# eTable 3. Summary estimates for postoperative pain at 6 hours assessment

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Subgroups** | |  | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  |  | |  | **I²**b |
|  |  |  |  |  | Gabapentinoids | Controls |  |  |  | MD [95% CI]a | |  |  |
| **Type of drug** | |  |  |  |  | |  | | --- | |  | |  |  |  |  |  |  | 79% |
|  | Pregabalin |  | 56 |  | 2634 | 1934 |  |  |  | -8 [-11, -6] | |  |  |
|  | Gabapentin |  | 70 |  | 2685 | 2686 |  |  |  | -13 [-15, -10] | |  |  |
|  | Mixedc |  | 3 |  | 180 | 90 |  |  |  | -10 [-11, 10] | |  |  |
| **Postoperative care pathway** | |  |  |  |  |  |  |  |  |  |  |  | 87% |
|  | Inpatient |  | 118 |  | 4811 | 4283 |  |  |  | -11 [-12, -9] | |  |  |
|  | Ambulatory |  | 9 |  | 628 | 367 |  |  |  | -6 [-10, -1] | |  |  |
|  | Unknown |  | 2 |  | 60 | 60 |  |  |  | -24 [-32, -17] | |  |  |
| **Dosage regimen**d | |  |  |  |  |  |  |  |  |  |  |  | 25% |
|  | High |  | 44 |  | 1584 | 1413 |  |  |  | -10 [-14, -7] | |  |  |
|  | Low |  | 70 |  | 2588 | 2807 |  |  |  | -11 [-13, -9] | |  |  |
|  | Mixedc |  | 15 |  | 1327 | 490 |  |  |  | -7 [-12, -2] | |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  |  |  |  |  | 82% |
|  | Single |  | 97 |  | 3803 | 3428 |  |  |  | -12 [-14, -10] | |  |  |
|  | Multiple |  | 31 |  | 1651 | 1267 |  |  |  | -7 [-10, -4] | |  |  |
|  | Mixedc |  | 1 |  | 45 | 15 |  |  |  | -4 [-10, 2] | |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  |  |  |  |  | 84% |
|  | Yes |  | 116 |  | 5082 | 4261 |  |  |  | -11 [-13, -9] | |  |  |
|  | No |  | 13 |  | 417 | 449 |  |  |  | -7 [-9, -4] | |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | High/unclear |  | 109 |  | 4557 | 3986 |  |  |  | -11 [-12, -9] | |  |  |
|  | Low |  | 20 |  | 942 | 724 |  |  |  | -9 [-14, -5] | |  |  |
| **Source of funding** | |  |  |  |  |  |  |  |  |  |  |  | 90% |
|  | Pharmaceutical industry |  | 3 |  | 502 | 192 |  |  |  | -2 [-5, 2] | |  |  |
|  | Not-pharmaceutical industry |  | 47 |  | 1832 | 1659 |  |  |  | -9 [-12, -7] | |  |  |
|  | Unknown |  | 79 |  | 3165 | 2859 |  |  |  | -11 [-13, -9] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Overall** | |  | 129 |  | 5499 | 4710 |  |  |  | -10 [-12, -9] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Favours gabapentinoids | | | Favours controls | | |  |  |

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |

# eTable 4. Summary estimates for postoperative pain at 12 hours assessment

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Subgroups** | |  | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  |  | |  | **I²**b |
|  |  |  |  |  | Gabapentinoids | Controls |  |  |  | MD [95% CI]a | |  |  |
| **Type of drug** | |  |  |  |  | |  | | --- | |  | |  |  |  |  |  |  | 85% |
|  | Pregabalin |  | 51 |  | 2217 | 1771 |  |  |  | -8 [-10, -5] | |  |  |
|  | Gabapentin |  | 71 |  | 3134 | 3167 |  |  |  | -10 [-12, -8] | |  |  |
|  | Mixedc |  | 8 |  | 520 | 260 |  |  |  | -4 [-7, -2] | |  |  |
| **Postoperative care pathway** | |  |  |  |  |  |  |  |  |  |  |  | 40% |
|  | Inpatient |  | 118 |  | 5371 | 4692 |  |  |  | -9 [-10, -7] | |  |  |
|  | Ambulatory |  | 7 |  | 223 | 233 |  |  |  | -5 [-9, -2] | |  |  |
|  | Unknown |  | 5 |  | 277 | 273 |  |  |  | -12 [-21, -2] | |  |  |
| **Dosage regimen**d | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | High |  | 41 |  | 1787 | 1661 |  |  |  | -10 [-13, -7] | |  |  |
|  | Low |  | 74 |  | 2951 | 3092 |  |  |  | -9 [-10, -7] | |  |  |
|  | Mixedc |  | 15 |  | 1133 | 445 |  |  |  | -7 [-12, -3] | |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  |  |  |  |  | 80% |
|  | Single |  | 93 |  | 3894 | 3462 |  |  |  | -9 [-11, -8] | |  |  |
|  | Multiple |  | 36 |  | 1932 | 1672 |  |  |  | -7 [-11, -4] | |  |  |
|  | Mixedc |  | 1 |  | 45 | 64 |  |  |  | -2 [-6, 3] | |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  |  |  |  |  | 53% |
|  | Yes |  | 111 |  | 5156 | 4535 |  |  |  | -9 [-11, -8] | |  |  |
|  | No |  | 19 |  | 715 | 663 |  |  |  | -6 [-10, -2] | |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | High/unclear |  | 116 |  | 4954 | 4390 |  |  |  | -9 [-11, -7] | |  |  |
|  | Low |  | 14 |  | 914 | 808 |  |  |  | -8 [-12, -3] | |  |  |
| **Source of funding** | |  |  |  |  |  |  |  |  |  |  |  | 40% |
|  | Pharmaceutical industry |  | 3 |  | 283 | 119 |  |  |  | -4 [-11, 2] | |  |  |
|  | Not-pharmaceutical industry |  | 42 |  | 2111 | 1941 |  |  |  | -7 [-10, -5] | |  |  |
|  | Unknown |  | 85 |  | 3477 | 3138 |  |  |  | -10 [-11, -8] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Overall** | |  | 130 |  | 5871 | 5198 |  |  |  | -9 [-10, -7] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Favours gabapentinoids | | | Favours controls | | |  |  |

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |

**eTable 5. Summary estimates for postoperative pain at 24 hours assessment**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Subgroups** | |  | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  |  | |  | **I²**b |
|  |  |  |  |  | Gabapentinoids | Controls |  |  |  | MD [95% CI]a | |  |  |
| **Type of drug** | |  |  |  |  | |  | | --- | |  | |  |  |  |  |  |  | 2% |
|  | Pregabalin |  | 59 |  | 3003 | 2166 |  |  |  | -6 [-8, -4] | |  |  |
|  | Gabapentin |  | 76 |  | 3240 | 3115 |  |  |  | -7 [-9, -6] | |  |  |
|  | Mixedc |  | 6 |  | 350 | 200 |  |  |  | -5 [-9, 0] | |  |  |
| **Postoperative care pathway** | |  |  |  |  |  |  |  |  |  |  |  | 51% |
|  | Inpatient |  | 127 |  | 5831 | 4977 |  |  |  | -7 [-8, -6] | |  |  |
|  | Ambulatory |  | 9 |  | 655 | 401 |  |  |  | -2 [-7, 3] | |  |  |
|  | Unknown |  | 2 |  | 107 | 103 |  |  |  | -7 [-13, -1] | |  |  |
| **Dosage regimen**d | |  |  |  |  |  |  |  |  |  |  |  | 55% |
|  | High |  | 48 |  | 1872 | 1612 |  |  |  | -5 [-7, -3] | |  |  |
|  | Low |  | 78 |  | 3135 | 3247 |  |  |  | -8 [-9, -6] | |  |  |
|  | Mixedc |  | 15 |  | 1586 | 622 |  |  |  | -6 [-11, -2] | |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  |  |  |  |  | 84% |
|  | Single |  | 94 |  | 3766 | 3346 |  |  |  | -8 [-9, -6] | |  |  |
|  | Multiple |  | 46 |  | 2782 | 2120 |  |  |  | -5 [-7, -3] | |  |  |
|  | Mixedc |  | 1 |  | 45 | 15 |  |  |  | 0 [-5, 5] | |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Yes |  | 127 |  | 6126 | 4976 |  |  |  | -7 [-8, -5] | |  |  |
|  | No |  | 14 |  | 467 | 505 |  |  |  | -7 [-12, -2] | |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  |  |  |  |  | 84% |
|  | High/unclear |  | 119 |  | 5416 | 4619 |  |  |  | -7 [-9, -6] | |  |  |
|  | Low |  | 22 |  | 1177 | 862 |  |  |  | -4 [-6, -1] | |  |  |
| **Source of funding** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry |  | 6 |  | 843 | 395 |  |  |  | -6 [-13, 1] | |  |  |
|  | Not-pharmaceutical industry |  | 56 |  | 2497 | 2182 |  |  |  | -6 [-8, -4] | |  |  |
|  | Unknown |  | 79 |  | 3253 | 2904 |  |  |  | -7 [-9, -6] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Overall** | |  | 141 |  | 6593 | 5481 |  |  |  | -7 [-8, -6] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Favours gabapentinoids | | | Favours controls | | |  |  |

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |

**eTable 6. Summary estimates for postoperative pain at 48 hours assessment**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Subgroups** | |  | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  |  | |  | **I²**b |
|  |  |  |  |  | Gabapentinoids | Controls |  |  |  | MD [95% CI]a | |  |  |
| **Type of drug** | |  |  |  |  | |  | | --- | |  | |  |  |  |  |  |  | 55% |
|  | Pregabalin |  | 24 |  | 1487 | 997 |  |  |  | -2 [-6, 1] | |  |  |
|  | Gabapentin |  | 34 |  | 1847 | 1731 |  |  |  | -3 [-6, -1] | |  |  |
|  | Mixedc |  | 1 |  | 100 | 50 |  |  |  | -13 [-22, -4] | |  |  |
| **Postoperative care pathway** | |  |  |  |  |  |  |  |  |  |  |  | 54% |
|  | Inpatient |  | 50 |  | 2771 | 2321 |  |  |  | -4 [-6, -1] | |  |  |
|  | Ambulatory |  | 8 |  | 596 | 394 |  |  |  | 1 [-3, 4] | |  |  |
|  | Unknown |  | 1 |  | 67 | 63 |  |  |  | -6 [-14, 2] | |  |  |
| **Dosage regimen**d | |  |  |  |  |  |  |  |  |  |  |  | 83% |
|  | High |  | 19 |  | 940 | 949 |  |  |  | -3 [-6, -0] | |  |  |
|  | Low |  | 34 |  | 1538 | 1418 |  |  |  | -4 [-7, -0] | |  |  |
|  | Mixedc |  | 6 |  | 956 | 411 |  |  |  | 1 [-0, 2] | |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Single |  | 36 |  | 2502 | 2044 |  |  |  | -3 [-5, -0] | |  |  |
|  | Multiple |  | 23 |  | 932 | 734 |  |  |  | -4 [-7, -1] | |  |  |
|  | Mixedc |  | 0 |  | - | - |  |  |  | - |  |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Yes |  | 55 |  | 3304 | 2652 |  |  |  | -3 [-5, -1] | |  |  |
|  | No |  | 4 |  | 130 | 126 |  |  |  | -4 [-17, 10] | |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  |  |  |  |  | 51% |
|  | High/unclear |  | 48 |  | 2685 | 2058 |  |  |  | -4 [-6, -1] | |  |  |
|  | Low |  | 11 |  | 749 | 720 |  |  |  | -1 [-4, 3] | |  |  |
| **Source of funding** | |  |  |  |  |  |  |  |  |  |  |  | 60% |
|  | Pharmaceutical industry |  | 4 |  | 791 | 341 |  |  |  | 1 [-2, 4] | |  |  |
|  | Not-pharmaceutical industry |  | 32 |  | 1750 | 1566 |  |  |  | -3 [-5, -1] | |  |  |
|  | Unknown |  | 23 |  | 893 | 871 |  |  |  | -4 [-8, -0] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Overall** | |  | 59 |  | 3434 | 2778 |  |  |  | -3 [-5, -1] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Favours gabapentinoids | | | Favours controls | | |  |  |

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |

**eTable 7. Summary estimates for postoperative pain at 72 hours assessment**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Subgroups** | |  | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  |  | |  | **I²**b |
|  |  |  |  |  | Gabapentinoids | Controls |  |  |  | MD [95% CI]a | |  |  |
| **Type of drug** | |  |  |  |  | |  | | --- | |  | |  |  |  |  |  |  | 0% |
|  | Pregabalin |  | 16 |  | 1327 | 724 |  |  |  | -2 [-6, 1] | |  |  |
|  | Gabapentin |  | 15 |  | 983 | 950 |  |  |  | -2 [-5, 2] | |  |  |
|  | Mixedc |  | 1 |  | 100 | 50 |  |  |  | -3 [-8, 2] | |  |  |
| **Postoperative care pathway** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Inpatient |  | 25 |  | 1767 | 1335 |  |  |  | -3 [-5, 0] | |  |  |
|  | Ambulatory |  | 6 |  | 576 | 326 |  |  |  | -1 [-4, 2] | |  |  |
|  | Unknown |  | 1 |  | 67 | 63 |  |  |  | -0 [-5, 5] | |  |  |
| **Dosage regimen**d | |  |  |  |  |  |  |  |  |  |  |  | 60% |
|  | High |  | 11 |  | 772 | 676 |  |  |  | 0 [-2, 3] | |  |  |
|  | Low |  | 16 |  | 787 | 772 |  |  |  | -5 [-8, -1] | |  |  |
|  | Mixedc |  | 5 |  | 851 | 276 |  |  |  | -1 [-4, 2] | |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  |  |  |  |  | 0% |
|  | Single |  | 5 |  | 198 | 146 |  |  |  | -2 [-7, 4] | |  |  |
|  | Multiple |  | 27 |  | 2212 | 1578 |  |  |  | -2 [-5, 0] | |  |  |
|  | Mixedc |  | 0 |  | - | - |  |  |  | - |  |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  |  |  |  |  | 75% |
|  | Yes |  | 30 |  | 2342 | 1655 |  |  |  | -2 [-4, 1] | |  |  |
|  | No |  | 2 |  | 68 | 69 |  |  |  | -5 [-8, -3] | |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  |  |  |  |  | 83% |
|  | High/unclear |  | 25 |  | 1703 | 1170 |  |  |  | -3 [-6, -1] | |  |  |
|  | Low |  | 7 |  | 707 | 554 |  |  |  | 1 [-1, 3] | |  |  |
| **Source of funding** | |  |  |  |  |  |  |  |  |  |  |  | 43% |
|  | Pharmaceutical industry |  | 6 |  | 887 | 362 |  |  |  | -5 [-12, 2] | |  |  |
|  | Not-pharmaceutical industry |  | 14 |  | 1090 | 910 |  |  |  | 0 [-2, 2] | |  |  |
|  | Unknown |  | 12 |  | 433 | 452 |  |  |  | -3 [-8, 1] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Overall** | |  | 32 |  | 2410 | 1724 |  |  |  | -2 [-4, 0] | |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Favours gabapentinoids | | | Favours controls | | |  |  |

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |

# eTable 8. Summary estimates for postoperative subacute pain assessment

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 11 |  | 462 | 342 |  | -6 [-10, -2] |  |  |
|  | Gabapentin | 7 |  | 288 | 300 |  | -5 [-14, 3] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 8 |  | 326 | 310 |  | -6 [-14, 3] |  |  |
|  | Low | 9 |  | 341 | 304 |  | -6 [-9, -3] |  |  |
|  | Mixedb | 1 |  | 83 | 28 |  | -3 [-13, 7] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 78% |
|  | Single dose | 4 |  | 133 | 123 |  | -10 [-15, -5] |  |  |
|  | Multiple dose | 14 |  | 617 | 519 |  | -4 [-6, -1] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 96% |
|  | Yes | 17 |  | 725 | 617 |  | -5 [-8, -2] |  |  |
|  | No | 1 |  | 25 | 25 |  | -28 [-37, -19] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 83% |
|  | High/unclear | 16 |  | 714 | 604 |  | -7 [-12, -2] |  |  |
|  | Low | 2 |  | 36 | 38 |  | -1 [-1, -0] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 72% |
|  | Pharmaceutical industry | 4 |  | 151 | 100 |  | -8 [-19, 3] |  |  |
|  | Not-pharmaceutical industry | 3 |  | 141 | 131 |  | -7 [-13, -1] |  |  |
|  | Unknown | 11 |  | 458 | 411 |  | 1 [-2, 4] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 18 |  | 750 | 642 |  | -6 [-9, -3] |  |  |

CI indicates confidence interval; MD, mean differences.

a On a 100-point scale.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 9. Summary estimates for postoperative chronic pain assessment

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 14 |  | 1174 | 787 |  | 0.77 [0.52, 1.15] |  |  |
|  | Gabapentin | 13 |  | 593 | 644 |  | 0.94 [0.77, 1.14] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 26% |
|  | High | 12 |  | 679 | 670 |  | 0.78 [0.54, 1.13] |  |  |
|  | Low | 12 |  | 405 | 462 |  | 0.92 [0.73, 1.15] |  |  |
|  | Mixedb | 3 |  | 683 | 299 |  | 1.27 [0.80, 2.02] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 9 |  | 323 | 305 |  | 0.76 [0.50, 1.15] |  |  |
|  | Multiple dose | 18 |  | 1444 | 1126 |  | 0.92 [0.73, 1.15] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 22% |
|  | Yes | 25 |  | 1656 | 1322 |  | 0.91 [0.75, 1.09] |  |  |
|  | No | 2 |  | 111 | 109 |  | 0.48 [0.17, 1.41] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 67% |
|  | High/unclear | 22 |  | 1433 | 1098 |  | 0.80 [0.62, 1.03] |  |  |
|  | Low | 5 |  | 334 | 333 |  | 1.06 [0.87, 1.28] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 37% |
|  | Pharmaceutical industry | 6 |  | 864 | 474 |  | 1.19 [0.83, 1.70] |  |  |
|  | Not-pharmaceutical industry | 8 |  | 469 | 449 |  | 0.87 [0.62, 1.22] |  |  |
|  | Unknown | 13 |  | 434 | 508 |  | 0.78 [0.58, 1.06] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 27 |  | 1767 | 1431 |  | 0.89 [0.74, 1.07] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 10. Summary estimates for cumulative dose of opioids administered within 24 hours following surgery

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 16% |
|  | Pregabalin | 42 |  | 1607 | 1330 |  | -7.09 [-8.30, -5.88] |  |  |
|  | Gabapentin | 68 |  | 2756 | 2702 |  | -8.58 [-10.04, -7.12] |  |  |
|  | Mixedb | 7 |  | 444 | 221 |  | -7.56 [-12.56, -2.56] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 69% |
|  | High | 36 |  | 1202 | 1069 |  | -9.53 [-11.44, -7.61] |  |  |
|  | Low | 70 |  | 2736 | 2839 |  | -6.94 [-8.05, -5.83] |  |  |
|  | Mixedb | 11 |  | 869 | 345 |  | -10.78 [-16.25, -5.32] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 74% |
|  | Single dose | 86 |  | 3408 | 3039 |  | -8.67 [-9.89, -7.45] |  |  |
|  | Multiple dose | 30 |  | 1354 | 1199 |  | -6.22 [-8.13, -4.32] |  |  |
|  | Mixedb | 1 |  | 45 | 15 |  | -10.45 [-12.94, -7.96] |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 78% |
|  | Yes | 116 |  | 4792 | 4238 |  | -7.92 [-8.85, -7.00] |  |  |
|  | No | 1 |  | 15 | 15 |  | -6.00 [-7.52, -4.48] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 87% |
|  | High/unclear | 105 |  | 4289 | 3803 |  | -8.24 [-9.21, -7.28] |  |  |
|  | Low | 12 |  | 518 | 450 |  | -4.68 [-7.00, -2.36] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 58% |
|  | Pharmaceutical industry | 3 |  | 283 | 170 |  | -14.10 [-20.58, -7.62] |  |  |
|  | Not-pharmaceutical industry | 41 |  | 1683 | 1498 |  | -7.22 [-8.42, -6.01] |  |  |
|  | Unknown | 73 |  | 2841 | 2585 |  | -8.15 [-9.45, -6.85] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 117 |  | 4807 | 4253 |  | -7.90 [-8.82, -6.98] |  |  |

CI indicates confidence interval; MD, mean differences.

a mg of intravenous morphine equivalent.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

**eTable 11. Summary estimates for cumulative dose of opioids administered within 48 hours following surgery**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 85% |
|  | Pregabalin | 12 |  | 333 | 309 |  | -13.46 [-17.98, -8.94] |  |  |
|  | Gabapentin | 12 |  | 475 | 383 |  | -5.46 [-9.60, -1.33] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 7 |  | 151 | 155 |  | -13.26 [-20.30, -6.22] |  |  |
|  | Low | 16 |  | 628 | 530 |  | -9.19 [-13.02, -5.36] |  |  |
|  | Mixedb | 1 |  | 29 | 7 |  | -26.10 [-72.03, 19.83] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 34% |
|  | Single dose | 12 |  | 457 | 344 |  | -12.18 [-16.87, -7.50] |  |  |
|  | Multiple dose | 12 |  | 351 | 348 |  | -7.98 [-12.76, -3.20] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | - |
|  | Yes | 24 |  | 808 | 692 |  | -9.79 [-12.81, -6.78] |  |  |
|  | No | 0 |  | - | - |  | - |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 20 |  | 685 | 571 |  | -9.64 [-12.80, -6.48] |  |  |
|  | Low | 4 |  | 123 | 121 |  | -8.67 [-20.40, 3.06] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 1 |  | 29 | 7 |  | -26.10 [-72.03, 19.83] |  |  |
|  | Not-pharmaceutical industry | 16 |  | 544 | 484 |  | -9.26 [-12.57, -5.96] |  |  |
|  | Unknown | 7 |  | 235 | 201 |  | -10.75 [-20.07, -1.42] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 24 |  | 808 | 692 |  | -9.79 [-12.81, -6.78] |  |  |

CI indicates confidence interval; MD, mean differences.

a mg of intravenous morphine equivalent.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 12. Summary estimates for cumulative dose of opioids administered within 72 hours following surgery

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 96% |
|  | Pregabalin | 1 |  | 40 | 40 |  | -48.60 [-56.39, -40.81] |  |  |
|  | Gabapentin | 2 |  | 100 | 103 |  | -5.38 [-17.25, 6.49] |  |  |
|  | Mixedb | 1 |  | 60 | 30 |  | -48.15 [-51.38, -44.92] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 62% |
|  | High | 1 |  | 60 | 30 |  | -48.15 [-51.38, -44.92] |  |  |
|  | Low | 3 |  | 140 | 143 |  | -20.61 [-53.78, 12.55] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 62% |
|  | Single dose | 1 |  | 60 | 30 |  | -48.15 [-51.38, -44.92] |  |  |
|  | Multiple dose | 3 |  | 140 | 143 |  | -20.61 [-53.78, 12.55] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | - |
|  | Yes | 4 |  | 200 | 173 |  | -29.18 [-46.89, -11.47] |  |  |
|  | No | 0 |  | - | - |  | - |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 2 |  | 88 | 94 |  | -27.23 [-70.04, 15.57] |  |  |
|  | Low | 2 |  | 112 | 79 |  | -28.35 [-69.40, 12.69] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | - |
|  | Pharmaceutical industry | 0 |  | - | - |  | - |  |  |
|  | Not-pharmaceutical industry | 4 |  | 200 | 173 |  | -29.18 [-46.89, -11.47] |  |  |
|  | Unknown | 0 |  | - | - |  | - |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 4 |  | 200 | 173 |  | -29.18 [-46.89, -11.47] |  |  |

CI indicates confidence interval; MD, mean differences.

a mg of intravenous morphine equivalent.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 13. Summary estimates for postanesthesia care unit length of stay

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 5 |  | 194 | 117 |  | 0.01 [-0.09, 0.11] |  |  |
|  | Gabapentin | 5 |  | 318 | 266 |  | -0.03 [-0.17, 0.10] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 5 |  | 282 | 184 |  | -0.02 [-0.12, 0.09] |  |  |
|  | Low | 3 |  | 113 | 154 |  | 0.01 [-0.22, 0.24] |  |  |
|  | Mixedb | 2 |  | 117 | 45 |  | 0.05 [-0.09, 0.18] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 6 |  | 228 | 205 |  | 0.01 [-0.11, 0.13] |  |  |
|  | Multiple dose | 4 |  | 284 | 178 |  | -0.02 [-0.10, 0.06] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 58% |
|  | Yes | 8 |  | 443 | 285 |  | 0.02 [-0.07, 0.12] |  |  |
|  | No | 2 |  | 69 | 98 |  | -0.09 [-0.20, 0.02] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 7 |  | 191 | 202 |  | -0.03 [-0.12, 0.06] |  |  |
|  | Low | 3 |  | 321 | 181 |  | 0.08 [-0.11, 0.26] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 80% |
|  | Pharmaceutical industry | 1 |  | 18 | 14 |  | 0.09 [0.03, 0.15] |  |  |
|  | Not-pharmaceutical industry | 4 |  | 290 | 234 |  | -0.08 [-0.16, 0.01] |  |  |
|  | Unknown | 5 |  |  |  |  | 0.00 [-0.08, 0.08] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 10 |  | 512 | 383 |  | -0.01 [-0.09, 0.07] |  |  |

CI indicates confidence interval; MD, mean differences.

a In hours.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 14. Summary estimates for intensive care unit length of stay

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Trials** (N) |  | **Patients** (N) |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 5 |  | 154 | 154 |  | 0.98 [-3.20, 5.17] |  |  |
|  | Gabapentin | 1 |  | 30 | 30 |  | -2.40 [-9.69, 4.89] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 3 |  | 95 | 93 |  | -1.51 [-8.22, 5.20] |  |  |
|  | Low | 3 |  | 89 | 91 |  | 2.01 [-4.64, 8.66] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 2 |  | 60 | 60 |  | 3.91 [-7.64, 15.46] |  |  |
|  | Multiple dose | 4 |  | 124 | 124 |  | -1.13 [-6.94, 4.68] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | - |
|  | Yes | 6 |  | 184 | 184 |  | 0,14 [-3,49, 3,78] |  |  |
|  | No | 0 |  | - | - |  | - |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 5 |  | 164 | 164 |  | 0.03 [-3.67, 3.72] |  |  |
|  | Low | 1 |  | 20 | 20 |  | 3.60 [-16.34, 23.54] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 70% |
|  | Pharmaceutical industry | 0 |  | - | - |  | - |  |  |
|  | Not-pharmaceutical industry | 4 |  | 109 | 111 |  | -0.99 [-4.82, 2.84] |  |  |
|  | Unknown | 2 |  | 75 | 73 |  | 10.36 [-1.12, 21.84] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 6 |  | 184 | 184 |  | 0.14 [-3.49, 3.78] |  |  |

CI indicates confidence interval; MD, mean differences.

a In hours.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 15. Summary estimates for hospital length of stay

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**b |
|  |  |  |  | Gabapentinoids | Controls |  | MD[95% CI]a |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 9 |  | 787 | 511 |  | 1.31 [-1.44, 4.06] |  |  |
|  | Gabapentin | 8 |  | 572 | 593 |  | 4.11 [-1.64, 9.87] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 47% |
|  | High | 6 |  | 571 | 589 |  | -0.39 [-2.48, 1.71] |  |  |
|  | Low | 8 |  | 251 | 257 |  | 6.41 [-1.65, 14.47] |  |  |
|  | Mixedb | 3 |  | 537 | 258 |  | 3.80 [-2.52, 10.11] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 7 |  | 223 | 190 |  | 2.82 [-1.47, 7.10] |  |  |
|  | Multiple dose | 10 |  | 1136 | 914 |  | 4.06 [-0.75, 8.87] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 0% |
|  | Yes | 16 |  | 1343 | 1087 |  | 2.99 [0.10, 5.88] |  |  |
|  | No | 1 |  | 16 | 17 |  | 3.30 [-2.60, 9.20] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 10 |  | 783 | 587 |  | 2.62 [-0.87, 6.10] |  |  |
|  | Low | 7 |  | 576 | 517 |  | 3.47 [-1.00, 7.95] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 3 |  | 569 | 346 |  | 3.93 [-3.31, 11.17] |  |  |
|  | Not-pharmaceutical industry | 8 |  | 578 | 581 |  | 3.34 [-5.16, 11.83] |  |  |
|  | Unknown | 6 |  | 212 | 177 |  | 3.13 [-1.13, 7.39] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 17 |  | 1359 | 1104 |  | 2.96 [0.28, 5.63] |  |  |

CI indicates confidence interval; MD, mean differences.

a In hours.

b Test for subgroup differences.

c The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

d High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 16. Summary estimates for postoperative nausea and vomiting

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 85 |  | 4516 | 3403 |  | 0.76 [0.69, 0.84] |  |  |
|  | Gabapentin | 92 |  | 4169 | 4079 |  | 0.77 [0.70, 0.85] |  |  |
|  | Mixedb | 10 |  | 652 | 326 |  | 0.72 [0.53, 0.99] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 60 |  | 2539 | 2304 |  | 0.72 [0.63, 0.82] |  |  |
|  | Low | 108 |  | 4788 | 4680 |  | 0.79 [0.73, 0.87] |  |  |
|  | Mixedb | 19 |  | 2010 | 824 |  | 0.76 [0.64, 0.89] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 75% |
|  | Single dose | 133 |  | 5773 | 5197 |  | 0.75 [0.69, 0.82] |  |  |
|  | Multiple dose | 52 |  | 3504 | 2581 |  | 0.80 [0.72, 0.88] |  |  |
|  | Mixedb | 2 |  | 60 | 30 |  | 0.13 [0.03, 0.47] |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 29% |
|  | Yes | 160 |  | 8090 | 6535 |  | 0.76 [0.70, 0.81] |  |  |
|  | No | 27 |  | 1247 | 1273 |  | 0.84 [0.72, 0.98] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 415 |
|  | High/unclear | 161 |  | 7893 | 6606 |  | 0.75 [0.70, 0.81] |  |  |
|  | Low | 26 |  | 1444 | 1202 |  | 0.83 [0.73, 0.96] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 15 |  | 1472 | 936 |  | 0.82 [0.73, 0.94] |  |  |
|  | Not-pharmaceutical industry | 77 |  | 3683 | 3221 |  | 0.75 [0.68, 0.83] |  |  |
|  | Unknown | 95 |  | 4182 | 3651 |  | 0.76 [0.68, 0.84] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 187 |  | 9337 | 7808 |  | 0.77 [0.72, 0.82] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 17. Summary estimates for dizziness

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 83% |
|  | Pregabalin | 69 |  | 3679 | 2741 |  | 1.47 [1.25, 1.74] |  |  |
|  | Gabapentin | 57 |  | 2486 | 2428 |  | 1.05 [0.95, 1.16] |  |  |
|  | Mixedb | 8 |  | 480 | 240 |  | 1.46 [0.70, 3.06] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 39% |
|  | High | 47 |  | 1991 | 1859 |  | 1.24 [1.05, 1.46] |  |  |
|  | Low | 70 |  | 2820 | 2762 |  | 1.18 [1.02, 1.37] |  |  |
|  | Mixedb | 17 |  | 1834 | 788 |  | 1.54 [1.20, 1.98] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 8% |
|  | Single dose | 86 |  | 3546 | 3070 |  | 1.33 [1.12, 1.57] |  |  |
|  | Multiple dose | 47 |  | 3054 | 2324 |  | 1.19 [1.04, 1.36] |  |  |
|  | Mixedb | 1 |  | 45 | 15 |  | 3.67 [0.52, 26.08] |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 71% |
|  | Yes | 111 |  | 5547 | 4403 |  | 1.20 [1.09, 1.33] |  |  |
|  | No | 23 |  | 1098 | 1006 |  | 1.85 [1.19, 2.88] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 117 |  | 5617 | 4517 |  | 1.27 [1.12, 1.44] |  |  |
|  | Low | 17 |  | 1028 | 892 |  | 1.17 [1.01, 1.35] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 1% |
|  | Pharmaceutical industry | 13 |  | 1281 | 831 |  | 1.29 [1.10, 1.53] |  |  |
|  | Not-pharmaceutical industry | 59 |  | 2811 | 2418 |  | 1.17 [1.02, 1.35] |  |  |
|  | Unknown | 62 |  | 2553 | 2160 |  | 1.40 [1.13, 1.73] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 134 |  | 6645 | 5409 |  | 1.25 [1.12, 1.39] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 18. Summary estimates for visual disturbance

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** | |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 75% |
|  | Pregabalin | 37 |  | 1483 | 1259 |  | 2.78 [1.97, 3.92] |  |  |
|  | Gabapentin | 15 |  | 891 | 824 |  | 1.49 [1.14, 1.95] |  |  |
|  | Mixedb | 2 |  | 120 | 60 |  | 2.54 [0.13, 51.31] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 48% |
|  | High | 23 |  | 1244 | 1103 |  | 1.75 [1.35, 2.28] |  |  |
|  | Low | 26 |  | 914 | 892 |  | 1.87 [1.27, 2.74] |  |  |
|  | Mixedb | 5 |  | 336 | 148 |  | 4.22 [1.82, 9.81] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 38% |
|  | Single dose | 34 |  | 1326 | 1179 |  | 2.50 [1.72, 3.64] |  |  |
|  | Multiple dose | 19 |  | 1123 | 949 |  | 1.66 [1.28, 2.14] |  |  |
|  | Mixedb | 1 |  | 45 | 15 |  | 2.50 [1.72, 3.64] |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 0% |
|  | Yes | 49 |  | 2256 | 1868 |  | 1.88 [1.52, 2.32] |  |  |
|  | No | 5 |  | 238 | 275 |  | 2.66 [0.21, 33.89] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 46 |  | 1808 | 1606 |  | 2.36 [1.69, 3.30] |  |  |
|  | Low | 8 |  | 686 | 537 |  | 1.85 [1.25, 2.75] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 5 |  | 210 | 227 |  | 2.29 [1.06, 4.91] |  |  |
|  | Not-pharmaceutical industry | 26 |  | 1457 | 1124 |  | 2.17 [1.15, 4.08] |  |  |
|  | Unknown | 23 |  | 827 | 792 |  | 1.93 [1.49, 2.50] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 54 |  | 2494 | 2143 |  | 1.89 [1.53, 2.33] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 19. Summary estimates for respiratory failure

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 22 |  | 1176 | 883 |  | 1.09 [0.50, 2.39] |  |  |
|  | Gabapentin | 15 |  | 775 | 1075 |  | 0.79 [0.30, 2.10] |  |  |
|  | Mixedb | 5 |  | 300 | 150 |  | 0.42 [0.14, 1.26] |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 11 |  | 415 | 467 |  | 0.99 [0.29, 3.47] |  |  |
|  | Low | 25 |  | 1025 | 1251 |  | 1.02 [0.46, 2.26] |  |  |
|  | Mixedb | 6 |  | 811 | 390 |  | 0.52 [0.22, 1.25] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 30 |  | 1447 | 1559 |  | 0.68 [0.35, 1.34] |  |  |
|  | Multiple dose | 12 |  | 804 | 549 |  | 1.01 [0.43, 2.42] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 0% |
|  | Yes | 33 |  | 1812 | 1599 |  | 0.81 [0.47, 1.39] |  |  |
|  | No | 9 |  | 439 | 509 |  | 0.34 [0.01, 8.13] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 11% |
|  | High/unclear | 35 |  | 1920 | 1849 |  | 0.71 [0.40, 1.26] |  |  |
|  | Low | 7 |  | 331 | 259 |  | 1.69 [0.38, 7.61] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 4 |  | 571 | 316 |  | 1.08 [0.24, 4.89] |  |  |
|  | Not-pharmaceutical industry | 21 |  | 881 | 766 |  | 0.77 [0.37, 1.59] |  |  |
|  | Unknown | 17 |  | 799 | 1026 |  | 0.73 [0.29, 1.86] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 42 |  | 2251 | 2108 |  | 0.79 [0.46, 1.35] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 20. Summary estimates for fall or ataxia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 0% |
|  | Pregabalin | 7 |  | 431 | 322 |  | 1.79 [0.74, 4.30] |  |  |
|  | Gabapentin | 7 |  | 797 | 785 |  | 1.14 [0.80, 1.62] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 0% |
|  | High | 4 |  | 628 | 618 |  | 2.74 [0.31, 24.07] |  |  |
|  | Low | 8 |  | 325 | 361 |  | 1.11 [0.57, 2.17] |  |  |
|  | Mixedb | 2 |  | 275 | 128 |  | 4.17 [0.53, 32.87] |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 70% |
|  | Single dose | 7 |  | 288 | 276 |  | 2.27 [1.20, 4.29] |  |  |
|  | Multiple dose | 7 |  | 940 | 831 |  | 1.12 [0.75, 1.68] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | 0% |
|  | Yes | 12 |  | 1171 | 1015 |  | 1.34 [0.89, 2.04] |  |  |
|  | No | 2 |  | 57 | 92 |  | 0.45 [0.02, 9.07] |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 0% |
|  | High/unclear | 10 |  | 612 | 502 |  | 1.75 [0.78, 3.90] |  |  |
|  | Low | 4 |  | 616 | 605 |  | 1.12 [0.61, 2.04] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 59% |
|  | Pharmaceutical industry | 3 |  | 262 | 205 |  | 2.16 [1.14, 4.10] |  |  |
|  | Not-pharmaceutical industry | 8 |  | 869 | 807 |  | 1.15 [0.73, 1.82] |  |  |
|  | Unknown | 3 |  | 97 | 95 |  | Not estimable |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 14 |  | 1228 | 1107 |  | 1.31 [0.88, 1.95] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 21. Summary estimates for delirium

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| **Subgroups** | | **Number of Trials** |  | **Number of Patients** |  |  | **Summary Estimate** |  | **I2**a |
|  |  |  |  | Gabapentinoids | Controls |  | RR[95% CI] |  |  |
| **Type of drug** | |  |  |  |  |  |  |  | 44% |
|  | Pregabalin | 2 |  | 66 | 66 |  | 0.26 [0.03, 2.26] |  |  |
|  | Gabapentin | 2 |  | 386 | 388 |  | 1.15 [0.87, 1.51] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Dosage regimen**c | |  |  |  |  |  |  |  | 55% |
|  | High | 1 |  | 350 | 347 |  | 1.16 [0.88, 1.53] |  |  |
|  | Low | 3 |  | 102 | 107 |  | 0.29 [0.05, 1.75] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Single or multiple intake** | |  |  |  |  |  |  |  | 0% |
|  | Single dose | 1 |  | 36 | 41 |  | 0.38 [0.02, 9.01] |  |  |
|  | Multiple dose | 3 |  | 416 | 413 |  | 1.13 [0.86, 1.49] |  |  |
|  | Mixedb | 0 |  | - | - |  | - |  |  |
| **Associated with opioids** | |  |  |  |  |  |  |  | - |
|  | Yes | 4 |  | 452 | 454 |  | 1.12 [0.85, 1.47] |  |  |
|  | No | 0 |  | - | - |  | - |  |  |
| **Risk of bias** | |  |  |  |  |  |  |  | 55% |
|  | High/unclear | 3 |  | 102 | 107 |  | 0.29 [0.05, 1.75] |  |  |
|  | Low | 1 |  | 350 | 347 |  | 1.16 [0.88, 1.53] |  |  |
| **Source of funding** | |  |  |  |  |  |  |  | 0% |
|  | Pharmaceutical industry | 0 |  | - | - |  | - |  |  |
|  | Not-pharmaceutical industry | 2 |  | 379 | 378 |  | 0.98 [0.37, 2.63] |  |  |
|  | Unknown | 2 |  | 73 | 76 |  | 0.35 [0.04, 3.25] |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Overall** | | 4 |  | 452 | 454 |  | 1.12 [0.85, 1.47] |  |  |

CI indicates confidence interval; RR, risk ratios.

a Test for subgroup differences.

b The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial).

c High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day). The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered.

# eTable 22. Exploratory analyses: Summary estimates for postoperative pain at 12 hours assessment





****

CI indicates confidence interval; MD, mean differences.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| a | On a 100-point scale. | | | | | | | | | | | |
| b | Test for subgroup differences. |  |  |  |  |  |  |  |  |  |  |  |
| c | The two subgroups were tested in the same trial in two different groups of patients (must have more than two groups in the same trial). | | | | | | | | | | | |
| d | Surgery associated with chronic pain (thoracotomy, mastectomy, inguinal hernia repair, coronary artery bypass, ceasarian, cholecystectomy and amputation). | | | | | | | | | | | |
| e | Sedation and/or local anesthesia. | | | | | | | | | | | |
| f | High dose (pregabalin ≥300mg/day or gabapentin ≥ 900mg/day); Low dose (pregabalin <300mg/day or gabapentin < 900mg/day. | | | | | | | | | | | |
|  | The dosage was estimated based on the cumulative dose of gabapentinoids administered within 24 hours of the first dose administered. | | | | | | | | | | | |
| g | Both covariates were present for all subjects included in the trial. | | | | | | | | | | | |
| h | At least one other type of analgesic drug was administered on a regular basis. | | | | | | | | | | | |
| i | Post-hoc analysis. |  |  |  |  |  |  |  |  |  |  |  |
| j | This classification is based on previous work and it has not been validated. |  |  |  |  |  |  |  |  |  |  |  |