0.49 | 0.61 |  | -0.53 | 0.59 |
| (-1.74, 0.56) | (0.18, 1.75) |  | (-1.47, 0.66) | (0.23, 1.93) |  | (-1.35, 0.68) | (0.26, 1.97) |  | (-1.30, 0.17) | (0.27, 1.19) |  | (-1.35, 0.16) | (0.26, 1.17) |
| Maternal race/ethnicity: Caucasian | 0.14 | 1.15 |  | 0.12 | 1.13 |  | 0.17 | 1.19 |  | 0.07 | 1.07 |  | 0.06 | 1.06 |
| (-0.74, 1.85) | (0.48, 6.36) |  | (-0.68, 1.63) | (0.51, 5.10) |  | (-0.96, 2.48) | (0.38, 11.94) |  | (-0.87, 2.47) | (0.42, 11.82) |  | (-0.78, 1.21) | (0.46, 3.35) |
| Maternal race/ethnicity: African American | 0.12 | 1.13 |  | 0.08 | 1.08 |  | 0.12 | 1.13 |  | 0.05 | 1.05 |  | 0.03 | 1.03 |
| (-0.75, 1.75) | (0.47, 5.75) |  | (-0.73, 1.53) | (0.48, 4.62) |  | (-1.08, 2.41) | (0.34, 11.13) |  | (-0.95, 1.18) | (0.39, 3.25) |  | (-0.91, 1.23) | (0.40, 3.42) |
| Maternal race/ethnicity: Hispanic | 0.10 | 1.11 |  | 0.07 | 1.07 |  | 0.12 | 1.13 |  | 0.00 | 1.00 |  | 0.05 | 1.05 |
| (-0.88, 1.70) | (0.41, 5.47) |  | (-0.74, 1.50) | (0.48, 4.48) |  | (-1.05, 2.48) | (0.35, 11.94) |  | (-1.04, 1.10) | (0.35, 3.00) |  | (-0.81, 1.21) | (0.44, 3.35) |
| DIC | 309.5 | |  | 309.3 | |  | 309.6 | |  | 309.3 | |  | 310.1 | |

The model coefficients (β) from the backwards model selection are displayed along with their 95% credible intervals. Each coefficient and interval is exponentiated to provide the multiplicative effect on the expected counts of EH. A dash (-) indicates that the variable was removed for that stage of selection. The abbreviation maternal suff/opt represents the dummy variable for the sufficient or optimal median 25(OH)D status; iPTH represents the cord blood iPTH concentration (pg/mL), and 1,25/10 represents the child cord blood measurement of 1,25(OH)2D (pg/mL) divided by 10.

Appendix Table 4. Entry parameter posterior probability means for Gibbs variable selection

|  |  |
| --- | --- |
| Model Term | mean |
| Child at birth iPTH | 0.48 |
| Child at birth 1,25/10 | 0.51 |
| Suff/opt\*Child at birth iPTH | 0.18 |
| Suff/opt\*Child at birth 1,25/10 | 0.31 |
| Antacid count | 0.32 |
| Gestational age/10 | 0.36 |

The entry parameter posterior probability means are provided for the Gibbs variable selection. Each mean is the average, across a sample 10,000, of the entry parameter for the model term listed. Each entry parameter is a Bernoulli random variable, and so the mean ranges from 0 to 1. Higher mean values indicate that the model term in question is included more often in the model.

Appendix Table 5. Model selection with continuous maternal median 25(OH)D utilizing truncated Poisson regression to model counts of positive EH scores (EH extent)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Model Selection Stage | | | | | | | | | | | | | |
|  |  | 1 | |  | 2 | |  | 3 | |  | 4 | |  | 5 | |
| Model Term |  | β | exp(β) |  | β | exp(β) |  | β | exp(β) |  | β | exp(β) |  | β | exp(β) |
| Maternal median 25(OH)D |  | 0.44 | 1.55 |  | 0.46 | 1.58 |  | 0.07 | 1.07 |  | 0.04 | 1.04 |  | 0.01 | 1.01 |
|  | (-0.42, 1.39) | (0.66, 4.01) |  | (-0.31, 1.41) | (0.73, 4.10) |  | (-0.18, 0.33) | (0.84, 1.39) |  | (-0.20, 0.29) | (0.82, 1.34) |  | (-0.23, 0.25) | (0.79, 1.28) |
| Child at birth iPTH |  | -0.08 | 0.92 |  | -0.05 | 0.95 |  | -0.05 | 0.95 |  | -0.05 | 0.95 |  | -0.06 | 0.94 |
|  | (-0.27, 0.07) | (0.76, 1.07) |  | (-0.11, 0.00) | (0.90, 1.00) |  | (-0.11, -0.01) | (0.90, 0.99) |  | (-0.11, 0.00) | (0.90, 1.00) |  | (-0.12, -0.01) | (0.89, 0.99) |
| Child at birth 1,25(OH)2D/10 |  | 0.61 | 1.84 |  | 0.59 | 1.80 |  | 0.24 | 1.27 |  | 0.24 | 1.27 |  | 0.24 | 1.27 |
|  | (-0.04, 1.35) | (0.96, 3.86) |  | (-0.08, 1.41) | (0.92, 4.10) |  | (0.03, 0.44) | (1.03, 1.55) |  | (0.01, 0.45) | (1.01, 1.57) |  | (0.01, 0.45) | (1.01, 1.57) |
| Child iPTH\*median 25(OH)D |  | 0.01 | 1.01 |  | - | - |  | - | - |  | - | - |  | - | - |
|  | (-0.04, 0.06) | (0.96, 1.06) |  |  |  |  |
| (Child 1,25(OH)2D/10)\* Maternal median 25(OH)D |  | -0.10 | 0.90 |  | -0.09 | 0.91 |  | - | - |  | - | - |  | - | - |
|  | (-0.29, 0.07) | (0.75, 1.07) |  | (-0.31, 0.07) | (0.73, 1.07) |  |  |  |
| Maternal antacid count |  | -0.12 | 0.89 |  | -0.12 | 0.89 |  | -0.12 | 0.89 |  | -0.12 | 0.89 |  | - | - |
|  | (-0.28, 0.03) | (0.76, 1.03) |  | (-0.27, 0.02) | (0.76, 1.02) |  | (-0.26, 0.02) | (0.77, 1.02) |  | (-0.27, 0.01) | (0.76, 1.01) |  |
| Gestational age/10 |  | -0.05 | 0.95 |  | -0.05 | 0.95 |  | -0.04 | 0.96 |  | - | - |  | - | - |
|  | (-0.14, 0.04) | (0.87, 1.04) |  | (-0.14, 0.03) | (0.87, 1.03) |  | (-0.12, 0.03) | (0.89, 1.03) |  |  |
| Maternal age |  | 0.08 | 1.08 |  | 0.08 | 1.08 |  | 0.10 | 1.11 |  | 0.09 | 1.09 |  | 0.10 | 1.11 |
|  | (-0.42, 0.59) | (0.66, 1.80) |  | (-0.40, 0.61) | (0.67, 1.84) |  | (-0.39, 0.59) | (0.68, 1.80) |  | (-0.41, 0.60) | (0.66, 1.82) |  | (-0.38, 0.63) | (0.68, 1.88) |
| Log(maternal BMI) |  | -0.45 | 0.64 |  | -0.44 | 0.64 |  | -0.18 | 0.84 |  | -0.47 | 0.63 |  | -0.52 | 0.59 |
|  | (-1.75, 0.61) | (0.17, 1.84) |  | (-1.65, 0.57) | (0.19, 1.77) |  | (-1.21, 0.72) | (0.30, 2.05) |  | (-1.27, 0.20) | (0.28, 1.22) |  | (-1.32, 0.14) | (0.27, 1.15) |
| Maternal race/ethnicity: white |  | 0.06 | 1.06 |  | 0.08 | 1.08 |  | 0.10 | 1.11 |  | 0.05 | 1.05 |  | 0.04 | 1.04 |
|  | (-0.90, 1.45) | (0.41, 4.26) |  | (-0.82, 1.43) | (0.44, 4.18) |  | (-0.77, 1.58) | (0.46, 4.85) |  | (-0.90, 1.12) | (0.41, 3.06) |  | (-0.78, 1.09) | (0.46, 2.97) |
| Maternal race/ethnicity: black |  | 0.08 | 1.08 |  | 0.11 | 1.12 |  | 0.08 | 1.08 |  | 0.06 | 1.06 |  | 0.04 | 1.04 |
|  | (-0.84, 1.53) | (0.43, 4.62) |  | (-0.70, 1.47) | (0.50, 4.35) |  | (-0.81, 1.55) | (0.44, 4.71) |  | (-0.89, 1.15) | (0.41, 3.16) |  | (-0.74, 1.11) | (0.48, 3.03) |
| Maternal race/ethnicity: Hispanic |  | 0.03 | 1.03 |  | 0.06 | 1.06 |  | 0.06 | 1.06 |  | 0.02 | 1.02 |  | 0.04 | 1.04 |
|  | (-0.87, 1.37) | (0.42, 3.94) |  | (-0.82, 1.42) | (0.44, 4.14) |  | (-0.85, 1.55) | (0.43, 4.71) |  | (-0.98, 1.06) | (0.38, 2.89) |  | (-0.76, 1.13) | (0.47, 3.10) |
| DIC |  | 307.8 | |  | 308.0 | |  | 309.6 | |  | 309.3 | |  | 310.1 | |

The model coefficients (β) from the backwards model selection are displayed along with their 95% credible intervals. Each coefficient and interval is exponentiated to provide the multiplicative effect on the expected counts of EH. A dash (-) indicates that the variable was removed for that stage of selection. The maternal median 25(OH)D represents the continuous dummy variable; iPTH represents the cord blood iPTH concentration (pg/mL), and 1,25/10 represents the child cord blood measurement of 1,25(OH)2D (pg/mL) divided by 10.

Appendix Table 6. DIC measures for models containing 25(OH)D concentrations as the longitudinal outcome

|  |  |  |  |
| --- | --- | --- | --- |
|  | Model | no BMI adjustment | BMI adjustment |
| EH Status (binary) | 1 | 8762.94 | 8745.65 |
| 2 | 8598.87 | 8580.77 |
| 3 | 8608.36 | 8589.89 |
| 4 | 8509.81 | 8510.83 |
| 5 | 8510.83 | 8511.79 |
| 6 | 8522.50 | 8521.47 |
| 7 | 8524.14 | 8522.91 |
| 8 | 8524.73 | 8522.94 |
| 9 | 8538.48 | 8539.21 |
| 10 | 8542.82 | 8541.86 |
| EH Extent Group | 1 | 8750.63 | 8738.74 |
| 2 | 8582.24 | 8564.27 |
| 3 | 8603.39 | 8588.15 |
| 4 | 8503.91 | 8506.75 |
| 5 | 8485.55 | 8486.42 |
| 6 | 8513.92 | 8518.43 |
| 7 | 8507.63 | 8505.92 |
| 8 | 8517.08 | 8516.17 |
| 9 | 8541.76 | 8541.21 |
| 10 | 8545.50 | 8544.72 |

The DIC for both EH categorizations and with or without BMI adjustment is shown for each model. The model descriptions are as follows: (1) intercept by EH status, (2) intercept by EH status + common time RW, (3) intercept by EH status + time RW by EH status, (4) intercept by EH status + common time RW + mean iPTH, (5) intercept by EH status + common time RW + mean iPTH per EH status, (6) intercept by EH status + common time RW + iPTH, (7) intercept by EH status + common time RW + iPTH per EH status, (8) intercept by EH status + common time RW + iPTH per visit, (9) intercept by EH status + common time RW + iPTH per EH status per visit, (10) intercept by EH status + time RW per EH status + iPTH per EH status per visit.

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).



with  and  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.



where 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.



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 D3 we were particularly interested in the association of EH with vitamin D3, both the substrate and active forms. While the RCT for which the data were gathered focused on the effect of vitamin D3 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 D3 using not only by treatment assignments for vitamin D3 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.