**S3 Table. Comparison between $l_{approx}$ and $l_{mean}$ in binary phenotype simulations**

| Scenario | | | GxE ($n = 1000$) | | | Marginal ($n = 1000$) | | | GxE ($n = 10000$) | | | Marginal ($n = 10000$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $(b_G, b_{GE}, b_Z)$ | M | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ |
| Base | (1,0,0) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| Base | (1,0,0) | d | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| Base | (0,0,1) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| Base | (0,0,1) | d | 1.01 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1a | (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 |
| | | | (0.00) | (0.03) | (0.02) | (0.00) | (0.04) | (0.04) | (0.00) | (0.02) | (0.02) | (0.00) | (0.04) | (0.04) |
| 1a | (1,0,0) | d | 1.01 | 1.02 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1a | (0,0,1) | r | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1a | (0,0,1) | d | 1.02 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (1,0,0) | a | 1.00 | 1.02 | 0.98 | 1.00 | 1.03 | 0.97 | 1.00 | 1.00 | 0.99 | 1.00 | 1.01 | 0.99 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.04) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (1,0,0) | d | 1.01 | 1.02 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.01 | 0.99 | 1.00 | 1.01 | 0.99 |
| | | | (0.02) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.04) | (0.03) |
| 1b | (0,1,0) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (0,0,1) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.99 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (0,0,1) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.01 | 0.99 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1b | (0,0,1) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.04) | (0.04) |
| 1c | (0,0,0) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (1,0,0) | a | 1.00 | 1.02 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (1,0,0) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (1,0,0) | d | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (0,0,1) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1c | (0,0,1) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 |
| | | | (0.01) | (0.03) | (0.03) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |

Mean and standard deviation (SD) for $l_{approx}$, $l_{mean}$ and the ratio $l_{approx}/l_{mean}$ are shown over 200 simulation runs for gene-environment (GxE) interaction and marginal association analyses for two sample sizes, $n = 1000$ and 10000. M, genotype model (a: additive, r: recessive, d: dominant). $b_G$, $b_{GE}$ and $b_Z$ are effect size parameters of genotype, gene-environment interaction and covariate, respectively; 0 and 1 denote absence and presence of effect.

**S3 Table (continued). Comparison between $l_{approx}$ and $l_{mean}$ in binary phenotype simulations**

| Scenario | | | GxE ($n = 1000$) | | | Marginal ($n = 1000$) | | | GxE ($n = 10000$) | | | Marginal ($n = 10000$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $(b_G, b_{GE}, b_Z)$ | M | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ |
| 1d | (0,0,0) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (1,0,0) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (1,0,0) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (1,0,0) | d | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 0.99 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (0,0,1) | a | 1.02 | 1.03 | 0.99 | 1.00 | 1.00 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.04) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 1d | (0,0,1) | d | 1.01 | 1.03 | 0.99 | 1.00 | 1.00 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2a | (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.03 | 0.97 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2a | (1,0,0) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2a | (0,0,1) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2a | (0,0,1) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (1,0,0) | a | 1.00 | 1.02 | 0.99 | 1.00 | 1.03 | 0.97 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.04) | (0.04) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (1,0,0) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (1,0,0) | d | 1.00 | 1.02 | 0.99 | 1.00 | 1.03 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 |
| | | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (0,0,1) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2b | (0,0,1) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2c | (1,0,0) | r | 0.89 | 0.90 | 0.99 | 1.00 | 1.01 | 0.99 | 0.85 | 0.86 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2c | (1,0,0) | d | 0.97 | 0.98 | 0.99 | 1.00 | 1.01 | 0.99 | 0.91 | 0.91 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2c | (0,0,1) | r | 0.86 | 0.86 | 1.00 | 1.00 | 1.00 | 1.00 | 0.85 | 0.85 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2c | (0,0,1) | d | 0.87 | 0.88 | 0.99 | 1.00 | 1.01 | 1.00 | 0.88 | 0.89 | 0.99 | 1.00 | 1.01 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.03) | (0.00) | (0.03) | (0.03) |

Mean and standard deviation (SD) for $l_{approx}$, $l_{mean}$ and the ratio $l_{approx}/l_{mean}$ are shown over 200 simulation runs for gene-environment (GxE) interaction and marginal association analyses for two sample sizes, $n = 1000$ and 10000. M, genotype model (a: additive, r: recessive, d: dominant). $b_G$, $b_{GE}$ and $b_Z$ are effect size parameters of genotype, gene-environment interaction and covariate, respectively; 0 and 1 denote absence and presence of effect.

**S3 Table (continued). Comparison between $l_{approx}$ and $l_{mean}$ in binary phenotype simulations**

| Scenario | | | GxE ($n = 1000$) | | | Marginal ($n = 1000$) | | | GxE ($n = 10000$) | | | Marginal ($n = 10000$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $(b_G, b_{GE}, b_Z)$ | | M | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ |
| 2d | (1,0,0) | r | 1.02 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.02 | 1.02 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.32) | (0.23) | (0.06) | (0.00) | (0.03) | (0.03) | (0.16) | (0.12) | (0.04) | (0.00) | (0.03) | (0.03) |
| 2d | (1,0,0) | d | 1.03 | 1.03 | 0.99 | 1.00 | 1.01 | 0.99 | 1.03 | 1.02 | 1.01 | 1.00 | 1.00 | 1.00 |
| | | | (0.29) | (0.21) | (0.06) | (0.00) | (0.03) | (0.03) | (0.18) | (0.14) | (0.04) | (0.00) | (0.03) | (0.03) |
| 2d | (0,0,1) | r | 1.74 | 1.52 | 1.09 | 1.00 | 1.01 | 1.00 | 2.00 | 1.98 | 1.01 | 1.00 | 1.00 | 1.00 |
| | | | (1.09) | (0.76) | (0.12) | (0.00) | (0.03) | (0.03) | (0.97) | (0.95) | (0.03) | (0.00) | (0.03) | (0.03) |
| 2d | (0,0,1) | d | 9.68 | 5.68 | 1.35 | 0.99 | 0.99 | 1.00 | 1.97 | 1.93 | 1.02 | 1.00 | 1.00 | 1.00 |
| | | | (9.66) | (5.14) | (0.41) | (0.01) | (0.03) | (0.03) | (0.95) | (0.92) | (0.03) | (0.00) | (0.03) | (0.03) |
| 2e | (0,0,0) | a | 1.05 | 1.05 | 1.01 | 1.00 | 1.00 | 1.01 | 1.05 | 1.04 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.04) | (0.04) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2e | (1,0,0) | a | 1.06 | 1.07 | 0.99 | 1.00 | 1.03 | 0.97 | 1.04 | 1.03 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.06) | (0.06) | (0.02) | (0.00) | (0.03) | (0.03) | (0.05) | (0.05) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2e | (1,0,0) | r | 1.06 | 1.06 | 1.00 | 1.00 | 1.01 | 0.99 | 1.04 | 1.03 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.03) | (0.04) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2e | (1,0,0) | d | 1.06 | 1.06 | 0.99 | 1.00 | 1.02 | 0.98 | 1.05 | 1.04 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.03) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.07) | (0.07) | (0.02) | (0.00) | (0.04) | (0.04) |
| 2e | (0,1,0) | a | 1.33 | 1.42 | 0.87 | 1.00 | 1.00 | 1.00 | 11.60 | 8.88 | 1.29 | 0.98 | 0.98 | 1.00 |
| | | | (1.91) | (1.04) | (0.10) | (0.00) | (0.03) | (0.03) | (3.00) | (1.38) | (0.15) | (0.00) | (0.03) | (0.03) |
| 2e | (0,0,1) | a | 1.06 | 1.06 | 1.00 | 1.00 | 1.00 | 1.00 | 4.20 | 4.14 | 0.97 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (2.32) | (1.92) | (0.10) | (0.00) | (0.03) | (0.03) |
| 2e | (0,0,1) | r | 1.06 | 1.07 | 0.99 | 1.00 | 1.00 | 1.00 | 1.04 | 1.04 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.04) | (0.04) | (0.03) | (0.00) | (0.03) | (0.03) | (0.04) | (0.05) | (0.02) | (0.00) | (0.03) | (0.03) |
| 2e | (0,0,1) | d | 1.25 | 1.32 | 0.90 | 1.00 | 1.00 | 1.00 | 9.76 | 8.06 | 1.19 | 0.99 | 0.99 | 1.00 |
| | | | (1.41) | (0.78) | (0.08) | (0.00) | (0.03) | (0.03) | (2.62) | (1.62) | (0.11) | (0.00) | (0.03) | (0.03) |
| 3a | (0,0,0) | a | 1.01 | 1.01 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (1,0,0) | a | 1.01 | 1.02 | 0.99 | 1.01 | 1.04 | 0.97 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (1,0,0) | r | 1.01 | 1.01 | 1.00 | 1.01 | 1.02 | 0.99 | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 |
| | | | (0.01) | (0.03) | (0.03) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (1,0,0) | d | 1.01 | 1.02 | 0.99 | 1.01 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (0,1,0) | a | 1.01 | 1.01 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (0,0,1) | a | 1.03 | 1.04 | 0.99 | 1.01 | 1.01 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (0,0,1) | r | 1.01 | 1.01 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3a | (0,0,1) | d | 1.01 | 1.02 | 0.99 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.03) | (0.03) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |

Mean and standard deviation (SD) for $l_{approx}$, $l_{mean}$ and the ratio $l_{approx}/l_{mean}$ are shown over 200 simulation runs for gene-environment (GxE) interaction and marginal association analyses for two sample sizes, $n = 1000$ and 10000. M, genotype model (a: additive, r: recessive, d: dominant). $b_G$, $b_{GE}$ and $b_Z$ are effect size parameters of genotype, gene-environment interaction and covariate, respectively; 0 and 1 denote absence and presence of effect.

**S3 Table (continued). Comparison between $l_{approx}$ and $l_{mean}$ in binary phenotype simulations**

| Scenario | | GxE ($n = 1000$) | | | Marginal ($n = 1000$) | | | GxE ($n = 10000$) | | | Marginal ($n = 10000$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $(b_G, b_{GE}, b_Z)$ | M | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ |
| 3b (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (1,0,0) | a | 1.00 | 1.02 | 0.98 | 1.00 | 1.03 | 0.97 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.03) | (0.02) | (0.00) | (0.04) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (1,0,0) | d | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.04) | (0.05) | (0.02) | (0.01) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (0,0,1) | a | 1.03 | 1.02 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3b (0,0,1) | d | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.02) | (0.02) | (0.00) | (0.04) | (0.04) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (1,0,0) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (1,0,0) | r | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (1,0,0) | d | 1.00 | 1.02 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.03) | (0.00) | (0.04) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (0,0,1) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (0,0,1) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.03 | 0.98 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3c (0,0,1) | d | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.03 | 0.97 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.04) | (0.04) |
| 3d (0,0,0) | a | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (1,0,0) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (1,0,0) | d | 1.00 | 1.02 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.03) | (0.04) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (0,0,1) | a | 1.01 | 1.01 | 1.00 | 1.00 | 1.03 | 0.97 | 1.03 | 1.03 | 1.00 | 1.00 | 0.99 | 1.00 |
| | | (0.01) | (0.03) | (0.02) | (0.00) | (0.04) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 3d (0,0,1) | d | 1.01 | 1.02 | 0.99 | 1.00 | 1.03 | 0.97 | 1.02 | 1.02 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |

Mean and standard deviation (SD) for $l_{approx}$, $l_{mean}$ and the ratio $l_{approx}/l_{mean}$ are shown over 200 simulation runs for gene-environment (GxE) interaction and marginal association analyses for two sample sizes, $n = 1000$ and 10000. M, genotype model (a: additive, r: recessive, d: dominant). $b_G$, $b_{GE}$ and $b_Z$ are effect size parameters of genotype, gene-environment interaction and covariate, respectively; 0 and 1 denote absence and presence of effect.

**S3 Table (continued). Comparison between $l_{approx}$ and $l_{mean}$ in binary phenotype simulations**

| Scenario | | | GxE ($n = 1000$) | | | Marginal ($n = 1000$) | | | GxE ($n = 10000$) | | | Marginal ($n = 10000$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $(b_G, b_{GE}, b_Z)$ | M | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ | $l_{approx}$ | $l_{mean}$ | $\frac{l_{approx}}{l_{mean}}$ |
| 4a | (0,0,0) | a | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 |
| | | | (0.00) | (0.07) | (0.07) | (0.00) | (0.10) | (0.09) | (0.00) | (0.07) | (0.07) | (0.00) | (0.09) | (0.09) |
| 4a | (1,0,0) | a | 1.00 | 1.19 | 0.84 | 1.00 | 1.39 | 0.73 | 1.00 | 2.25 | 0.45 | 1.00 | 3.58 | 0.28 |
| | | | (0.02) | (0.09) | (0.06) | (0.00) | (0.17) | (0.09) | (0.01) | (0.22) | (0.05) | (0.00) | (0.42) | (0.04) |
| 4a | (1,0,0) | r | 1.00 | 1.00 | 1.01 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 |
| | | | (0.00) | (0.06) | (0.06) | (0.00) | (0.09) | (0.08) | (0.00) | (0.06) | (0.06) | (0.00) | (0.09) | (0.09) |
| 4a | (1,0,0) | d | 1.00 | 1.05 | 0.96 | 1.00 | 1.10 | 0.92 | 1.00 | 1.59 | 0.63 | 1.00 | 2.17 | 0.47 |
| | | | (0.01) | (0.07) | (0.07) | (0.00) | (0.12) | (0.10) | (0.00) | (0.14) | (0.06) | (0.00) | (0.27) | (0.06) |
| 4a | (0,1,0) | a | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 |
| | | | (0.02) | (0.07) | (0.07) | (0.00) | (0.09) | (0.09) | (0.01) | (0.07) | (0.07) | (0.00) | (0.09) | (0.09) |
| 4a | (0,0,1) | a | 1.01 | 1.12 | 0.91 | 1.00 | 1.00 | 1.01 | 1.02 | 2.28 | 0.45 | 1.00 | 0.99 | 1.01 |
| | | | (0.01) | (0.09) | (0.07) | (0.00) | (0.09) | (0.09) | (0.01) | (0.16) | (0.03) | (0.00) | (0.09) | (0.09) |
| 4a | (0,0,1) | r | 1.00 | 1.02 | 0.99 | 1.00 | 1.01 | 1.00 | 1.00 | 1.17 | 0.86 | 1.00 | 1.00 | 1.01 |
| | | | (0.00) | (0.07) | (0.06) | (0.00) | (0.10) | (0.09) | (0.00) | (0.10) | (0.07) | (0.00) | (0.08) | (0.08) |
| 4a | (0,0,1) | d | 1.02 | 1.09 | 0.94 | 1.00 | 1.01 | 1.00 | 1.01 | 1.85 | 0.55 | 1.00 | 1.00 | 1.01 |
| | | | (0.02) | (0.09) | (0.07) | (0.00) | (0.09) | (0.09) | (0.01) | (0.16) | (0.05) | (0.00) | (0.09) | (0.09) |
| 4b | (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.04) | (0.04) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (1,0,0) | a | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (1,0,0) | d | 1.00 | 1.01 | 0.99 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (0,1,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (0,0,1) | a | 1.02 | 1.03 | 0.99 | 1.00 | 1.00 | 1.00 | 1.02 | 1.02 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.02) | (0.03) | (0.02) | (0.00) | (0.03) | (0.03) | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (0,0,1) | r | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4b | (0,0,1) | d | 1.01 | 1.02 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) | (0.00) | (0.02) | (0.02) | (0.00) | (0.03) | (0.03) |
| 4c | (0,0,0) | a | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| | | | (0.00) | (0.05) | (0.05) | (0.00) | (0.07) | (0.07) | (0.00) | (0.06) | (0.06) | (0.00) | (0.09) | (0.08) |
| 4c | (1,0,0) | a | 1.00 | 1.11 | 0.91 | 1.00 | 1.23 | 0.83 | 1.00 | 1.07 | 0.94 | 1.00 | 1.14 | 0.89 |
| | | | (0.01) | (0.08) | (0.06) | (0.00) | (0.13) | (0.09) | (0.00) | (0.06) | (0.06) | (0.00) | (0.11) | (0.09) |
| 4c | (1,0,0) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.27 | 0.79 | 1.00 | 1.55 | 0.65 |
| | | | (0.00) | (0.05) | (0.05) | (0.00) | (0.07) | (0.07) | (0.00) | (0.09) | (0.06) | (0.00) | (0.17) | (0.07) |
| 4c | (1,0,0) | d | 1.00 | 1.09 | 0.92 | 1.00 | 1.18 | 0.86 | 1.00 | 1.25 | 0.80 | 1.00 | 1.50 | 0.68 |
| | | | (0.01) | (0.06) | (0.06) | (0.00) | (0.11) | (0.08) | (0.00) | (0.10) | (0.06) | (0.00) | (0.17) | (0.07) |
| 4c | (0,1,0) | a | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 |
| | | | (0.02) | (0.05) | (0.05) | (0.00) | (0.08) | (0.08) | (0.01) | (0.05) | (0.05) | (0.00) | (0.09) | (0.08) |
| 4c | (0,0,1) | a | 1.03 | 1.14 | 0.91 | 1.00 | 0.99 | 1.02 | 1.00 | 1.06 | 0.95 | 1.00 | 1.00 | 1.01 |
| | | | (0.02) | (0.08) | (0.06) | (0.00) | (0.07) | (0.07) | (0.00) | (0.06) | (0.05) | (0.00) | (0.08) | (0.08) |
| 4c | (0,0,1) | r | 1.00 | 1.01 | 1.00 | 1.00 | 1.00 | 1.01 | 1.00 | 1.02 | 0.98 | 1.00 | 1.00 | 1.01 |
| | | | (0.00) | (0.05) | (0.05) | (0.00) | (0.08) | (0.08) | (0.00) | (0.06) | (0.06) | (0.00) | (0.08) | (0.08) |
| 4c | (0,0,1) | d | 1.01 | 1.06 | 0.95 | 1.00 | 1.01 | 0.99 | 1.01 | 1.69 | 0.60 | 1.00 | 1.00 | 1.00 |
| | | | (0.01) | (0.06) | (0.06) | (0.00) | (0.08) | (0.08) | (0.00) | (0.14) | (0.05) | (0.00) | (0.08) | (0.08) |

Mean and standard deviation (SD) for $l_{approx}$, $l_{mean}$ and the ratio $l_{approx}/l_{mean}$ are shown over 200 simulation runs for gene-environment (GxE) interaction and marginal association analyses for two sample sizes, $n = 1000$ and 10000. M, genotype model (a: additive, r: recessive, d: dominant). $b_G$, $b_{GE}$ and $b_Z$ are effect size parameters of genotype, gene-environment interaction and covariate, respectively; 0 and 1 denote absence and presence of effect.