**Supplemental Digital Content 5.** Analysis of GEE parameter estimates for gastrointestinal symptom outcomes

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Effect** | | **Estimate**  **(log Odds Ratio)** | **SE** | **95% Confidence Limits** | | **Z** | **Pr > |Z|** |
| **Lower** | **Upper** |
| *Borborygmus* | A2 milk vs. Conventional milk | | −1.0361 | 0.1760 | −1.3810 | −0.6912 | −5.89 | <0.0001\*\*\* |
|  | Conventional milk | D1 vs. BL | 2.0090 | 0.3862 | 1.2521 | 2.7659 | 5.20 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.6921 | 0.4235 | 0.8622 | 2.5221 | 4.00 | <0.0001\*\*\* |
|  |  | D3 vs. BL | 1.8410 | 0.4304 | 0.9974 | 2.6845 | 4.28 | <0.0001\*\*\* |
|  |  | D4 vs. BL | 1.5908 | 0.4197 | 0.7682 | 2.4134 | 3.79 | 0.0002\*\*\* |
|  |  | D5 vs. BL | 1.4952 | 0.4316 | 0.6493 | 2.3412 | 3.46 | 0.0005\*\*\* |
|  | A2 milk | D1 vs. BL | 0.1988 | 0.4218 | −0.6279 | 1.0255 | 0.47 | 0.6374 |
|  |  | D2 vs. BL | 0.5338 | 0.4175 | −0.2846 | 1.3522 | 1.28 | 0.2011 |
|  |  | D3 vs. BL | 0.3747 | 0.4398 | −0.4872 | 1.2366 | 0.85 | 0.3942 |
|  |  | D4 vs. BL | 0.3747 | 0.4398 | −0.4872 | 1.2367 | 0.85 | 0.3942 |
|  |  | D5 vs. BL | 0.2892 | 0.4420 | −0.5771 | 1.1555 | 0.65 | 0.5129 |
| *Bloating* | A2 milk vs. Conventional milk | | −1.1090 | 0.1723 | −1.4468 | −0.7713 | −6.44 | <0.0001\*\*\* |
| Conventional milk | D1 vs. BL | 1.4121 | 0.3367 | 0.7523 | 2.0719 | 4.19 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.5119 | 0.3977 | 0.7325 | 2.2914 | 3.80 | 0.0001\*\*\* |
|  |  | D3 vs. BL | 1.5305 | 0.3750 | 0.7954 | 2.2655 | 4.08 | <0.0001\*\*\* |
|  |  | D4 vs. BL | 1.6969 | 0.4030 | 0.9070 | 2.4869 | 4.21 | <0.0001\*\*\* |
|  |  | D5 vs. BL | 1.6095 | 0.4143 | 0.7974 | 2.4216 | 3.88 | 0.0001\*\*\* |
|  | A2 milk | D1 vs. BL | 0.3170 | 0.4061 | −0.4790 | 1.1130 | 0.78 | 0.4351 |
|  |  | D2 vs. BL | 0.2601 | 0.3880 | −0.5003 | 1.0207 | 0.67 | 0.5025 |
|  |  | D3 vs. BL | 0.1659 | 0.4563 | −0.7284 | 1.0601 | 0.36 | 0.7162 |
|  |  | D4 vs. BL | −0.0899 | 0.4135 | −0.9004 | 0.7206 | −0.22 | 0.8279 |
|  |  | D5 vs. BL | 0.3346 | 0.3397 | −0.3313 | 1.0005 | 0.98 | 0.3246 |
| *Break Wind* | A2 milk vs. Conventional milk | | −0.8897 | 0.1804 | −1.2433 | −0.5362 | −4.93 | <0.0001\*\*\* |
|  | Conventional milk | D1 vs. BL | 1.0621 | 0.2915 | 0.4907 | 1.6334 | 3.64 | 0.0003\*\*\* |
|  |  | D2 vs. BL | 1.1498 | 0.2831 | 0.5949 | 1.7046 | 4.06 | <0.0001\*\*\* |
|  |  | D3 vs. BL | 1.1493 | 0.2704 | 0.6194 | 1.6793 | 4.25 | <0.0001\*\*\* |
|  |  | D4 vs. BL | 1.1248 | 0.3198 | 0.4980 | 1.7517 | 3.52 | 0.0004\*\*\* |
|  |  | D5 vs. BL | 1.1373 | 0.3180 | 0.5140 | 1.7606 | 3.58 | 0.0003\*\*\* |
|  | A2 milk | D1 vs. BL | 0.2474 | 0.3214 | −0.3826 | 0.8774 | 0.77 | 0.4415 |
|  |  | D2 vs. BL | 0.3882 | 0.3190 | −0.2371 | 1.0135 | 1.22 | 0.2236 |
|  |  | D3 vs. BL | 0.6461 | 0.3444 | 0.0290 | 1.3212 | 1.88 | 0.0607 |
|  |  | D4 vs. BL | 0.5698 | 0.3419 | −0.1003 | 1.2399 | 1.67 | 0.0956 |
|  |  | D5 vs. BL | 0.2816 | 0.3186 | −0.3429 | 0.9062 | 0.88 | 0.3768 |
| *Abdominal Pain* | A2 milk vs. Conventional milk | | −1.5276 | 0.2403 | −1.9987 | −1.0565 | −6.36 | <0.0001\*\*\* |
| Conventional milk | D1 vs. BL | 2.0640 | 0.4917 | 1.1002 | 3.0277 | 4.20 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.6175 | 0.4829 | 0.6709 | 2.5641 | 3.35 | 0.0008\*\*\* |
|  |  | D3 vs. BL | 1.6176 | 0.4516 | 0.7325 | 2.5027 | 3.58 | 0.0003\*\*\* |
|  |  | D4 vs. BL | 1.6176 | 0.5115 | 0.6150 | 2.6201 | 3.16 | 0.0016\*\* |
|  |  | D5 vs. BL | 1.4602 | 0.5739 | 0.3354 | 2.5850 | 2.54 | 0.0109\* |
|  | A2 milk | D1 vs. BL | 0.1968 | 0.6533 | −1.0837 | 1.4773 | 0.30 | 0.7633 |
|  |  | D2 vs. BL | 0.0000 | 0.6778 | −1.3286 | 1.3286 | 0.00 | 1.0000 |
|  |  | D3 vs. BL | 0.3656 | 0.5798 | −0.7707 | 1.5019 | 0.63 | 0.5283 |
|  |  | D4 vs. BL | −0.2374 | 0.7133 | −1.6354 | 1.1606 | -0.33 | 0.7392 |
|  |  | D5 vs. BL | −0.5391 | 0.6654 | −1.8433 | 0.7650 | −0.81 | 0.4178 |
| *Diarrhea* | A2 milk vs. Conventional milk | | −2.8450 | 0.4037 | −3.6363 | −2.0537 | −7.05 | <0.0001\*\*\* |
|  | Conventional milk | D1 vs. BL | 1.9196 | 0.4682 | 1.0020 | 2.8373 | 4.10 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 2.0167 | 0.4948 | 1.0470 | 2.9865 | 4.08 | <0.0001\*\*\* |
|  |  | D3 vs. BL | 2.0390 | 0.5473 | 0.9662 | 3.1117 | 3.73 | 0.0002\*\*\* |
|  |  | D4 vs. BL | 1.8754 | 0.5198 | 0.8566 | 2.8942 | 3.61 | 0.0003\*\*\* |
|  |  | D5 vs. BL | 2.0356 | 0.5070 | 1.0419 | 3.0293 | 4.02 | <0.0001\*\*\* |
|  | A2 milk | D1 vs. BL | −0.7068 | 1.2468 | −3.1505 | 1.7370 | −0.57 | 0.5708 |
|  |  | D2 vs. BL | −0.7068 | 1.2471 | −3.1511 | 1.7376 | −0.57 | 0.5709 |
|  |  | D3 vs. BL | −0.7068 | 1.2469 | −3.1507 | 1.7372 | −0.57 | 0.5708 |
|  |  | D4 vs. BL | 0.4193 | 0.9432 | −1.4293 | 2.2679 | 0.44 | 0.6566 |
|  |  | D5 vs. BL | −0.7068 | 1.2469 | −3.1507 | 1.7372 | −0.57 | 0.5708 |

Empirical Standard Error Estimates

Daily VAS scores were analyzed using the Generalized Estimating Equation (GEE) for ordinal repeated outcomes, with fixed effects for study product (A1 or A2), study phase (phase 1 or phase 2), measurement time (baseline, days during intervention in each phase), and interaction between study product and measurement time. A random subject effect was also nested within the intervention sequence (conventional milk followed by milk containing A2 beta-casein only or milk containing A2 beta-casein only following by conventional milk). A2 milk = milk containing A2 beta-casein only.

\*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001; no symbol: p≥0.05