**Appendix Table D53. Dose response effect on adverse effects with topiramate in children (results from randomized controlled clinical trials)**

| **Compared**  **doses** | **Type of outcome** | **Reference** | **Events/**  **randomized with smaller dose** | **Events/**  **randomized with larger dose** | **Relative risk**  **(95% CI)** | **Absolute risk difference**  **(95% CI)** | **Arcsine transformed**  **Risk difference**  **(95% CI)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 50mg vs. 100mg | Abdominal pain | Winner, 200615 | 0/12 | 2/13 | 0.2  (0.0 to 4.4) | -0.14 (-0.36 to 0.07) | -0.39 (-0.77 to 0.00) |
| 50mg vs. 200mg | Abdominal pain | Winner, 200615 | 0/12 | 2/14 | 0.2  (0.0 to 4.1) | -0.14 (-0.36 to 0.07) | -0.39 (-0.77 to -0.01) |
| 100mg vs. 200mg | Abdominal pain | Winner, 200615 | 2/13 | 2/14 | 1.0  (0.1 to 6.7) | 0.00 (-0.11 to 0.11) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Abdominal pain | Lewis, 20097 | 3/35 | 5/35 | 0.6  (0.2 to 2.3) | -0.06 (-0.21 to 0.09) | -0.09 (-0.32 to 0.14) |
| 50mg vs. 100mg | Abnormal vision | Lewis, 20097 | 1/35 | 2/35 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Allergy | Lewis, 20097 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Anorexia | Winner, 200615 | 1/12 | 1/13 | 1.0  (0.1 to 15.4) | 0.00 (-0.08 to 0.08) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 200mg | Anorexia | Winner, 200615 | 1/12 | 2/14 | 0.5  (0.1 to 5.3) | -0.07 (-0.30 to 0.17) | -0.11 (-0.48 to 0.27) |
| 100mg vs. 200mg | Anorexia | Winner, 200615 | 1/13 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Anorexia | Lewis, 20097  Pandina, 201017 | 3/35 | 4/35 | 0.8  (0.2 to 3.1) | -0.03 (-0.17 to 0.11) | -0.05 (-0.28 to 0.19) |
| 50mg vs. 100mg | Any adverse event | Winner, 200615 | 8/12 | 11/13 | 0.8  (0.5 to 1.4) | -0.12 (-0.46 to 0.22) | -0.13 (-0.52 to 0.25) |
| 50mg vs. 200mg | Any adverse event | Winner, 200615 | 8/12 | 12/14 | 0.7  (0.3 to 1.4) | -0.11 (-0.32 to 0.10) | -0.13 (-0.36 to 0.11) |
| 50mg vs. 100mg | Any adverse event | Lewis, 20097 | 26/35 | 26/35 | 1.0  (0.8 to 1.3) | 0.00 (-0.20 to 0.20) | 0.00 (-0.23 to 0.23) |
| 100mg vs. 200mg | Any adverse event | Winner, 200615 | 11/13 | 12/14 | 0.9  (0.5 to 1.8) | -0.03 (-0.25 to 0.19) | -0.03 (-0.26 to 0.20) |
| 50mg vs. 100mg | Asthma | Lewis, 20097 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Back pain | Lewis, 20097 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Bronchitis | Winner, 200615 | 0/12 | 1/13 | 0.4  (0.0 to 8.1) | -0.07 (-0.25 to 0.11) | -0.27 (-0.65 to 0.11) |
| 100mg vs. 200mg | Bronchitis | Winner, 200615 | 1/13 | 0/14 | 3.0  (0.1 to 71.2) | 0.03 (-0.05 to 0.10) | 0.17 (-0.06 to 0.40) |
| 50mg vs. 100mg | Conjunctivitis | Lewis, 20097 | 3/35 | 1/35 | 3.0  (0.3 to 27.5) | 0.06 (-0.05 to 0.17) | 0.13 (-0.11 to 0.36) |
| 50mg vs. 100mg | Cough | Lewis, 20097 | 3/35 | 1/35 | 3.0  (0.3 to 27.5) | 0.06 (-0.05 to 0.17) | 0.13 (-0.11 to 0.36) |
| 50mg vs. 100mg | Depression | Pandina, 201017 | 1/35 | 0/35 | 3.2  (0.1 to 72.5) | 0.08 (-0.12 to 0.28) | 0.29 (-0.10 to 0.69) |
| 50mg vs. 100mg | Diarrhea | Winner, 200615 | 0/12 | 1/13 | 0.4  (0.0 to 8.7) | -0.07 (-0.26 to 0.11) | -0.27 (-0.66 to 0.11) |
| 50mg vs. 200mg | Diarrhea | Winner, 200615 | 0/12 | 1/14 | 0.4  (0.0 to 8.1) | -0.07 (-0.25 to 0.11) | -0.27 (-0.65 to 0.11) |
| 100mg vs. 200mg | Diarrhea | Winner, 200615 | 1/13 | 1/14 | 1.2  (0.1 to 16.7) | 0.01 (-0.19 to 0.22) | 0.02 (-0.36 to 0.41) |
| 50mg vs. 200mg | Difficulty concentration/attention | Winner, 200615 | 0/12 | 2/14 | 0.2  (0.0 to 4.1) | -0.14 (-0.36 to 0.07) | -0.39 (-0.77 to -0.01) |
| 100mg vs. 200mg | Difficulty concentration/attention | Winner, 200615 | 0/13 | 2/14 | 0.2  (0.0 to 4.4) | -0.14 (-0.36 to 0.07) | -0.39 (-0.77 to 0.00) |
| 50mg vs. 200mg | Difficulty memory numbers | Winner, 200615 | 0/12 | 1/14 | 0.4  (0.0 to 8.1) | -0.07 (-0.25 to 0.11) | -0.27 (-0.65 to 0.11) |
| 100mg vs. 200mg | Difficulty memory numbers | Winner, 200615 | 0/13 | 1/14 | 0.3  (0.0 to 7.9) | -0.03 (-0.10 to 0.05) | -0.17 (-0.40 to 0.06) |
| 50mg vs. 100mg | Difficulty with concentration or attention | Pandina, 201017 | 0/35 | 1/35 | 0.3  (0.0 to 7.9) | -0.03 (-0.10 to 0.05) | -0.17 (-0.40 to 0.06) |
| 50mg vs. 100mg | Dizziness | Lewis, 20097  Pandina, 201017 | 2/35 | 3/35 | 0.7  (0.1 to 3.7) | -0.03 (-0.15 to 0.09) | -0.06 (-0.29 to 0.18) |
| 50mg vs. 100mg | Emotional lability | Pandina, 201017 | 1/35 | 0/35 | 3.0  (0.1 to 71.2) | 0.03 (-0.05 to 0.10) | 0.17 (-0.06 to 0.40) |
| 50mg vs. 100mg | Eye pain | Lewis, 20097 | 1/35 | 1/35 | 1.0  (0.1 to 15.4) | 0.00 (-0.08 to 0.08) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Fatigue | Winner, 200615 | 0/12 | 1/13 | 0.3  (0.0 to 7.9) | -0.03 (-0.10 to 0.05) | -0.17 (-0.40 to 0.06) |
| 50mg s. 200mg | Fatigue | Winner, 200615 | 0/12 | 2/14 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Fatigue | Lewis, 20097  Pandina, 201017 | 2/35 | 3/35 | 0.7  (0.1 to 3.7) | -0.03 (-0.15 to 0.09) | -0.06 (-0.29 to 0.18) |
| 100mg vs. 200mg | Fatigue | Winner, 200615 | 1/13 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Fever | Lewis, 20097 | 2/35 | 2/35 | 1.0  (0.1 to 6.7) | 0.00 (-0.11 to 0.11) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Infection, viral | Winner, 200615 | 1/12 | 1/13 | 1.2  (0.1 to 16.7) | 0.01 (-0.19 to 0.22) | 0.02 (-0.36 to 0.41) |
| 50mg vs. 200mg | Infection, viral | Winner, 200615 | 1/12 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Infection, viral | Lewis, 20097 | 1/35 | 3/35 | 0.3  (0.0 to 3.1) | -0.06 (-0.17 to 0.05) | -0.13 (-0.36 to 0.11) |
| 100mg vs. 200mg | Infection, viral | Winner, 200615 | 1/13 | 2/14 | 0.5  (0.1 to 5.2) | -0.07 (-0.32 to 0.18) | -0.11 (-0.50 to 0.28) |
| 50mg vs. 100mg | Injury | Winner, 200615 | 1/12 | 1/13 | 1.2  (0.1 to 16.7) | 0.01 (-0.19 to 0.22) | 0.02 (-0.36 to 0.41) |
| 50mg vs. 200mg | Injury | Winner, 200615 | 1/12 | 1/14 | 1.1  (0.1 to 15.5) | 0.01 (-0.19 to 0.20) | 0.01 (-0.37 to 0.39) |
| 100mg vs. 200mg | Injury | Winner, 200615 | 1/13 | 1/14 | 1.0  (0.1 to 15.4) | 0.00 (-0.08 to 0.08) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Injury | Lewis, 20097 | 3/35 | 4/35 | 0.8  (0.2 to 3.1) | -0.03 (-0.17 to 0.11) | -0.05 (-0.28 to 0.19) |
| 50mg vs. 100mg | Insomnia | Lewis, 20097  Pandina, 201017 | 3/35 | 1/35 | 3.0  (0.3 to 27.5) | 0.06 (-0.05 to 0.17) | 0.13 (-0.11 to 0.36) |
| 50mg vs. 200mg | Language problems | Winner, 200615 | 0/12 | 2/14 | 0.2  (0.0 to 4.1) | -0.14 (-0.36 to 0.07) | -0.39 (-0.77 to -0.01) |
| 100mg vs. 200mg | Language problems | Winner, 200615 | 0/13 | 2/14 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Mood problems | Pandina, 201017 | 1/35 | 1/35 | 1.2  (0.1 to 16.7) | 0.01 (-0.19 to 0.22) | 0.02 (-0.36 to 0.41) |
| 50mg vs. 200mg | Mood problems | Winner, 200615 | 0/12 | 1/14 | 0.4  (0.0 to 8.1) | -0.07 (-0.25 to 0.11) | -0.27 (-0.65 to 0.11) |
| 100mg vs. 200mg | Mood problems | Winner, 200615 | 0/13 | 1/14 | 0.3  (0.0 to 7.9) | -0.03 (-0.10 to 0.05) | -0.17 (-0.40 to 0.06) |
| 50mg vs. 100mg | Nausea | Lewis, 20097 | 2/35 | 3/35 | 0.7  (0.1 to 3.7) | -0.03 (-0.15 to 0.09) | -0.06 (-0.29 to 0.18) |
| 50mg vs. 100mg | Nervousness | Lewis, 20097  Pandina, 201017 | 2/35 | 1/35 | 2.0  (0.2 to 21.1) | 0.03 (-0.07 to 0.12) | 0.07 (-0.16 to 0.31) |
| 50mg vs. 100mg | Paresthesia | Winner, 200615 | 1/12 | 5/13 | 0.2  (0.0 to 1.7) | -0.27 (-0.57 to 0.02) | -0.35 (-0.73 to 0.04) |
| 50mg vs. 200mg | Paresthesia | Winner, 200615 | 1/12 | 5/14 | 0.2  (0.0 to 1.6) | -0.28 (-0.57 to 0.01) | -0.36 (-0.74 to 0.02) |
| 100mg vs. 200mg | Paresthesia | Winner, 200615 | 5/13 | 5/14 | 1.0  (0.3 to 3.2) | 0.00 (-0.16 to 0.16) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Paresthesia | Lewis, 20097 | 8/35 | 4/35 | 2.0  (0.7 to 6.0) | 0.11 (-0.06 to 0.29) | 0.15 (-0.08 to 0.39) |
| 50mg vs. 100mg | Pharyngitis | Lewis, 20097 | 1/35 | 3/35 | 0.3  (0.0 to 3.1) | -0.06 (-0.17 to 0.05) | -0.13 (-0.36 to 0.11) |
| 50mg vs. 100mg | Pneumonia | Lewis, 20097 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Psychomotor slowing | Winner, 200615 | 1/12 | 0/13 | 3.5  (0.2 to 77.9) | 0.08 (-0.11 to 0.28) | 0.29 (-0.09 to 0.68) |
| 50mg vs. 200mg | Psychomotor slowing | Winner, 200615 | 1/12 | 1/14 | 1.1  (0.1 to 15.5) | 0.01 (-0.19 to 0.20) | 0.01 (-0.37 to 0.39) |
| 100mg vs. 200mg | Psychomotor slowing | Winner, 200615 | 0/13 | 1/14 | 0.3  (0.0 to 7.9) | -0.03 (-0.10 to 0.05) | -0.17 (-0.40 to 0.06) |
| 50mg vs. 100mg | Rhinitis | Lewis, 20097 | 3/35 | 2/35 | 1.5  (0.3 to 8.4) | 0.03 (-0.09 to 0.15) | 0.06 (-0.18 to 0.29) |
| 50mg vs. 100mg | Sinusitis | Winner, 200615 | 1/12 | 1/13 | 1.2  (0.1 to 16.7) | 0.01 (-0.19 to 0.22) | 0.02 (-0.36 to 0.41) |
| 50mg vs. 200mg | Sinusitis | Winner, 200615 | 1/12 | 2/14 | 0.5  (0.1 to 5.3) | -0.07 (-0.30 to 0.17) | -0.11 (-0.48 to 0.27) |
| 100mg vs. 200mg | Sinusitis | Winner, 200615 | 1/13 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Sinusitis | Lewis, 20097 | 2/35 | 1/35 | 2.0  (0.2 to 21.1) | 0.03 (-0.07 to 0.12) | 0.07 (-0.16 to 0.31) |
| 50mg vs. 100mg | Somnolence | Winner, 200615 | 1/12 | 1/13 | 1.0  (0.1 to 15.4) | 0.00 (-0.08 to 0.08) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 200mg | Somnolence | Winner, 200615 | 1/12 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Somnolence | Lewis, 20097  Pandina, 201017 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 100mg vs. 200mg | Somnolence | Winner, 200615 | 1/13 | 2/14 | 0.5  (0.0 to 5.3) | -0.03 (-0.12 to 0.07) | -0.07 (-0.31 to 0.16) |
| 50mg vs. 100mg | Taste perversion | Lewis, 20097 | 1/35 | 3/35 | 0.3  (0.0 to 3.1) | -0.06 (-0.17 to 0.05) | -0.13 (-0.36 to 0.11) |
| 50mg vs. 100mg | Upper respiratory tract infection | Winner, 200615 | 5/12 | 3/13 | 1.9  (0.6 to 6.5) | 0.20 (-0.15 to 0.55) | 0.22 (-0.17 to 0.61) |
| 50mg vs. 200mg | Upper respiratory tract infection | Winner, 200615 | 5/12 | 3/14 | 1.8  (0.5 to 6.1) | 0.17 (-0.17 to 0.51) | 0.19 (-0.19 to 0.57) |
| 100mg vs. 200mg | Upper respiratory tract infection | Winner, 200615 | 3/13 | 3/14 | 1.0  (0.2 to 4.6) | 0.00 (-0.13 to 0.13) | 0.00 (-0.23 to 0.23) |
| 50mg vs. 100mg | Upper respiratory tract infection | Lewis, 20097 | 7/35 | 8/35 | 0.9  (0.4 to 2.2) | -0.03 (-0.22 to 0.16) | -0.03 (-0.27 to 0.20) |
| 50mg vs. 100mg | Vomiting | Lewis, 20097 | 0/35 | 2/35 | 0.2  (0.0 to 4.0) | -0.06 (-0.15 to 0.03) | -0.24 (-0.48 to -0.01) |
| 50mg vs. 100mg | Weight decrease | Winner, 200615 | 2/12 | 2/13 | 1.2  (0.2 to 7.1) | 0.02 (-0.26 to 0.30) | 0.03 (-0.35 to 0.42) |
| 50mg vs. 200mg | Weight decrease | Winner, 200615 | 2/12 | 4/14 | 0.5  (0.1 to 2.6) | -0.06 (-0.19 to 0.07) | -0.10 (-0.34 to 0.13) |
| 50mg vs. 100mg | Weight decrease | Lewis, 20097 | 10/35 | 17/35 | 0.6  (0.3 to 1.1) | -0.20 (-0.42 to 0.02) | -0.21 (-0.44 to 0.03) |
| 100mg vs. 200mg | Weight decrease | Winner, 200615 | 2/13 | 4/14 | 0.5  (0.1 to 2.5) | -0.13 (-0.44 to 0.18) | -0.16 (-0.54 to 0.22) |