Table S2a. Differences on risk ratio and odds ratio for *MTHFR* 677 genotypes in breast cancer (BC) (82 Studies).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Genotype  (number of studies) | BC Case  N=36683  n (%) | Control  N=40689  n (%) | Ratio Type | Test of Heterogeneity | | | Statistical Model | Test of Association | |
| Q | *p* | *I2* | Risk Ratio  (95% Cl) | *p* |
| TT (82) | 4568 (12.45) | 4652 (11.43) | Risk | 172.93 | <.0001 | 53.2% | Random | 1.13 (1.06 – 1.21) | .0004 |
|  |  |  | Odds | 176.61 | <.0001 | 54.1% | Random | 1.15 (1.07 – 1.25) | .0004 |
| CT (82) | 15443 (42.1) | 16984 (41.74) | Risk | 117.83 | .0047 | 31.3% | Random | 1.00 (0.98 – 1.03) | .6596 |
|  |  |  | Odds | 119.42 | .0036 | 32.2% | Random | 1.01 (0.97 – 1.05) | .7122 |
| CC (82) | 16671 (45.45) | 19053 (46.83) | Risk | 150.35 | <.0001 | 46.1% | Random | 0.97 (0.95 – 0.99) | .0068 |
|  |  |  | Odds | 152.02 | <.0001 | 46.7% | Random | 0.93 (0.89 – 0.98) | .0029 |
| TT +CT (82) | 20011 (54.55) | 21636 (53.17) | Risk | 150.07 | <.0001 | 46% | Random | 1.03 (1.01 – 1.05) | .0026 |
|  |  |  | Odds | 152.31 | <.0001 | 46.8 | Random | 1.07 (1.02 – 1.12) | .003 |

Table S2b. Differences on risk ratio and odds ratio for *MTHFR* 1298 genotypes in breast cancer (BC) (50 Studies).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Genotype  (number of studies) | BC Case  N=23252  n (%) | Control  N=27094  n (%) | Ratio Type | Test of Heterogeneity | | | Statistical Model | Test of Association | |
| Q | *p* | I2 | Risk Ratio  (95% Cl) | *p* |
| CC (50) | 2290 (9.84) | 2529 (9.33) | Risk | 63.78 | .0632 | 24.7% | Fixed | 1.03 (0.98 – 1.08) | .2706 |
|  |  |  | Odds | 64.77 | .0535 | 25.9% | Fixed | 1.03 (0.97 – 1.10) | .2783 |
| AC (50) | 9116 (39.21) | 10534 (38.88) | Risk | 68.20 | .0362 | 28.1% | Fixed | 1.00 (0.98 – 1.02) | .8507 |
|  |  |  | Odds | 67.83 | .0386 | 27.8% | Fixed | 1.00 (0.97 – 1.04) | .8581 |
| AA (50) | 11846 (50.95) | 14031 (51.79) | Risk | 89.67 | .0004 | 45.4% | Random | 0.99 (0.97 – 1.02) | .5506 |
|  |  |  | Odds | 94.21 | .0001 | 48% | Random | 0.98 (0.93 – 1.04) | .4750 |
| CC+AC (50) | 11406 (49.05) | 13063 (48.21) | Risk | 95.10 | <.0001 | 48.5% | Random | 1.01 (0.98 – 1.04) | .4179 |
|  |  |  | Odds | 94.21 | .0001 | 48% | Random | 1.02 (0.96 – 1.08) | .475 |

**Q = Cochran’s Q test to determine the differences between three or more matched sets of frequencies or proportions**

***p* = *p*-value or calculated probability**

***I2* = I–square or percentage of variation across studies**

**CI = confidence interval**