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-DFollowup: 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-DFollowup: 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-Dfollowup: 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)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| 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