| Study | Experimental Events | Total | Control Events | Total | Risk Ratio | RR | 95%–CI | Weight (common) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|
| **days = NR** | | | | | | | | | |
| 207 Silberstein 2009 | 62 | 165 | 47 | 163 | | 1.30 | [0.95; 1.78] | 23.6% | 22.2% |
| **days = >median** | | | | | | | | | |
| 421 Brandes 2004 | 159 | 353 | 26 | 114 | | 1.97 | [1.38; 2.82] | 19.6% | 19.5% |
| 999 Diener 2007 | 7 | 32 | 0 | 27 | | 12.69 | [0.76; 212.36] | 0.3% | 0.6% |
| Common effect model | | 385 | | 141 | | 2.12 | [1.49; 3.02] | 19.9% | -- |
| Random effects model | | | | | | 2.90 | [0.66; 12.68] | -- | 20.1% |
| Heterogeneity: $I^2 = 39\%$, $\tau^2 = 0.6810$, $p = 0.20$ | | | | | | | | | |
| **days = </=median** | | | | | | | | | |
| 479 Silberstein 2004 | 168 | 354 | 26 | 115 | | 2.10 | [1.47; 3.00] | 19.6% | 19.5% |
| 646 Silberstein 2006 | 55 | 138 | 25 | 73 | | 1.16 | [0.80; 1.70] | 16.3% | 18.3% |
| 920 Diener 2004 | 101 | 282 | 31 | 143 | | 1.65 | [1.17; 2.34] | 20.5% | 19.9% |
| Common effect model | | 774 | | 331 | | 1.67 | [1.35; 2.05] | 56.5% | -- |
| Random effects model | | | | | | 1.60 | [1.15; 2.23] | -- | 57.8% |
| Heterogeneity: $I^2 = 60\%$, $\tau^2 = 0.0513$, $p = 0.08$ | | | | | | | | | |
| **Common effect model** | | **1324** | | **635** | | **1.67** | **[1.43; 1.95]** | **100.0%** | **--** |
| **Random effects model** | | | | | | **1.61** | **[1.29; 2.01]** | **--** | **100.0%** |

Heterogeneity: $I^2 = 50\%$, $\tau^2 = 0.0322$, $p = 0.07$
Test for subgroup differences (fixed effect): $\chi^2_2 = 4.16$, df = 2 ($p = 0.12$)
Test for subgroup differences (random effects): $\chi^2_2 = 1.64$, df = 2 ($p = 0.44$)
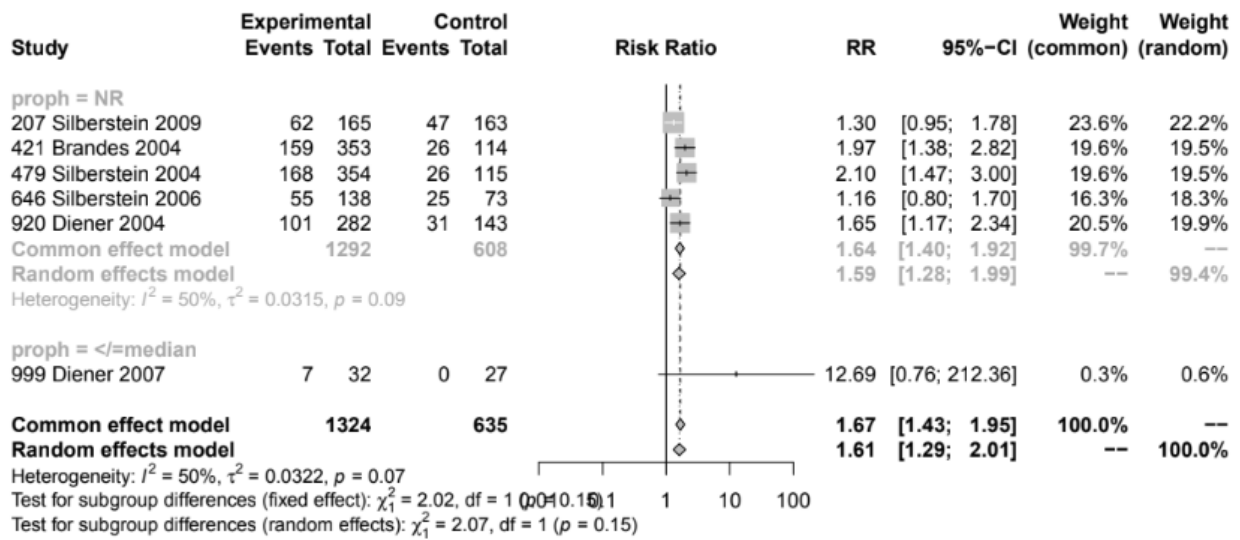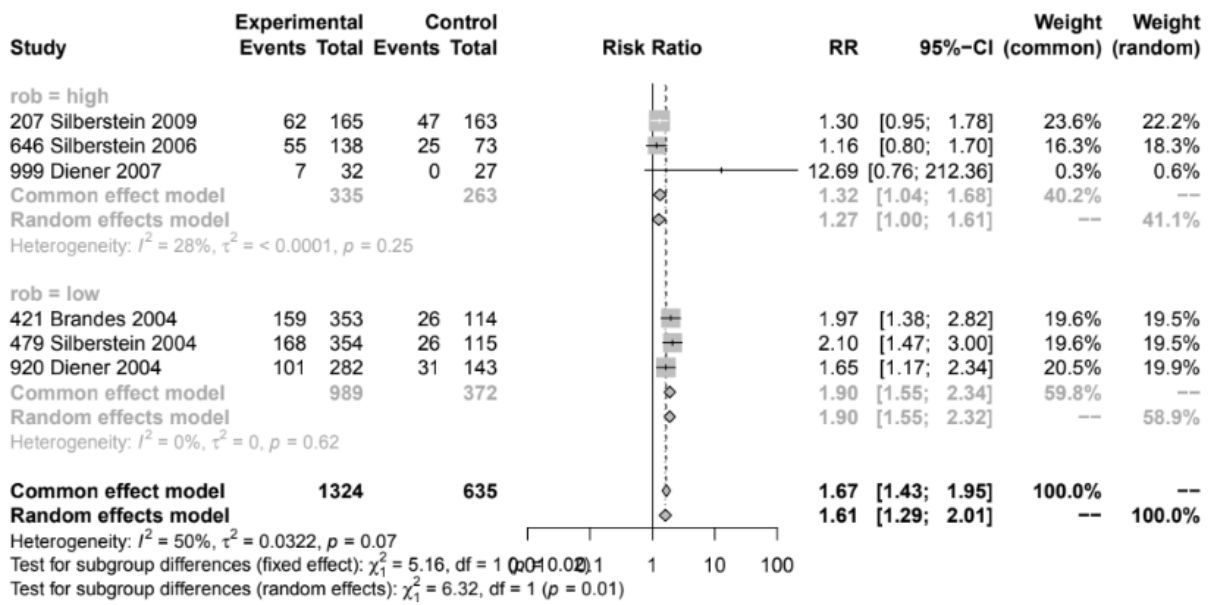
Risk Ratio axis: 0.01 0.1 1 10 100

**Supplementary Material 3.1:** Subgroup analysis for the 50% responder rate based on the number of monthly migraine days at baseline (below vs. above the median value). NR = not reported.

| Study | Experimental Events | Total | Control Events | Total | Risk Ratio | RR | 95%-CI | Weight (common) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|
| proph = NR | | | | | | | | | |
| 207 Silberstein 2009 | 62 | 165 | 47 | 163 | | 1.30 | [0.95; 1.78] | 23.6% | 22.2% |
| 421 Brandes 2004 | 159 | 353 | 26 | 114 | | 1.97 | [1.38; 2.82] | 19.6% | 19.5% |
| 479 Silberstein 2004 | 168 | 354 | 26 | 115 | | 2.10 | [1.47; 3.00] | 19.6% | 19.5% |
| 646 Silberstein 2006 | 55 | 138 | 25 | 73 | | 1.16 | [0.80; 1.70] | 16.3% | 18.3% |
| 920 Diener 2004 | 101 | 282 | 31 | 143 | | 1.65 | [1.17; 2.34] | 20.5% | 19.9% |
| Common effect model | | 1292 | | 608 | | 1.64 | [1.40; 1.92] | 99.7% | -- |
| Random effects model | | | | | | 1.59 | [1.28; 1.99] | -- | 99.4% |
| Heterogeneity: $I^2 = 50\%$, $\tau^2 = 0.0315$, $p = 0.09$ | | | | | | | | | |
| | | | | | | | | | |
| proph = </=median | | | | | | | | | |
| 999 Diener 2007 | 7 | 32 | 0 | 27 | | 12.69 | [0.76; 212.36] | 0.3% | 0.6% |
| | | | | | | | | | |
| Common effect model | | 1324 | | 635 | | 1.67 | [1.43; 1.95] | 100.0% | -- |
| Random effects model | | | | | | 1.61 | [1.29; 2.01] | -- | 100.0% |

Heterogeneity: $I^2 = 50\%$, $\tau^2 = 0.0322$, $p = 0.07$

Test for subgroup differences (fixed effect): $\chi^2_1 = 2.02$, df = 1 ($p = 0.15$)

Test for subgroup differences (random effects): $\chi^2_1 = 2.07$, df = 1 ($p = 0.15$)

0.01  0.1  1  10  100

**Supplementary Material 3.2:** Subgroup analysis for the 50% responder rate based on the proportion of patients that had previously used prophylactic therapy (below vs. above the median value). NR = not reported.

| Study | Experimental Events | Total | Control Events | Total | Risk Ratio | RR | 95%-CI | Weight (common) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|
| rob = high | | | | | | | | | |
| 207 Silberstein 2009 | 62 | 165 | 47 | 163 | | 1.30 | [0.95; 1.78] | 23.6% | 22.2% |
| 646 Silberstein 2006 | 55 | 138 | 25 | 73 | | 1.16 | [0.80; 1.70] | 16.3% | 18.3% |
| 999 Diener 2007 | 7 | 32 | 0 | 27 | | 12.69 | [0.76; 212.36] | 0.3% | 0.6% |
| Common effect model | | 335 | | 263 | | 1.32 | [1.04; 1.68] | 40.2% | -- |
| Random effects model | | | | | | 1.27 | [1.00; 1.61] | -- | 41.1% |
| Heterogeneity: $I^2$ = 28%, $\tau^2$ = < 0.0001, $p$ = 0.25 | | | | | | | | | |
| | | | | | | | | | |
| rob = low | | | | | | | | | |
| 421 Brandes 2004 | 159 | 353 | 26 | 114 | | 1.97 | [1.38; 2.82] | 19.6% | 19.5% |
| 479 Silberstein 2004 | 168 | 354 | 26 | 115 | | 2.10 | [1.47; 3.00] | 19.6% | 19.5% |
| 920 Diener 2004 | 101 | 282 | 31 | 143 | | 1.65 | [1.17; 2.34] | 20.5% | 19.9% |
| Common effect model | | 989 | | 372 | | 1.90 | [1.55; 2.34] | 59.8% | -- |
| Random effects model | | | | | | 1.90 | [1.55; 2.32] | -- | 58.9% |
| Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.62 | | | | | | | | | |
| | | | | | | | | | |
| Common effect model | | 1324 | | 635 | | 1.67 | [1.43; 1.95] | 100.0% | -- |
| Random effects model | | | | | | 1.61 | [1.29; 2.01] | -- | 100.0% |

Heterogeneity: $I^2$ = 50%, $\tau^2$ = 0.0322, $p$ = 0.07
Test for subgroup differences (fixed effect): $\chi^2_1$ = 5.16, df = 1 ($p$ = 0.02)
Test for subgroup differences (random effects): $\chi^2_1$ = 6.32, df = 1 ($p$ = 0.01)

Risk Ratio axis: 0.01 0.1 1 10 100

**Supplementary Material 3.3:** Subgroup analysis for the 50% responder rate based on the risk of bias (high vs. low). Rob = risk of bias.