Table E15. Benefits and risks of second-generation antidepressants compared with St. John’s wort monotherapy

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| --- | --- | --- | --- | --- | --- | --- |
| Outcomes | Anticipated Absolute Effectsa:  *Benefit and risk with St. John’s Wort* | Anticipated Absolute Effectsa (95% CI):  *Benefit and risk with SGA* | Relative Effect (95% CI) | Number of Participants  (Trials) | Strength of Evidence | Comments |
| **Response** Assessed with: HAM-D Followup: range 4-12 weeks | 54 per 100 | 52 per 100 (45 to 60) | RR, 0.96 (0.83 to 1.10) | 1517 (9 trials30-39) | Lowb,c | Evidence is based on the comparison of SSRIs with SJW. |
| **Response in subgroup of older adults**  Assessed with: HAM-D  Followup: mean 6 weeks | 64 per 100 | 55 per 100  (43 to 71) | RR, 0.83 (0.67 to 1.11) | 161  (1 trial36) | Lowe | Comparison limited to fluoxetine and SJW in older adults (60 to 80 years) |
| **Remission** Assessed with: HAM-D followup: mean 13 weeks | 36 per 100 | 30 per 100 (24 to 36) | RR, 0.82 (0.67 to 1.00) | 768 (5 trials31,33,37,39-41) | Lowc,d | Evidence is based on the comparison of SSRIs with SJW. |
| **Quality of life** | NA | NA | NA | 0 (0 trials) | Insufficient | None |
| **Functional capacity** | NA | NA | NA | 0 (0 trials) | Insufficient | None |
| **Suicidal ideas or behaviors** | 1 per 100 | 1 per 100 (0 to 6) | RR, 1.03 (0.11 to 9.81) | 331 (2 trials34,42) | Insufficiente,g | None |
| **Serious adverse events** | 2 per 100 | 1 per 100 (0 to 5) | RR, 0.79 (0.23 to 2.72) | 840 (4 trials34,35,39,42) | Lowe | None |
| **Overall risk for adverse events** | 39 per 100 | 47 per 100 (41 to 53) | RR, 1.19 (1.05 to 1.34) | 1427 (8 trials30,31,34-36,38,39,42) | Moderated | None |
| **Overall risk for adverse events**  **in subgroup based on older age** | 16 per 100 | 20 per 100  (10 to 40) | RR, 1.30 (0.66 to 2.54) | 131  (1 trial36) | Lowe | Comparison limited to fluoxetine and SJW in older adults (60 to 80 years) |
| **Overall discontinuation** | 15 per 100 | 19 per 100 15 to 24) | RR, 1.28 (1.01 to 1.62) | 1651 (9 trials30,31,33-36,38,39,42) | Moderatec | None |
| **Discontinuation because of adverse events** | 4 per 100 | 7 per 100 (5 to 11) | RR, 1.7 (1.12 to 2.6) | 1651 (9 trials30,31,33-36,38,39,42) | Moderatec | None |

Table E15. Benefits and risks of second-generation antidepressants compared with St. John’s wort monotherapy (continued)

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| --- | --- | --- | --- | --- | --- | --- |
| Outcomes | Anticipated Absolute Effectsa:  *Benefit and risk with St. John’s Wort* | Anticipated Absolute Effectsa (95% CI):  *Benefit and risk with SGA* | Relative Effect (95% CI) | Number of Participants  (Trials) | Strength of Evidence | Comments |
| **Discontinuation because of adverse events in subgroup based on older age** | 65 per 100 | 79 per 100  (29 to 218) | RR, 1.22 (0.44 to 3.36) | 161  (1 trial29) | Lowe | Comparison limited to fluoxetine and SJW in older adults (60 to 80 years) |

a The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

b Downgraded for inconsistency: moderate heterogeneity (I2=47%).

c Downgraded for indirectness: most studies compared to low or moderate dose SGA.

d Downgraded for imprecision: few events.

e Downgraded 2 steps for serious imprecision: few events overall and confidence interval crosses threshold of appreciable difference.

f Downgraded for risk of bias: Conflicting definitions of suicidal ideas or behaviors and suspected outcomes reporting bias.

CI = confidence interval; HAM-D = Hamilton Depression Rating Scale; N = number of participants; NWMA = network meta-analyses; OIS = optimal information size; RR: Risk ratio; SGA = second-generation antidepressant; SJW = St. John’s wort; SSRI = selective serotonin reuptake inhibitor