# Appendix 16c: Clinical evidence profiles for pharmacological and physical interventions

This appendix contains evidence profiles for reviews substantially updated or added to the guideline update (summary evidence profiles are included in the evidence chapters). The use of evidence profiles was introduced since the previous guideline was published.

Evidence profile tables summarise both the quality of the evidence and the results of the evidence synthesis. Each table includes details about the quality assessment of each outcome: quality of the included studies, number of studies and participants, limitations, information about the consistency of the evidence (based on heterogeneity – see Chapter 3), directness of the evidence (that is, how closely the outcome measures, interventions and participants match those of interest) and any other considerations (for example, effect sizes with wide confidence intervals [CIs] would be described as imprecise data). Each evidence profile also includes a summary of the findings: number of patients included in each group, an estimate of the magnitude of effect, quality of the evidence, and the importance of the evidence (where appropriate). The quality of the evidence was based on the quality assessment components (study design, limitations to study quality, consistency, directness and any other considerations) and graded using the following definitions:

**High** = further research is very unlikely to change our confidence in the estimate of the effects

**Moderate** = further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate

**Low** = further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate

**Very low** = any estimate of effect is very uncertain.

For further information about the process and the rationale of producing an evidence profile table see GRADE (2004) Grading quality of evidence and strength of recommendations. *British Medical Journal*, 328, 1490-1497.

# Contents

# Tricyclic antidepressants (TCAs)

## Are TCAs effective in depression? (TCAs versus placebo – efficacy data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | TCAs | Placebo | Relative (95% CI) | Absolute | | |
| **Mean endpoint depression scores (Better indicated by lower values)** | | | | | | | | | | | | |
| 22 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 1225 | 1220 | - | SMD 0.48 lower (0.59 to 0.37 lower) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint depression scores - Amitriptyline (Better indicated by lower values)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 176 | 172 | - | SMD 0.61 lower (0.83 to 0.4 lower) | ⊕⊕⊕⊕ HIGH | |
| **Mean endpoint depression scores - Dosulepin (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 194 | 192 | - | SMD 0.49 lower (0.7 to 0.29 lower) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean endpoint depression scores - Imipramine (Better indicated by lower values)** | | | | | | | | | | | | |
| 13 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 803 | 800 | - | SMD 0.41 lower (0.54 to 0.27 lower) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint depression scores - Nortriptyline (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 52 | 56 | - | SMD 0.8 lower (1.37 to 0.24 lower) | ⊕⊕⊕O MODERATE | |
| **Mean depression change scores (Better indicated by lower values)** | | | | | | | | | | | | |
| 8 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 676 | 643 | - | SMD 0.47 lower (0.74 to 0.21 lower) | ⊕⊕⊕O MODERATE | |
| **Mean depression change scores - Amitriptyline (Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 387 | 404 | - | SMD 0.69 lower (1.07 to 0.3 lower) | ⊕⊕⊕O MODERATE | |
| **Mean depression change scores - Imipramine (Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised | no serious | no serious | no serious | no serious | none | 289 | 239 | - | SMD 0.21 lower (0.41 | ⊕⊕⊕⊕ | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | imprecision | | | | | to 0.01 lower) | HIGH | |
| **Sensitivity analysis: Mean depression change scores (Better indicated by lower values)** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 604 | 569 | - | SMD 0.35 lower (0.53 to 0.18 lower) | ⊕⊕⊕O MODERATE | |
| **Sensitivity analysis: Mean depression change scores - Amitriptyline (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 315 | 330 | - | SMD 0.5 lower (0.67 to 0.34 lower) | ⊕⊕⊕⊕ HIGH | |
| **Sensitivity analysis: Mean depression change scores - Imipramine (Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 289 | 239 | - | SMD 0.21 lower (0.41 to 0.01 lower) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving remission** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 301/478 (63%) | 393/476 (82.6%)<br>79% | RR 0.74 (0.65 to 0.84) | 215 fewer per 1000 (from 132 fewer to 289 fewer)<br>205 fewer per 1000 | ⊕⊕⊕O MODERATE | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (from 126 fewer to 277 fewer) | | |
| **Number not achieving remission - Amitriptyline** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 42/81 (51.9%) | 59/71 (83.1%) | RR 0.66 (0.44 to 1) | 283 fewer per 1000 (from 465 fewer to 0 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 76.7% | | 261 fewer per 1000 (from 430 fewer to 0 more) | | |
| **Number not achieving remission - Clomipramine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 9/20 (45%) | 14/18 (77.8%) | RR 0.58 (0.34 to 1) | 327 fewer per 1000 (from 513 fewer to 0 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 77.8% | | 327 fewer per 1000 (from 513 fewer to 0 more) | | |
| **Number not achieving remission - Dosulepin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 2/17 (11.8%) | 2/20 (10%) | RR 1.18 (0.18 to 7.48) | 18 more per 1000 (from 82 fewer to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 648 more) | | |
| | | | | | | | | 10% | | 18 more per 1000 (from 82 fewer to 648 more) | | |
| **Number not achieving remission - Imipramine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[5] | none | 207/294 (70.4%) | 258/302 (85.4%) | RR 0.83 (0.75 to 0.91) | 145 fewer per 1000 (from 77 fewer to 214 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 83.1% | | 141 fewer per 1000 (from 75 fewer to 208 fewer) | | |
| **Number not achieving remission - Nortriptyline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 41/66 (62.1%) | 60/65 (92.3%) | RR 0.68 (0.52 to 0.88) | 295 fewer per 1000 (from 111 fewer to 443 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 92.4% | | 296 fewer per 1000 (from 111 fewer to 444 fewer) | | |
| | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number not achieving response (50% reduction in depression scores)** | | | | | | | | | | | | |
| 35 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1041/2444 (42.6%) | 1529/2419 (63.2%)<br>65.9% | RR 0.69 (0.64 to 0.74) | 196 fewer per 1000 (from 164 fewer to 228 fewer)<br>204 fewer per 1000 (from 171 fewer to 237 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving response (50% reduction in depression scores) - Amitriptyline** | | | | | | | | | | | | |
| 14 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 485/1144 (42.4%) | 718/1147 (62.6%)<br>67.3% | RR 0.69 (0.61 to 0.78) | 194 fewer per 1000 (from 138 fewer to 244 fewer)<br>209 fewer per 1000 (from 148 fewer to 262 fewer) | ⊕⊕⊕O MODERATE | |
| **Number not achieving response (50% reduction in depression scores) - Dosulepin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 94/194 (48.5%) | 126/192 (65.6%)<br>65.6% | RR 0.74 (0.62 to 0.88) | 171 fewer per 1000 (from 79 fewer to 249 fewer)<br>171 fewer | ⊕⊕⊕⊕ HIGH | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 1000 (from 79 fewer to 249 fewer) | | |
| **Number not achieving response (50% reduction in depression scores) - Imipramine** | | | | | | | | | | | | |
| 20 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 462/1106 (41.8%) | 685/1080 (63.4%)<br>65.2% | RR 0.69 (0.62 to 0.76) | 197 fewer per 1000 (from 152 fewer to 241 fewer)<br>202 fewer per 1000 (from 156 fewer to 248 fewer) | ⊕⊕⊕O MODERATE | |
| **Sensitivity analysis: Number not achieving response (50% reduction in depression scores)** | | | | | | | | | | | | |
| 34 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1022/2372 (43.1%) | 1471/2345 (62.7%)<br>65.8% | RR 0.7 (0.66 to 0.75) | 188 fewer per 1000 (from 157 fewer to 213 fewer)<br>197 fewer per 1000 (from 165 fewer to 224 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Sensitivity analysis: Number not achieving response (50% reduction in depression scores) - Amitriptyline** | | | | | | | | | | | | |
| 13 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 466/1072 (43.5%) | 660/1073 (61.5%) | RR 0.71 (0.65 to | 178 fewer per 1000 (from 135 | ⊕⊕⊕⊕ HIGH | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 0.78) | fewer to 215 fewer) | | |
| | | | | | | | | 67.3% | | 195 fewer per 1000 (from 148 fewer to 236 fewer) | | |
| **Sensitivity analysis: Number not achieving response (50% reduction in depression scores) - Dosulepin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 94/194 (48.5%) | 126/192 (65.6%) | RR 0.74 (0.62 to 0.88) | 171 fewer per 1000 (from 79 fewer to 249 fewer) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 65.6% | | 171 fewer per 1000 (from 79 fewer to 249 fewer) | | |
| **Sensitivity analysis: Number not achieving response (50% reduction in depression scores) - Imipramine** | | | | | | | | | | | | |
| 20 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 462/1106 (41.8%) | 685/1080 (63.4%) | RR 0.69 (0.62 to 0.76) | 197 fewer per 1000 (from 152 fewer to 241 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 65.2% | | 202 fewer per 1000 (from 156 fewer to 248 fewer) | | |

[1] Moderate heterogeneity

[2] Single study

[3] Large heterogeneity
[4] Inconclusive effect size
[5] Uncertain clinical importance

## Are TCAs effective in depression? (TCAs versus placebo – acceptability/tolerability data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | TCAs | Placebo | Relative (95% CI) | Absolute | | |
| **Number leaving treatment early for any reason** | | | | | | | | | | | | |
| 85 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 1864/5039 (37%) | 1830/4862 (37.6%)<br>39% | RR 0.99 (0.92 to 1.06) | 4 fewer per 1000 (from 30 fewer to 23 more)<br>4 fewer per 1000 (from 31 fewer to 23 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason - Amitriptyline** | | | | | | | | | | | | |
| 23 | randomised trials | no serious limitations | serious[2,3] | no serious indirectness | no serious imprecision | none | 464/1424 (32.6%) | 474/1381 (34.3%)<br>35.7% | RR 0.93 (0.79 to 1.1) | 24 fewer per 1000 (from 72 fewer to 34 more)<br>25 fewer per 1000 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (from 75 fewer to 36 more) | | |
| **Number leaving treatment early for any reason - Clomipramine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 6/30 (20%) | 7/28 (25%)<br><br>23.9% | RR 0.82 (0.3 to 2.19) | 45 fewer per 1000 (from 175 fewer to 298 more)<br><br>43 fewer per 1000 (from 167 fewer to 284 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason - Dosulepin** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 96/236 (40.7%) | 94/239 (39.3%)<br><br>33.3% | RR 1.09 (0.79 to 1.5) | 35 more per 1000 (from 83 fewer to 197 more)<br><br>30 more per 1000 (from 70 fewer to 167 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason - Imipramine** | | | | | | | | | | | | |
| 54 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 1253/3222 (38.9%) | 1198/3090 (38.8%) | RR 1.01 (0.93 to | 4 more per 1000 (from 27 fewer to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.09) | 35 more) | | |
| | | | | | | | | 41% | | 4 more per 1000 (from 29 fewer to 37 more) | | |
| **Number leaving treatment early for any reason - Nortriptyline** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[2] | no serious indirectness | serious[1] | none | 45/127 (35.4%) | 57/124 (46%) | RR 0.73 (0.27 to 2.03) | 124 fewer per 1000 (from 336 fewer to 473 more) | ⊕⊕OO LOW | |
| | | | | | | | | 42.9% | | 116 fewer per 1000 (from 313 fewer to 442 more) | | |
| **Number leaving treatment early due to side effects** | | | | | | | | | | | | |
| 65 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 777/4151 (18.7%) | 184/4022 (4.6%) | RR 4.02 (3.46 to 4.67) | 138 more per 1000 (from 113 more to 168 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 4.6% | | 139 more per 1000 (from 113 more to 169 more) | | |
| **Number leaving treatment early due to side effects - Amitriptyline** | | | | | | | | | | | | |
| 16 | randomised | no serious | no serious | no serious | no serious | none | 199/1193 | 40/1157 | RR 4.66 | 127 more | ⊕⊕⊕⊕ | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | imprecision | | (16.7%) | (3.5%) | (3.38 to 6.44) | per 1000 (from 82 more to 188 more) | HIGH | |
| | | | | | | | | 3.2% | | 117 more per 1000 (from 76 more to 174 more) | | |
| **Number leaving treatment early due to side effects - Clomipramine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[1] | none | 2/20 (10%) | 2/18 (11.1%) | RR 0.9 (0.14 to 5.74) | 11 fewer per 1000 (from 96 fewer to 527 more) | ⊕⊕OO LOW | |
| | | | | | | | | 11.1% | | 11 fewer per 1000 (from 95 fewer to 526 more) | | |
| **Number leaving treatment early due to side effects - Dosulepin** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 30/207 (14.5%) | 10/202 (5%) | RR 2.92 (1.47 to 5.8) | 95 more per 1000 (from 23 more to 238 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 7.3% | | 140 more per 1000 (from 34 more to | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 350 more) | | |
| **Number leaving treatment early due to side effects - Imipramine** | | | | | | | | | | | | |
| 44 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 534/2665 (20%) | 131/2580 (5.1%) | RR 3.91 (3.27 to 4.67) | 148 more per 1000 (from 115 more to 186 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 4.7% | | 137 more per 1000 (from 107 more to 172 more) | | |
| **Number leaving treatment early due to side effects - Nortriptyline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 12/66 (18.2%) | 1/65 (1.5%) | RR 7.98 (1.51 to 42.09) | 107 more per 1000 (from 8 more to 632 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 1.4% | | 98 more per 1000 (from 7 more to 575 more) | | |
| **Number reporting side effects** | | | | | | | | | | | | |
| 31 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 1756/2343 (74.9%) | 1248/2204 (56.6%) | RR 1.4 (1.25 to 1.56) | 226 more per 1000 (from 142 more to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 317 more) | | |
| | | | | | | | | 60% | | 240 more per 1000 (from 150 more to 336 more) | | |
| **Number reporting side effects - Amitriptyline** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 367/485 (75.7%) | 228/447 (51%) | RR 1.44 (1.15 to 1.79) | 224 more per 1000 (from 77 more to 403 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 48.4% | | 213 more per 1000 (from 73 more to 382 more) | | |
| **Number reporting side effects - Clomipramine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[1] | none | 8/10 (80%) | 5/10 (50%) | RR 1.6 (0.8 to 3.2) | 300 more per 1000 (from 100 fewer to 1100 more) | ⊕⊕OO LOW | |
| | | | | | | | | 50% | | 300 more per 1000 (from 100 fewer to 1100 more) | | |
| **Number reporting side effects - Dosulepin** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | serious[4] | no serious indirectness | no serious imprecision | none | 14/25 (56%) | 5/27 (18.5%) | RR 3.02 (1.27 to 7.18) | 374 more per 1000 (from 50 more to 1144 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 18.5% | | 374 more per 1000 (from 50 more to 1143 more) | | |
| **Number reporting side effects - Imipramine** | | | | | | | | | | | | |
| 20 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 1304/1757 (74.2%) | 959/1657 (57.9%) | RR 1.39 (1.21 to 1.59) | 226 more per 1000 (from 122 more to 341 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 63.3% | | 247 more per 1000 (from 133 more to 373 more) | | |
| **Number reporting side effects - Nortriptyline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 63/66 (95.5%) | 51/63 (81%) | RR 1.18 (1.03 to 1.34) | 146 more per 1000 (from 24 more to 275 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 80.7% | | 145 more per 1000 (from 24 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | more to 274 more) | | |

[1] Inconclusive effect size
[2] Large heterogeneity
[3] Moderate heterogeneity
[4] Single study

# Escitalopram

## Should escitalopram be used in depression? (Escitalopram versus placebo)

| Quality assessment | | | | | | | Summary of findings | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | Importance |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Escitalopram | Placebo | Relative (95% CI) | Absolute | | |
| **Non-response - ordered by baseline severity** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 936/1881 (49.8%) | 971/1614 (60.2%) | RR 0.81 (0.75 to 0.88) | 114 fewer per 1000 (from 72 fewer to 150 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 58.5% | | 111 fewer per 1000 (from 70 fewer to 146 fewer) | | |
| **Non-response - Escitalopram 10mg** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 407/758 (53.7%) | 388/628 (61.8%) | RR 0.84 (0.72 to 0.98) | 99 fewer per 1000 (from 12 fewer to 173 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 63.4% | | 101 fewer per 1000 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (from 13 fewer to 178 fewer) | | |
| **Non-response - Escitalopram 20mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 62/125 (49.6%) | 89/122 (73%)<br>73% | RR 0.68 (0.55 to 0.84) | 233 fewer per 1000 (from 117 fewer to 328 fewer)<br>234 fewer per 1000 (from 117 fewer to 329 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Non-remission - vs Placebo** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 921/1508 (61.1%) | 935/1363 (68.6%)<br>71.1% | RR 0.88 (0.82 to 0.94) | 82 fewer per 1000 (from 41 fewer to 123 fewer)<br>85 fewer per 1000 (from 43 fewer to 128 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Non-remission - Escitalopram 10mg vs Placebo** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 397/639 (62.1%) | 331/506 (65.4%) | RR 0.92 (0.81 to | 52 fewer per 1000 (from 124 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.06) | fewer to 39 more) | | |
| | | | | | | | | 66.1% | | 53 fewer per 1000 (from 126 fewer to 40 more) | | |
| **Mean endpoint depression scores (clinician-rated) - vs Placebo (better indicated by lower scores) (Better indicated by lower values)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 903 | 918 | - | SMD 0.24 lower (0.35 to 0.13 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 10mg vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | strong association[4] | 476 | 488 | - | SMD 0.23 lower (0.46 to 0.01 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 20mg vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 123 | 119 | - | SMD 0.46 lower (0.71 to 0.2 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1533 | 1397 | - | SMD 0.26 lower (0.34 to 0.19 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | lower) | | |
| **Mean change depression scores (clinician-rated) - Escitalopram 10mg vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[5] | none | 580 | 445 | - | SMD 0.28 lower (0.41 to 0.15 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean change depression scores (clinician-rated) - Escitalopram 20mg vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 123 | 119 | - | SMD 0.48 lower (0.74 to 0.22 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Leaving treatment early for any reason - vs Placebo** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 413/1881 (22%) | 309/1614 (19.1%) | RR 1.11 (0.95 to 1.29) | 21 more per 1000 (from 10 fewer to 56 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 19.3% | | 21 more per 1000 (from 10 fewer to 56 more) | | |
| **Leaving treatment early for any reason - Escitalopram 10mg vs Placebo** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[6] | none | 151/758 (19.9%) | 119/628 (18.9%) | RR 0.99 (0.75 to | 2 fewer per 1000 (from 47 | ⊕⊕OO LOW | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.3) | fewer to 57 more) | | |
| | | | | | | | | 20% | | 2 fewer per 1000 (from 50 fewer to 60 more) | | |
| **Leaving treatment early for any reason - Escitalopram 20mg vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[6] | none | 36/125 (28.8%) | 30/122 (24.6%) | RR 1.17 (0.77 to 1.77) | 42 more per 1000 (from 57 fewer to 189 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 24.6% | | 42 more per 1000 (from 57 fewer to 189 more) | | |
| **Leaving treatment early due to side effects - vs Placebo** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 117/1855 (6.3%) | 51/1601 (3.2%) | RR 1.8 (1.18 to 2.73) | 25 more per 1000 (from 6 more to 55 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 3% | | 24 more per 1000 (from 5 more to 52 more) | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early due to side effects - Escitalopram 10mg vs Placebo** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[2] | no serious indirectness | serious[6] | none | 45/758 (5.9%) | 18/628 (2.9%)<br><br>2.6% | RR 2.02 (0.9 to 4.54) | 29 more per 1000 (from 3 fewer to 101 more)<br><br>27 more per 1000 (from 3 fewer to 92 more) | ⊕⊕OO LOW | CRITICAL |
| **Leaving treatment early due to side effects - Escitalopram 20mg vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[7] | none | 13/125 (10.4%) | 3/122 (2.5%)<br><br>2.5% | RR 4.23 (1.24 to 14.47) | 79 more per 1000 (from 6 more to 331 more)<br><br>81 more per 1000 (from 6 more to 337 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Patients reporting side effects - vs Placebo** | | | | | | | | | | | | |
| 8 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 932/1299 (71.7%) | 771/1191 (64.7%)<br><br>66.5% | RR 1.09 (1.04 to 1.15) | 58 more per 1000 (from 26 more to 97 more)<br><br>60 more | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 1000 (from 27 more to 100 more) | | |
| **Patients reporting side effects - Escitalopram 10mg vs Placebo** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 295/483 (61.1%) | 288/491 (58.7%) | RR 1.04 (0.94 to 1.15) | 23 more per 1000 (from 35 fewer to 88 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 56.1% | | 22 more per 1000 (from 34 fewer to 84 more) | | |
| **Patients reporting side effects - Escitalopram 20mg vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 107/125 (85.6%) | 86/122 (70.5%) | RR 1.21 (1.06 to 1.39) | 148 more per 1000 (from 42 more to 275 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 70.5% | | 148 more per 1000 (from 42 more to 275 more) | | |

[1] Moderate heterogeneity
[2] Large heterogeneity
[3] Single study
[4] Large studies
[5] Unclear clinical importance

[6] Inconclusive effect size
[7] Large confidence interval

## Is escitalopram more effective than other antidepressants in depression?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Escitalopram | All other ADs | Relative (95% CI) | Absolute | | |
| **Non-response - vs other AD** | | | | | | | | | | | | |
| 20 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1131/3090 (36.6%) | 1199/2961 (40.5%) | RR 0.89 (0.84 to 0.95) | 45 fewer per 1000 (from 20 fewer to 65 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 40.2% | | 44 fewer per 1000 (from 20 fewer to 64 fewer) | | |
| **Non-response - vs other AD (sensitivity analysis)** | | | | | | | | | | | | |
| 19 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1125/2981 (37.7%) | 1179/2851 (41.4%) | RR 0.9 (0.85 to 0.96) | 41 fewer per 1000 (from 17 fewer to 62 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 41.3% | | 41 fewer | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 1000 (from 17 fewer to 62 fewer) | | |
| **Non-remission - vs other AD** | | | | | | | | | | | | |
| 18 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 1220/2717 (44.9%) | 1346/2708 (49.7%) | RR 0.9 (0.85 to 0.95) | 50 fewer per 1000 (from 25 fewer to 75 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 52.5% | | 53 fewer per 1000 (from 26 fewer to 79 fewer) | | |
| **Non-remission - vs other AD (sensitivity analysis)** | | | | | | | | | | | | |
| 17 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1208/2608 (46.3%) | 1291/2598 (49.7%) | RR 0.93 (0.88 to 0.98) | 35 fewer per 1000 (from 10 fewer to 60 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 55.1% | | 39 fewer per 1000 (from 11 fewer to 66 fewer) | | |
| **Mean endpoint depression scores (clinician-rated) - vs other AD (Better indicated by lower values)** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1506 | 1503 | - | SMD 0.1 lower (0.17 to | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 0.02 lower) | | |
| **Mean change depression scores (clinician-rated) - vs other AD (Better indicated by lower values)** | | | | | | | | | | | | |
| 19 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 2586 | 2572 | - | SMD 0.07 lower (0.12 to 0.02 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Leaving treatment early for any reason - vs other AD** | | | | | | | | | | | | |
| 21 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 587/3106 (18.9%) | 667/3086 (21.6%) | RR 0.85 (0.74 to 0.98) | 32 fewer per 1000 (from 4 fewer to 56 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 23.2% | | 35 fewer per 1000 (from 5 fewer to 60 fewer) | | |
| **Leaving treatment early due to side effects - vs other AD** | | | | | | | | | | | | |
| 20 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 167/2968 (5.6%) | 245/2839 (8.6%) | RR 0.64 (0.53 to 0.78) | 31 fewer per 1000 (from 19 fewer to 41 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 7.7% | | 28 fewer per 1000 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (from 17 fewer to 36 fewer) | | |
| **Number reporting side effects - vs other AD** | | | | | | | | | | | | |
| 17 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1550/2425 (63.9%) | 1555/2414 (64.4%) | RR 0.94 (0.91 to 0.98) | 39 fewer per 1000 (from 13 fewer to 58 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 71.4% | | 43 fewer per 1000 (from 14 fewer to 64 fewer) | | |

[1] Large heterogeneity
[2] Moderate heterogeneity

## Is escitalopram more effective than SSRIs in depression?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Escitalopram | SSRIs | Relative (95% CI) | Absolute | | |
| **Non-response (vs SSRIs) - SSRI Citalopram** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 346/955 (36.2%) | 361/858 (42.1%) | RR 0.82 (0.73 to 0.92) | 76 fewer per 1000 (from 34 fewer to 114 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 46.9% | | 84 fewer per 1000 (from 38 fewer to 127 fewer) | | |
| **Non-response (vs SSRIs) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 159/399 (39.8%) | 166/384 (43.2%) | RR 0.92 (0.78 to 1.08) | 35 fewer per 1000 (from 95 fewer to 35 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 35.9% | | 29 fewer per 1000 (from 79 fewer to 29 more) | | |
| **Non-response (vs SSRIs) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 87/243 (35.8%) | 87/246 (35.4%) | RR 1.01 (0.8 to 1.28) | 4 more per 1000 (from 71 fewer to 99 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 34.8% | | 3 more per 1000 (from 70 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 97 more) | | |
| **Non-response (vs SSRIs) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 99/398 (24.9%) | 104/386 (26.9%) | RR 0.92 (0.73 to 1.17) | 22 fewer per 1000 (from 73 fewer to 46 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 27.4% | | 22 fewer per 1000 (from 74 fewer to 47 more) | | |
| **Non-response (sensitivity analysis)** | | | | | | | | | | | | |
| 12 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 685/1886 (36.3%) | 698/1764 (39.6%) | RR 0.89 (0.82 to 0.97) | 44 fewer per 1000 (from 12 fewer to 71 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 37.5% | | 41 fewer per 1000 (from 11 fewer to 68 fewer) | | |
| **Non-response (sensitivity analysis) - SSRI Citalopram** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | strong association[3] | 340/846 (40.2%) | 341/748 (45.6%) | RR 0.85 (0.76 to 0.95) | 68 fewer per 1000 (from 23 fewer to | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 109 fewer) | | |
| | | | | | | | | 50.9% | | 76 fewer per 1000 (from 25 fewer to 122 fewer) | | |
| **Non-response (sensitivity analysis) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 159/399 (39.8%) | 166/384 (43.2%) | RR 0.92 (0.78 to 1.08) | 35 fewer per 1000 (from 95 fewer to 35 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 35.9% | | 29 fewer per 1000 (from 79 fewer to 29 more) | | |
| **Non-response (sensitivity analysis) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 87/243 (35.8%) | 87/246 (35.4%) | RR 1.01 (0.8 to 1.28) | 4 more per 1000 (from 71 fewer to 99 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 34.8% | | 3 more per 1000 (from 70 fewer to 97 more) | | |
| **Non-response (sensitivity analysis) - SSRI Paroxetine** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[2] | none | 99/398 (24.9%) | 104/386 (26.9%) | RR 0.92 (0.73 to 1.17) | 22 fewer per 1000 (from 73 fewer to 46 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 27.4% | | 22 fewer per 1000 (from 74 fewer to 47 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs)** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 642/1622 (39.6%) | 753/1621 (46.5%) | RR 0.85 (0.79 to 0.92) | 70 fewer per 1000 (from 37 fewer to 98 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 42.6% | | 64 fewer per 1000 (from 34 fewer to 89 fewer) | | |
| **Number not achieving remission at endpoint (vs SSRIs) - SSRI Citalopram** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 206/582 (35.4%) | 303/605 (50.1%) | RR 0.71 (0.62 to 0.81) | 145 fewer per 1000 (from 95 fewer to 190 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 54.9% | | 159 fewer per 1000 (from 104 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 209 fewer) | | |
| **Number not achieving remission at endpoint (vs SSRIs) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 123/243 (50.6%) | 122/246 (49.6%) | RR 1.02 (0.86 to 1.22) | 10 more per 1000 (from 69 fewer to 109 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 48.8% | | 10 more per 1000 (from 68 fewer to 107 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 179/399 (44.9%) | 187/384 (48.7%) | RR 0.92 (0.8 to 1.06) | 39 fewer per 1000 (from 97 fewer to 29 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 40.8% | | 33 fewer per 1000 (from 82 fewer to 24 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 134/398 (33.7%) | 141/386 (36.5%) | RR 0.92 (0.76 to 1.11) | 29 fewer per 1000 (from 88 fewer to | ⊕⊕OO LOW | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 40 more) | | |
| | | | | | | | | 37% | | 30 fewer per 1000 (from 89 fewer to 41 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs) (sensitivity analysis)** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 630/1513 (41.6%) | 698/1511 (46.2%) | RR 0.9 (0.83 to 0.98) | 46 fewer per 1000 (from 9 fewer to 79 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 41.7% | | 42 fewer per 1000 (from 8 fewer to 71 fewer) | | |
| **Number not achieving remission at endpoint (vs SSRIs) (sensitivity analysis) - SSRI Citalopram** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 194/473 (41%) | 248/495 (50.1%) | RR 0.82 (0.72 to 0.94) | 90 fewer per 1000 (from 30 fewer to 140 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 59.9% | | 108 fewer per 1000 (from 36 fewer to 168 fewer) | | |
| **Number not achieving remission at endpoint (vs SSRIs) (sensitivity analysis) - SSRI Sertraline** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 123/243 (50.6%) | 122/246 (49.6%) | RR 1.02 (0.86 to 1.22) | 10 more per 1000 (from 69 fewer to 109 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 48.8% | | 10 more per 1000 (from 68 fewer to 107 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs) (sensitivity analysis) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 179/399 (44.9%) | 187/384 (48.7%) | RR 0.92 (0.8 to 1.06) | 39 fewer per 1000 (from 97 fewer to 29 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 40.8% | | 33 fewer per 1000 (from 82 fewer to 24 more) | | |
| **Number not achieving remission at endpoint (vs SSRIs) (sensitivity analysis) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 134/398 (33.7%) | 141/386 (36.5%) | RR 0.92 (0.76 to 1.11) | 29 fewer per 1000 (from 88 fewer to 40 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 37% | | 30 fewer per 1000 (from 89 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 41 more) | | |
| **Mean endpoint scores (clinician rated) (vs SSRIs) (Better indicated by lower values)** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1219 | 1215 | - | SMD 0.11 lower (0.19 to 0.03 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint scores (clinician rated) (vs SSRIs) - SSRI Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 566 | 577 | - | SMD 0.12 lower (0.24 lower to 0 higher) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint scores (clinician rated) (vs SSRIs) - SSRI Fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 384 | 375 | - | SMD 0.2 lower (0.34 to 0.06 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint scores (clinician rated) (vs SSRIs) - SSRI Sertraline (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 104 | 107 | - | SMD 0.02 lower (0.29 lower to 0.25 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | higher) | | |
| **Mean endpoint scores (clinician rated) (vs SSRIs) - SSRI Paroxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 165 | 156 | - | SMD 0.11 higher (0.11 lower to 0.33 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean change (clinician rated) (vs SSRIs) (Better indicated by lower values)** | | | | | | | | | | | | |
| 13 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1667 | 1670 | - | SMD 0.1 lower (0.18 to 0.02 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change (clinician rated) (vs SSRIs) - SSRI Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 812 | 827 | - | SMD 0.17 lower (0.28 to 0.05 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change (clinician rated) (vs SSRIs) - SSRI Fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 227 | 222 | - | SMD 0.06 lower (0.24 lower to 0.13 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | higher) | | |
| **Mean change (clinician rated) (vs SSRIs) - SSRI Sertraline (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 235 | 242 | - | SMD 0.01 higher (0.17 lower to 0.19 higher) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change (clinician rated) (vs SSRIs) - SSRI Paroxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | very serious[1] | no serious indirectness | serious[2] | none | 393 | 379 | - | SMD 0.06 lower (0.38 lower to 0.27 higher) | ⊕OOO VERY LOW | CRITICAL |
| **Leaving the study early for any reason (vs SSRIs)** | | | | | | | | | | | | |
| 14 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 338/2011 (16.8%) | 372/1999 (18.6%) | RR 0.86 (0.71 to 1.03) | 26 fewer per 1000 (from 54 fewer to 6 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 17.3% | | 24 fewer per 1000 (from 50 fewer to 5 more) | | |

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| **Leaving the study early for any reason (vs SSRIs) - SSRI Citalopram** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[2] | none | 145/955 (15.2%) | 149/969 (15.4%) | RR 0.82 (0.6 to 1.11) | 28 fewer per 1000 (from 62 fewer to 17 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 19.6% | | 35 fewer per 1000 (from 78 fewer to 22 more) | | |
| **Leaving the study early for any reason (vs SSRIs) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 82/415 (19.8%) | 87/398 (21.9%) | RR 0.91 (0.58 to 1.42) | 20 fewer per 1000 (from 92 fewer to 92 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 19.9% | | 18 fewer per 1000 (from 84 fewer to 84 more) | | |
| **Leaving the study early for any reason (vs SSRIs) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 47/243 (19.3%) | 40/246 (16.3%) | RR 1.19 (0.81 to 1.74) | 31 more per 1000 (from 31 fewer to 120 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 16% | | 30 more | | |

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| | | | | | | | | | | per 1000 (from 30 fewer to 118 more) | | |
| **Leaving the study early for any reason (vs SSRIs) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 64/398 (16.1%) | 96/386 (24.9%) | RR 0.65 (0.49 to 0.85) | 87 fewer per 1000 (from 37 fewer to 127 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 23.2% | | 81 fewer per 1000 (from 35 fewer to 118 fewer) | | |
| **Leaving the study early due to side effects (vs SSRIs)** | | | | | | | | | | | | |
| 13 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 109/1883 (5.8%) | 133/1756 (7.6%) | RR 0.75 (0.58 to 0.96) | 19 fewer per 1000 (from 3 fewer to 32 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 6.3% | | 16 fewer per 1000 (from 3 fewer to 26 fewer) | | |
| **Leaving the study early due to side effects (vs SSRIs) - SSRI Citalopram** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 47/837 (5.6%) | 49/732 (6.7%) | RR 0.8 (0.49 to | 13 fewer per 1000 (from 34 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.29) | fewer to 19 more) | | |
| | | | | | | | | 6.3% | | 13 fewer per 1000 (from 32 fewer to 18 more) | | |
| **Leaving the study early due to side effects (vs SSRIs) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 27/411 (6.6%) | 34/394 (8.6%) | RR 0.77 (0.47 to 1.26) | 20 fewer per 1000 (from 46 fewer to 22 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 7.6% | | 17 fewer per 1000 (from 40 fewer to 20 more) | | |
| **Leaving the study early due to side effects (vs SSRIs) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 10/238 (4.2%) | 9/245 (3.7%) | RR 1.11 (0.38 to 3.22) | 4 more per 1000 (from 23 fewer to 82 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 3.7% | | 4 more per 1000 (from 23 fewer to 82 more) | | |

| | | | | | | | | | | | | |
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| **Leaving the study early due to side effects (vs SSRIs) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[2] | none | 25/397 (6.3%) | 41/385 (10.6%)<br><br>9.6% | RR 0.65 (0.31 to 1.36) | 37 fewer per 1000 (from 73 fewer to 38 more)<br><br>34 fewer per 1000 (from 66 fewer to 35 more) | ⊕⊕OO LOW | CRITICAL |
| **Patients reporting side effects (vs SSRIs)** | | | | | | | | | | | | |
| 14 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1229/1994 (61.6%) | 1230/1980 (62.1%)<br><br>71.4% | RR 0.94 (0.91 to 0.98) | 37 fewer per 1000 (from 12 fewer to 56 fewer)<br><br>43 fewer per 1000 (from 14 fewer to 64 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Patients reporting side effects (vs SSRIs) - SSRI Citalopram** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 551/949 (58.1%) | 511/956 (53.5%)<br><br>70.9% | RR 0.95 (0.86 to 1.04) | 27 fewer per 1000 (from 75 fewer to 21 more)<br><br>35 fewer | ⊕⊕OO LOW | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 1000 (from 99 fewer to 28 more) | | |
| **Patients reporting side effects (vs SSRIs) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 231/410 (56.3%) | 243/394 (61.7%) | RR 0.92 (0.83 to 1.01) | 49 fewer per 1000 (from 105 fewer to 6 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 64.1% | | 51 fewer per 1000 (from 109 fewer to 6 more) | | |
| **Patients reporting side effects (vs SSRIs) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 198/238 (83.2%) | 218/245 (89%) | RR 0.94 (0.86 to 1.02) | 53 fewer per 1000 (from 125 fewer to 18 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 88.8% | | 53 fewer per 1000 (from 124 fewer to 18 more) | | |
| **Patients reporting side effects (vs SSRIs) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 249/397 (62.7%) | 258/385 (67%) | RR 0.93 (0.84 to | 47 fewer per 1000 (from 107 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.04) | fewer to 27 more) | | |
| | | | | | | | | 66.1% | | 46 fewer per 1000 (from 106 fewer to 26 more) | | |
| **Patients reporting side effects (vs SSRIs) (sensitivity analysis)** | | | | | | | | | | | | |
| 13 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1222/1886 (64.8%) | 1195/1766 (67.7%) | RR 0.94 (0.9 to 0.98) | 41 fewer per 1000 (from 14 fewer to 68 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 71.4% | | 43 fewer per 1000 (from 14 fewer to 71 fewer) | | |
| **Patients reporting side effects (vs SSRIs) (sensitivity analysis) - SSRI Citalopram** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 544/841 (64.7%) | 476/742 (64.2%) | RR 0.95 (0.89 to 1.02) | 32 fewer per 1000 (from 71 fewer to 13 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 73.1% | | 37 fewer per 1000 (from 80 fewer to 15 more) | | |

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| **Patients reporting side effects (vs SSRIs) (sensitivity analysis) - SSRI Fluoxetine** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 231/410 (56.3%) | 243/394 (61.7%)<br><br>64.1% | RR 0.92 (0.82 to 1.03) | 49 fewer per 1000 (from 111 fewer to 19 more)<br><br>51 fewer per 1000 (from 115 fewer to 19 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Patients reporting side effects (vs SSRIs) (sensitivity analysis) - SSRI Sertraline** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 198/238 (83.2%) | 218/245 (89%)<br><br>88.8% | RR 0.93 (0.87 to 1) | 62 fewer per 1000 (from 116 fewer to 0 more)<br><br>62 fewer per 1000 (from 115 fewer to 0 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Patients reporting side effects (vs SSRIs) (sensitivity analysis) - SSRI Paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 249/397 (62.7%) | 258/385 (67%)<br><br>66.1% | RR 0.94 (0.85 to 1.04) | 40 fewer per 1000 (from 101 fewer to 27 more)<br><br>40 fewer | ⊕⊕⊕⊕ HIGH | CRITICAL |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 1000 (from 99 fewer to 26 more) | | |

[1] Large heterogeneity
[2] Inconclusive effect size
[3] Small confidence interval
[4] Moderate heterogeneity

## Is escitalopram more effective than non-SSRI antidepressants in depression?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Escitalopram | Other ADs (non SSRIs) | Relative (95% CI) | Absolute | | |
| **Non-response - SNRI Duloxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 242/558 (43.4%) | 274/562 (48.8%) | RR 0.81 (0.57 to 1.15) | 93 fewer per 1000 (from 210 fewer to 73 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 54.4% | | 103 fewer per 1000 (from 234 fewer to 82 more) | | |
| **Non-response - SNRI Venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 79/246 (32.1%) | 90/245 (36.7%) | RR 0.86 (0.68 to 1.09) | 51 fewer per 1000 (from 118 fewer to 33 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 39.3% | | 55 fewer per 1000 (from 126 | | |

| | | | | | | | | | | | | |
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| | | | | | | | | | | fewer to 35 more) | | |
| **Non-response - Bupropion XL** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 119/291 (40.9%) | 117/280 (41.8%) | RR 0.98 (0.78 to 1.22) | 8 fewer per 1000 (from 92 fewer to 92 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 41.8% | | 8 fewer per 1000 (from 92 fewer to 92 more) | | |
| **Number not achieving remission at endpoint - SNRI Duloxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 310/558 (55.6%) | 315/562 (56%) | RR 0.97 (0.83 to 1.13) | 17 fewer per 1000 (from 95 fewer to 73 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 64.5% | | 19 fewer per 1000 (from 110 fewer to 84 more) | | |
| **Number not achieving remission at endpoint - SNRI Venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 98/246 (39.8%) | 111/245 (45.3%) | RR 0.88 (0.72 to 1.07) | 54 fewer per 1000 (from 127 fewer to 32 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 47.4% | | 57 fewer per 1000 (from 133 fewer to 33 more) | | |
| **Number not achieving remission at endpoint - Bupropion xl** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 170/291 (58.4%) | 167/280 (59.6%) | RR 0.98 (0.79 to 1.21) | 12 fewer per 1000 (from 125 fewer to 125 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 59.6% | | 12 fewer per 1000 (from 125 fewer to 125 more) | | |
| **Mean endpoint scores (clinician rated) - SNRI Duloxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 141 | 146 | - | SMD 0.19 lower (0.42 lower to 0.04 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean endpoint scores (clinician rated) - SNRI Venlafaxine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 146 | 142 | - | SMD 0.08 higher (0.15 lower to 0.32 higher) | ⊕⊕⊕O MODERATE | CRITICAL |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean change (clinician rated) - SNRI Duloxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 410 | 399 | - | SMD 0.03 higher (0.11 lower to 0.17 higher) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change (clinician rated) - SNRI Venlafaxine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 243 | 240 | - | SMD 0.04 lower (0.37 lower to 0.29 higher) | ⊕⊕OO LOW | CRITICAL |
| **Mean change (clinician rated) - Bupropion XL (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 266 | 263 | - | SMD 0.05 lower (0.22 lower to 0.12 higher) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Leaving the study early for any reason - SNRI Duloxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 119/558 (21.3%) | 168/562 (29.9%) | RR 0.7 (0.49 to 1) | 90 fewer per 1000 (from 152 fewer to 0 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 31.1% | | 93 fewer per 1000 | | |

| | | | | | | | | | | | | |
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| | | | | | | | | | | (from 159 fewer to 0 more) | | |
| **Leaving the study early for any reason - SNRI Venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 49/246 (19.9%) | 55/245 (22.4%) | RR 0.88 (0.63 to 1.23) | 27 fewer per 1000 (from 83 fewer to 52 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 24.2% | | 29 fewer per 1000 (from 90 fewer to 56 more) | | |
| **Leaving the study early for any reason - Bupropion XL** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 81/291 (27.8%) | 72/280 (25.7%) | RR 1.08 (0.82 to 1.41) | 21 more per 1000 (from 46 fewer to 105 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 25.8% | | 21 more per 1000 (from 46 fewer to 106 more) | | |
| **Leaving the study early due to side effects - SNRI Duloxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 30/558 (5.4%) | 63/562 (11.2%) | RR 0.47 (0.25 to | 59 fewer per 1000 (from 12 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 0.89) | fewer to 84 fewer) | | |
| | | | | | | | | 12.3% | | 65 fewer per 1000 (from 14 fewer to 92 fewer) | | |
| **Leaving the study early due to side effects - SNRI Venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 16/246 (6.5%) | 32/245 (13.1%) | RR 0.47 (0.17 to 1.31) | 69 fewer per 1000 (from 108 fewer to 40 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 13.5% | | 72 fewer per 1000 (from 112 fewer to 42 more) | | |
| **Leaving the study early due to side effects - Bupropion XL** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | very serious[1] | no serious indirectness | serious[2] | none | 12/281 (4.3%) | 17/276 (6.2%) | RR 0.78 (0.16 to 3.7) | 14 fewer per 1000 (from 52 fewer to 166 more) | ⊕OOO VERY LOW | CRITICAL |
| | | | | | | | | 6.2% | | 14 fewer per 1000 (from 52 fewer to 167 more) | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Patients reporting side effects - SNRI Duloxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 223/283 (78.8%) | 223/289 (77.2%)<br>77.3% | RR 1.02 (0.94 to 1.11) | 15 more per 1000 (from 46 fewer to 85 more)<br>15 more per 1000 (from 46 fewer to 85 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Patients reporting side effects - SNRI Venlafaxine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 98/148 (66.2%) | 102/145 (70.3%)<br>70.3% | RR 0.94 (0.81 to 1.1) | 42 fewer per 1000 (from 134 fewer to 70 more)<br>42 fewer per 1000 (from 134 fewer to 70 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |

[1] Large heterogeneity
[2] Inconclusive effect size

## Is escitalopram more effective than other antidepressants in depression? (Sub-analysis highlighting citalopram)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Escitalopram | All other ADs (citalopram separated) | Relative (95% CI) | Absolute | | |
| **Non-response** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 635/1713 (37.1%) | 730/1724 (42.3%) | RR 0.87 (0.81 to 0.94) | 55 fewer per 1000 (from 25 fewer to 80 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 42.8% | | 56 fewer per 1000 (from 26 fewer to 81 fewer) | | |
| **Non-response - Escitalopram 10mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 315/678 (46.5%) | 322/662 (48.6%) | RR 0.96 (0.86 to 1.06) | 19 fewer per 1000 (from 68 fewer to 29 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 44.6% | | 18 fewer per 1000 (from 62 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 27 more) | | |
| **Non-response - Escitalopram 10mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 108/294 (36.7%) | 127/307 (41.4%)<br>43.4% | RR 0.89 (0.73 to 1.08) | 46 fewer per 1000 (from 112 fewer to 33 more)<br>48 fewer per 1000 (from 117 fewer to 35 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Non-response - Escitalopram 20mg vs Other antidepressant** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 113/474 (23.8%) | 148/478 (31%)<br>25.8% | RR 0.77 (0.63 to 0.95) | 71 fewer per 1000 (from 15 fewer to 115 fewer)<br>59 fewer per 1000 (from 13 fewer to 95 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Non-response - Escitalopram 20mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 99/267 (37.1%) | 133/277 (48%) | RR 0.77 (0.63 to | 110 fewer per 1000 (from 34 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 0.93) | fewer to 178 fewer) | | |
| | | | | | | | | 48.6% | | 112 fewer per 1000 (from 34 fewer to 180 fewer) | | |
| **Non-remission** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 639/1469 (43.5%) | 703/1474 (47.7%) | RR 0.91 (0.82 to 1) | 43 fewer per 1000 (from 86 fewer to 0 more) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 42.6% | | 38 fewer per 1000 (from 77 fewer to 0 more) | | |
| **Non-remission - Escitalopram 10mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 372/678 (54.9%) | 367/662 (55.4%) | RR 0.98 (0.88 to 1.11) | 11 fewer per 1000 (from 67 fewer to 61 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 53.5% | | 11 fewer per 1000 (from 64 fewer to | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 59 more) | | |
| **Non-remission - Escitalopram 10mg vs Citalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 49/175 (28%) | 59/182 (32.4%) | RR 0.86 (0.63 to 1.19) | 45 fewer per 1000 (from 120 fewer to 62 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 32.4% | | 45 fewer per 1000 (from 120 fewer to 62 more) | | |
| **Non-remission - Escitalopram 20mg vs Other antidepressant** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 151/474 (31.9%) | 186/478 (38.9%) | RR 0.82 (0.7 to 0.97) | 70 fewer per 1000 (from 12 fewer to 117 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 34.4% | | 62 fewer per 1000 (from 10 fewer to 103 fewer) | | |
| **Non-remission - Escitalopram 20mg vs Citalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 67/142 (47.2%) | 91/152 (59.9%) | RR 0.79 (0.63 to | 126 fewer per 1000 (from 12 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 0.98) | fewer to 222 fewer) | | |
| | | | | | | | | 59.9% | | 126 fewer per 1000 (from 12 fewer to 222 fewer) | | |
| **Mean endpoint depression scores (clinician-rated) (Better indicated by lower values)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 938 | 954 | - | SMD 0.19 lower (0.28 to 0.1 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 10mg vs Other antidepressant (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 392 | 384 | - | SMD 0.19 lower (0.33 to 0.05 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 10mg vs Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 282 | 299 | - | SMD 0.17 lower (0.33 to 0.01 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | lower) | | |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 20mg vs Other antidepressant (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 141 | 146 | - | SMD 0.19 lower (0.42 lower to 0.04 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean endpoint depression scores (clinician-rated) - Escitalopram 20mg vs Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 123 | 125 | - | SMD 0.22 lower (0.47 lower to 0.03 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean change scores (clinician-rated) (Better indicated by lower values)** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 1408 | 1434 | - | SMD 0.13 lower (0.2 to 0.05 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change scores (clinician-rated) - Escitalopram 10mg vs Other antidepressant (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 496 | 493 | - | SMD 0 higher (0.13 lower to 0.12 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | higher) | | |
| **Mean change scores (clinician-rated) - Escitalopram 10mg vs Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 390 | 407 | - | SMD 0.17 lower (0.31 to 0.03 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Mean change scores (clinician-rated) - Escitalopram 20mg vs Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 261 | 267 | - | SMD 0.22 lower (0.39 to 0.05 lower) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Mean change scores (clinician-rated) - Escitalopram 20mg vs Citalopram (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | no methodology chosen | | | | | none | 261 | 267 | - | SMD 0.22 lower (0.39 to 0.05 lower) | | |
| **Leaving treatment early for any reason** | | | | | | | | | | | | |
| 12 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 338/1838 (18.4%) | 444/1848 (24%) | RR 0.76 (0.68 to 0.87) | 58 fewer per 1000 (from 31 fewer to 77 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 25.6% | | 61 fewer per 1000 (from 33 fewer to 82 fewer) | | |
| **Leaving treatment early for any reason - Escitalopram 10mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 130/678 (19.2%) | 159/662 (24%) | RR 0.8 (0.65 to 0.98) | 48 fewer per 1000 (from 5 fewer to 84 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 20.1% | | 40 fewer per 1000 (from 4 fewer to 70 fewer) | | |
| **Leaving treatment early for any reason - Escitalopram 10mg vs Citalopram** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 56/403 (13.9%) | 81/417 (19.4%) | RR 0.72 (0.53 to 0.98) | 54 fewer per 1000 (from 4 fewer to 91 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 25.6% | | 72 fewer per 1000 (from 5 fewer to 120 fewer) | | |
| **Leaving treatment early for any reason - Escitalopram 20mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised | no serious | no serious | no serious | no serious | none | 106/490 | 147/492 | RR 0.73 | 81 fewer | ⊕⊕⊕⊕ | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | imprecision | | (21.6%) | (29.9%) | (0.58 to 0.9) | per 1000 (from 30 fewer to 125 fewer) | HIGH | |
| | | | | | | | | 28.6% | | 77 fewer per 1000 (from 29 fewer to 120 fewer) | | |
| **Leaving treatment early for any reason - Escitalopram 20mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | serious[1] | none | 46/267 (17.2%) | 57/277 (20.6%) | RR 0.83 (0.58 to 1.17) | 35 fewer per 1000 (from 86 fewer to 35 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 21% | | 36 fewer per 1000 (from 88 fewer to 36 more) | | |
| **Leaving treatment early due to side effects** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 107/1722 (6.2%) | 176/1728 (10.2%) | RR 0.61 (0.48 to 0.77) | 40 fewer per 1000 (from 23 fewer to 53 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 8.8% | | 34 fewer per 1000 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (from 20 fewer to 46 fewer) | | |
| **Leaving treatment early due to side effects - Escitalopram 10mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 39/675 (5.8%) | 49/662 (7.4%) | RR 0.77 (0.52 to 1.16) | 17 fewer per 1000 (from 36 fewer to 12 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 5.8% | | 13 fewer per 1000 (from 28 fewer to 9 more) | | |
| **Leaving treatment early due to side effects - Escitalopram 10mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 15/294 (5.1%) | 29/307 (9.4%) | RR 0.54 (0.3 to 0.99) | 43 fewer per 1000 (from 1 fewer to 66 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 9.4% | | 43 fewer per 1000 (from 1 fewer to 66 fewer) | | |
| **Leaving treatment early due to side effects - Escitalopram 20mg vs Other antidepressant** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 36/490 (7.3%) | 78/492 (15.9%) | RR 0.46 (0.32 to | 86 fewer per 1000 (from 51 | ⊕⊕⊕⊕ HIGH | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 0.68) | fewer to 108 fewer) | | |
| | | | | | | | | 15.7% | | 85 fewer per 1000 (from 50 fewer to 107 fewer) | | |
| **Leaving treatment early due to side effects - Escitalopram 20mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 17/263 (6.5%) | 20/267 (7.5%) | RR 0.86 (0.46 to 1.6) | 10 fewer per 1000 (from 40 fewer to 45 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 7.6% | | 11 fewer per 1000 (from 41 fewer to 46 more) | | |
| **Number reporting side effects** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 839/1352 (62.1%) | 901/1365 (66%) | RR 0.94 (0.89 to 0.99) | 40 fewer per 1000 (from 7 fewer to 73 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| | | | | | | | | 72.3% | | 43 fewer per 1000 (from 7 fewer to | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 80 fewer) | | |
| **Number reporting side effects - Escitalopram 10mg vs Other antidepressant** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 232/400 (58%) | 242/389 (62.2%)<br>56.7% | RR 0.94 (0.85 to 1.05) | 37 fewer per 1000 (from 93 fewer to 31 more)<br>34 fewer per 1000 (from 85 fewer to 28 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Number reporting side effects - Escitalopram 10mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 204/294 (69.4%) | 241/307 (78.5%)<br>79.7% | RR 0.88 (0.8 to 0.97) | 94 fewer per 1000 (from 24 fewer to 157 fewer)<br>96 fewer per 1000 (from 24 fewer to 159 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Number reporting side effects - Escitalopram 20mg vs Other antidepressant** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 275/391 (70.3%) | 285/392 (72.7%) | RR 0.97 (0.89 to | 22 fewer per 1000 (from 80 | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.06) | fewer to 44 more) | | |
| | | | | | | | | 71.4% | | 21 fewer per 1000 (from 79 fewer to 43 more) | | |
| **Number reporting side effects - Escitalopram 20mg vs Citalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 128/267 (47.9%) | 133/277 (48%) | RR 0.97 (0.86 to 1.1) | 14 fewer per 1000 (from 67 fewer to 48 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| | | | | | | | | 51.4% | | 15 fewer per 1000 (from 72 fewer to 51 more) | | |

[1] Inconclusive effect size

[2] Large heterogeneity

# Duloxetine

## Should duloxetine be used for depression? (Acute phase efficacy data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine | Placebo | Relative (95% CI) | Absolute | | |
| **Mean change scores at endpoint - data for doses above licensed dose (60 mg) - Sensitivity analysis: 60 mg (measured with: HAMD-17; range of scores: 0-52; Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 729 | 511 | - | MD 1.85 lower (2.71 to 0.98 lower) | ⊕⊕⊕O MODERATE | |
| **Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 80 mg (Better indicated by lower values)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 353 | 369 | - | MD 1.97 lower (2.83 to 1.11 lower) | ⊕⊕⊕O MODERATE | |
| **Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 120 mg (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 261 | 260 | - | MD 2.57 lower (3.77 to 1.37 lower) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean change scores at endpoint - data for doses above licensed dose (60 mg) - 40 mg - 120 mg (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 81 | 72 | - | MD 0.9 lower (3.08 lower to 1.28 higher) | ⊕OOO VERY LOW | |
| **Mean change scores at endpoint - overall (Better indicated by lower values)** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 1229 | 1020 | - | MD 1.9 lower (2.44 to 1.35 lower) | ⊕⊕⊕O MODERATE | |
| **Non-response - data for doses above licensed dose (60 mg) - 60 mg (HAMD < 50% reduction)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 589/1034 (57%) | 565/808 (69.9%) | RR 0.8 (0.73 to 0.88) | 14 fewer per 100 (from 8 fewer to 19 fewer) | ⊕⊕⊕O MODERATE | |
| **Non-response - data for doses above licensed dose (60 mg) - 80 mg (HAMD < 50% reduction)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 235/566 (41.5%) | 228/371 (61.5%) | RR 0.74 (0.6 to 0.9) | 16 fewer per 100 (from 6 fewer to 25 fewer) | ⊕⊕OO LOW | |
| **Non-response - data for doses above licensed dose (60 mg) - 120 mg (HAMD < 50% reduction)** | | | | | | | | | | | | |
| 1 | randomised | no serious | no serious | serious[1] | very | none | 38/70 | 45/70 | RR 0.84 (0.64 to | 10 fewer per 100 | ⊕OOO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | | serious[2] | | (54.3%) | (64.3%) | 1.11) | (from 23 fewer to 7 more) | VERY LOW | |
| **Non-response - data for doses above licensed dose (60 mg) - 40 mg - 120 mg (HAMD < 50% reduction)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[2] | none | 42/82 (51.2%) | 54/77 (70.1%) | RR 0.73 (0.57 to 0.94) | 19 fewer per 100 (from 4 fewer to 30 fewer) | ⊕OOO VERY LOW | |
| **Non-response - overall (HAMD < 50% reduction )** | | | | | | | | | | | | |
| 12 | randomised trials | no serious limitations | serious | serious[1] | no serious imprecision | none | 904/1752 (51.6%) | 892/1326 (67.3%) | RR 0.78 (0.74 to 0.83) | 15 fewer per 100 (from 11 fewer to 17 fewer) | ⊕⊕OO LOW | |
| **Non-remission - data for doses above licensed dose (60 mg) - Sensitivity analysis: 60 mg** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 583/893 (65.3%) | 519/667 (77.8%) | RR 0.83 (0.78 to 0.89) | 13 fewer per 100 (from 9 fewer to 17 fewer) | ⊕⊕⊕O MODERATE | |
| **Non-remission - data for doses above licensed dose (60 mg) - 80 mg** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 213/363 (58.7%) | 266/371 (71.7%) | RR 0.82 (0.74 to 0.91) | 13 fewer per 100 (from 6 fewer to 19 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer) | | |
| **Non-remission - data for doses above licensed dose (60 mg) - 40 mg - 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 50/82 (61%) | 54/77 (70.1%) | RR 0.87 (0.69 to 1.09) | 9 fewer per 100 (from 22 fewer to 6 more) | ⊕OOO VERY LOW | |
| **Non-remission - data for doses above licensed dose (60 mg) - 120 mg** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 149/266 (56%) | 183/262 (69.8%) | RR 0.8 (0.7 to 0.92) | 14 fewer per 100 (from 6 fewer to 21 fewer) | ⊕⊕⊕O MODERATE | |
| **Non-remission - overall** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 995/1604 (62%) | 891/1185 (75.2%) | RR 0.83 (0.79 to 0.87) | 13 fewer per 100 (from 10 fewer to 16 fewer) | ⊕⊕⊕O MODERATE | |
| **Depression-related pain: BPI item 5 average pain (measured with: BP item 5 average pain in last 24 hrs; range of scores: 1-11; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 288 | 295 | - | MD 0.74 lower (1.13 to 0.34 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | lower) | | |

[1] Selective outpatients from multiple sites
[2] Single study; inconclusive effect size
[3] Significant heterogeneity (> 50%) random effects model used

## Is duloxetine effective for depression? (Acute phase acceptability and tolerability data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine | Placebo - acceptability and tolerability | Relative (95% CI) | Absolute | | |
| **Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 60 mg** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 318/1034 (30.8%) | 227/808 (28.1%) | RR 1.13 (0.98 to 1.3) | 4 more per 100 (from 1 fewer to 8 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - any reason (data by doses above licensed dose 60mg) - Sensitivity analysis: 80 mg** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 60/279 (21.5%) | 68/281 (24.2%) | RR 0.88 (0.66 to 1.17) | 3 fewer per 100 (from 8 fewer to 4 more) | ⊕OOO VERY LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 120 mg** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 44/266 (16.5%) | 55/262 (21%) | RR 0.79 (0.56 to 1.12) | 4 fewer per 100 (from 9 fewer to 3 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - any reason (data by doses above licensed dose 60mg) - 40 mg - 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 25/82 (30.5%) | 31/75 (41.3%) | RR 0.74 (0.48 to 1.13) | 11 fewer per 100 (from 21 fewer to 5 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - any reason (overall)** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[4] | none | 447/1661 (26.9%) | 350/1234 (28.4%) | RR 1.02 (0.91 to 1.15) | 1 more per 100 (from 3 fewer to 4 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 60 mg** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[5] | serious[1] | no serious imprecision | none | 110/1034 (10.6%) | 38/808 (4.7%) | RR 2.29 (1.31 to 4) | 6 more per 100 (from 1 more to 14 more) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 80 mg** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 35/363 (9.6%) | 16/371 (4.3%) | RR 2.11 (1.18 to 3.76) | 5 more per 100 (from 1 more to 12 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - adverse reactions (data by doses above licensed dose 60 mg) - 120 mg** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[6] | none | 14/266 (5.3%) | 8/262 (3.1%) | RR 1.72 (0.72 to 4.07) | 2 more per 100 (from 1 fewer to 9 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions (overall)** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 159/1663 (9.6%) | 57/1249 (4.6%) | RR 2.22 (1.66 to 2.95) | 6 more per 100 (from 3 more to 9 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 60 mg (sensitivity analysis)** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 38/911 (4.2%) | 60/686 (8.7%) | RR 0.30 (0.18 to 0.51) | 6 fewer per 100 (from 4 fewer to 7 fewer) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 6/188 (3.2%) | 11/192 (5.7%) | RR 0.55 (0.21 to 1.46) | 3 fewer per 100 (from 5 fewer to 3 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - lack of efficacy (data by doses above licensed dose 60 mg) - 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 4/196 (2%) | 11/192 (5.7%) | RR 0.36 (0.12 to 1.1) | 4 fewer per 100 (from 5 fewer to 1 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - lack of efficacy (overall): sensitivity analysis** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 48/1295 (3.7%) | 71/878 (8.1%) | RR 0.34 (0.22 to 0.54) | 5 fewer per 100 (from 4 fewer to 6 fewer) | ⊕⊕⊕O MODERATE | |
| **Number reporting side effects (data by doses above licensed dose 60 mg) - 60 mg** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | serious[5] | serious[1] | no serious imprecision | none | 705/893 (78.9%) | 455/667 (68.2%) | RR 1.14 (1.06 to 1.23) | 10 more per 100 (from 4 more to 16 more) | ⊕⊕OO LOW | |
| **Number reporting side effects (data by doses above licensed dose 60 mg) - 120 mg** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 143/266 (53.8%) | 122/262 (46.6%) | RR 1.12 (0.97 to 1.28) | 6 more per 100 (from 1 fewer to 13 more) | ⊕⊕⊕O MODERATE | |
| **Number reporting side effects (data by doses above licensed dose 60 mg) - 40 mg - 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[7] | none | 73/82 (89%) | 55/75 (73.3%) | RR 1.21 (1.04 to 1.42) | 15 more per 100 (from 3 more to 31 more) | ⊕⊕OO LOW | |
| **Number reporting side effects (data by doses above licensed dose 60 mg) - 80 mg** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 239/363 (65.8%) | 188/371 (50.7%) | RR 1.27 (1.15 to 1.41) | 14 more per 100 (from 8 more to 21 more) | ⊕⊕⊕O MODERATE | |
| **Number reporting side effects (overall)** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision | none | 1098/1534 (71.6%) | 698/1113 (62.7%) | RR 1.18 (1.12 to 1.24) | 11 more per 100 (from 8 more to 15 more) | ⊕⊕⊕O MODERATE | |
| **Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 60 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised | no serious | serious[5] | serious[1] | no serious | none | 479 | 364 | - | MD 0.49 lower | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | | | imprecision | | | | | (1.04 lower to 0.05 higher) | LOW | |
| **Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 80 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[5] | serious[1] | no serious imprecision | none | 265 | 271 | - | MD 0.70 lower (1.28 to 0.12 lower) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 120 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[5] | serious[1] | serious[2] | none | 158 | 159 | - | MD 0.61 lower (1.72 lower to 0.49 higher) | ⊕OOO VERY LOW | |
| **Mean weight change (kg) at endpoint (by doses above licensed dose 60 mg) - 40 mg - 120 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[5] | none | 81 | 72 | - | MD 1.09 lower (1.71 to 0.47 lower) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint (overall) (measured with: kg ; Better indicated by lower values)** | | | | | | | | | | | | |
| 8 | randomised | no serious | serious[5] | serious[1] | no serious | none | 890 | 773 | - | MD 0.69 lower (1 | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | | | imprecision | | | | | to 0.38 lower) | LOW | |

[1] Selected outpatients from multiple sites
[2] Inconclusive effect size
[3] Inconsistent effect size; single study
[4] Wide range of control group risks in individual studies (13% to 42%)
[5] Significant heterogeneity; random effects model used
[6] Inconclusive effect size
[7] Single study

## Is one dose of duloxetine more effective than others for depression? (Acute phase efficacy data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine at different doses | Control | Relative (95% CI) | Absolute | | |
| **Mean change scores at endpoint - 30 mg vs 60 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 202 | 198 | - | MD 0.83 higher (0.43 lower to 2.09 higher) | ⊕OOO VERY LOW | |
| **Mean change scores at endpoint - 40 mg vs 80 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 174 | 167 | - | MD 0.58 higher (0.87 lower to 2.03 higher) | ⊕OOO VERY LOW | |
| **Mean change scores at endpoint - 80 mg vs 120 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 186 | 195 | - | MD 0.7 higher (0.28 lower to 1.68 higher) | ⊕OOO VERY LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Non-response - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision[4] | none | 136/219 (62.1%) | 278/428 (65%) | RR 0.96 (0.84 to 1.08) | 3 fewer per 100 (from 10 fewer to 5 more) | ⊕⊕⊕O MODERATE | |
| **Non-response - 40 mg vs 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 110/177 (62.1%) | 103/175 (58.9%) | RR 1.05 (0.89 to 1.24) | 3 more per 100 (from 6 fewer to 14 more) | ⊕⊕OO LOW | |
| **Non-response - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 66/188 (35.1%) | 61/196 (31.1%) | RR 1.13 (0.85 to 1.5) | 4 more per 100 (from 5 fewer to 16 more) | ⊕⊕OO LOW | |
| **Non-remission - 40 mg vs 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[5] | serious[1] | serious[3] | none | 128/177 (72.3%) | 109/175 (62.3%) | RR 1.15 (0.92 to 1.44) | 9 more per 100 (from 5 fewer to 27 more) | ⊕OOO VERY LOW | |
| **Non-remission - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision[4] | none | 125/219 (57.1%) | 252/428 (58.9%) | RR 0.97 (0.84 to 1.11) | 2 fewer per 100 (from 9 fewer to 6 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | more) | | |
| **Non-remission - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[4] | none | 104/188 (55.3%) | 107/196 (54.6%) | RR 1.01 (0.83 to 1.23) | 1 more per 100 (from 9 fewer to 13 more) | ⊕⊕OO LOW | |

[1] Selective outpatients from multiple sites
[2] Inconclusive effect size; single study
[3] Inconclusive effect size
[4] Unlikely to be a difference
[5] Significant heterogeneity; random effects model used

## Is one dose of duloxetine more effective than others for depression? (Acute phase acceptability and tolerability data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine at different doses - acceptability and tolerability | Control | Relative (95% CI) | Absolute | Quality | |
| **Leaving treatment early - any reason - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 54/219 (24.7%) | 129/428 (30.1%) | RR 0.82 (0.62 to 1.07) | 5 fewer per 100 (from 11 fewer to 2 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - any reason - 40 mg vs 80 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 31/86 (36%) | 41.8% | RR 0.86 (0.6 to 1.25) | 59 fewer per 1000 (from 167 fewer to 104 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - any reason - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 22/188 (11.7%) | 20/196 (10.2%) | RR 1.15 (0.65 to 2.03) | 2 more per 100 (from 4 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 11 more) | | |
| **Leaving treatment early - due to adverse reaction - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[4] | none | 10/219 (4.6%) | 42/428 (9.8%) | RR 0.47 (0.24 to 0.91) | 5 fewer per 100 (from 1 fewer to 7 fewer) | ⊕⊕OO LOW | |
| **Leaving treatment early - due to adverse reaction - 40 mg vs 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 21/177 (11.9%) | 27/175 (15.4%) | RR 0.77 (0.45 to 1.31) | 4 fewer per 100 (from 8 fewer to 5 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - due to adverse reaction - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 8/188 (4.3%) | 7/196 (3.6%) | RR 1.2 (0.44 to 3.24) | 1 more per 100 (from 2 fewer to 8 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - lack of efficacy - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[2] | none | 3/219 (1.4%) | 6/428 (1.4%) | RR 0.98 (0.25 to 3.87) | 0 fewer per 100 (from 1 fewer to 4 more) | ⊕OOO VERY LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - lack of efficacy - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[1] | none | 6/188 (3.2%) | 2.1% | RR 1.56 (0.45 to 5.44) | 12 more per 1000 (from 12 fewer to 93 more) | ⊕OOO VERY LOW | |
| **No reporting side effects - 30 mg vs 60 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[4] | none | 160/219 (73.1%) | 315/428 (73.6%) | RR 0.99 (0.9 to 1.1) | 1 fewer per 100 (from 7 fewer to 7 more) | ⊕⊕OO LOW | |
| **No reporting side effects - 40 mg vs 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | no serious imprecision[5] | none | 151/177 (85.3%) | 151/175 (86.3%) | RR 0.99 (0.91 to 1.07) | 9 fewer per 1000 (from 78 fewer to 60 more) | ⊕⊕⊕O MODERATE | |
| **No reporting side effects - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 88/188 (46.8%) | 81/196 (41.3%) | RR 1.12 (0.9 to 1.4) | 5 more per 100 (from 4 fewer to 17 more) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean weight change (kg) at endpoint - 30 mg vs 60 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[4] | none | 168 | 155 | - | MD 0.35 lower (1 lower to 0.3 higher) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint - 40 mg vs 80 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 158 | 167 | - | MD 0.19 lower (0.69 lower to 0.31 higher) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint - 80 mg vs 120 mg (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[3] | none | 93 | 93 | - | MD 0.08 lower (0.69 lower to 0.53 higher) | ⊕⊕OO LOW | |

[1] Selected outpatients from multiple sites
[2] Inconclusive effect size; single study
[3] Inconclusive effect size
[4] Single study
[5] Unlikely to be a difference

## Is duloxetine more effective than other antidepressants for depression? (Acute phase efficacy data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine | Other antidepressants | Relative (95% CI) | Absolute | | |
| **Mean change scores at endpoint (all data) (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 12 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision[3] | none | 1601 | 1544 | - | MD 0.19 higher (0.44 lower to 0.81 higher) | ⊕⊕OO LOW | |
| **Mean change scores at endpoint - paroxetine (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 591 | 593 | - | MD 0.2 lower (1.14 lower to 0.74 higher) | ⊕⊕OO LOW | |
| **Mean change scores at endpoint - fluoxetine (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[4] | none | 147 | 70 | - | MD 1.1 lower (3.03 lower to | ⊕OOO VERY LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 0.83 higher) | | |
| **Mean change scores at endpoint - escitalopram (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 545 | 551 | - | MD 0.66 higher (0.61 lower to 1.93 higher) | ⊕⊕OO LOW | |
| **Mean change scores at endpoint - venlafaxine (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 318 | 330 | - | MD 1.06 higher (0.02 lower to 2.14 higher) | ⊕⊕⊕O MODERATE | |
| **Non-response (all data)** | | | | | | | | | | | | |
| 12 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 805/1645 (48.9%) | 718/1563 (45.9%) | RR 1.05 (0.95 to 1.17) | 2 more per 100 (from 2 fewer to 8 more) | ⊕⊕OO LOW | |
| **Non-response - paroxetine** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 | randomised trials | no serious limitations | serious[1] | serious[1] | no serious imprecision | none | 263/601 (43.8%) | 257/599 (42.9%) | RR 1.01 (0.81 to 1.26) | 0 more per 100 (from 8 fewer to 11 more) | ⊕⊕OO LOW | |
| **Non-response - fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[4] | none | 80/152 (52.6%) | 37/70 (52.9%) | RR 0.99 (0.72 to 1.36) | 1 fewer per 100 (from 15 fewer to 19 more) | ⊕⊕OO LOW | |
| **Non-response - escitalopram** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 331/562 (58.9%) | 315/557 (56.6%) | RR 1.04 (0.94 to 1.16) | 2 more per 100 (from 3 fewer to 9 more) | ⊕⊕⊕O MODERATE | |
| **Non-response - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | serious[2] | serious[4] | none | 131/330 (39.7%) | 109/337 (32.3%) | RR 1.23 (0.92 to 1.64) | 7 more per 100 (from 3 fewer to 21 more) | ⊕OOO VERY LOW | |
| **Non-remission (all data)** | | | | | | | | | | | | |
| 12 | randomised | no serious | serious[1] | serious[2] | no serious | none | 948/1645 | 879/1563 | RR 1.02 (0.94 to | 1 more per 100 | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | | | imprecision | | (57.6%) | (56.2%) | 1.11) | (from 3 fewer to 6 more) | LOW | |
| **Non-remission - paroxetine** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 334/601 (55.6%) | 337/599 (56.3%) | RR 0.99 (0.9 to 1.1) | 1 fewer per 100 (from 6 fewer to 6 more) | ⊕⊕⊕O MODERATE | |
| **Non-remission - fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | very serious[1] | serious[2] | very serious[4] | none | 92/152 (60.5%) | 51.8% | RR 1.21 (0.56 to 2.61) | 109 more per 1000 (from 228 fewer to 834 more) | ⊕OOO VERY LOW | |
| **Non-remission - escitalopram** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 345/562 (61.4%) | 334/557 (60%) | RR 1.06 (0.89 to 1.26) | 4 more per 100 (from 7 fewer to 16 more) | ⊕⊕OO LOW | |
| **Non-remission - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 177/330 (53.6%) | 171/337 (50.7%) | RR 1.06 (0.88 to | 3 more per 100 (from 6 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.27) | fewer to 14 more) | | |

[1] Significant heterogeneity; random effects model used
[2] Selected outpatients from multiple sites
[3] Unlikely to be a difference
[4] Inconclusive effect size

**Is duloxetine more effective than other antidepressants for depression? (Acute phase acceptability and tolerability data)**

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Duloxetine | Other antidepressants - acceptability and tolerability | Relative (95% CI) | Absolute | | |
| **Leaving treatment early - any reason** | | | | | | | | | | | | |
| 11 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 472/1494 (31.6%) | 344/1420 (24.2%) | RR 1.27 (1.1 to 1.47) | 7 more per 100 (from 2 more to 11 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - any reason - paroxetine** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 176/601 (29.3%) | 145/599 (24.2%) | RR 1.21 (1.01 to 1.45) | 5 more per 100 (from 0 more to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 11 more) | | |
| **Leaving treatment early - any reason - fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[3] | none | 49/152 (32.2%) | 26/70 (37.1%) | RR 0.87 (0.59 to 1.27) | 5 fewer per 100 (from 15 fewer to 10 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - any reason - escitalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 131/411 (31.9%) | 87/414 (21%) | RR 1.64 (0.97 to 2.78) | 13 more per 100 (from 1 fewer to 37 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - any reason - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 116/330 (35.2%) | 86/337 (25.5%) | RR 1.37 (1.09 to 1.72) | 9 more per 100 (from 2 more to 18 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - adverse reactions** | | | | | | | | | | | | |
| 10 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 147/1412 (10.4%) | 91/1383 (6.6%) | RR 1.54 (1.2 to 1.99) | 4 more per 100 (from 1 more to 7 more) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - adverse reactions - paroxetine** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[3] | none | 55/601 (9.2%) | 42/599 (7%) | RR 1.32 (0.9 to 1.93) | 2 more per 100 (from 1 fewer to 7 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions - fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[4] | none | 7/70 (10%) | 1/33 (3%) | RR 3.3 (0.42 to 25.74) | 7 more per 100 (from 2 fewer to 75 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - adverse reactions - escitalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | serious[2] | serious[3] | none | 37/411 (9%) | 17/414 (4.1%) | RR 2.62 (0.67 to 10.3) | 7 more per 100 (from 1 fewer to 38 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - adverse reactions - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 48/330 (14.5%) | 31/337 (9.2%) | RR 1.58 (1.04 to 2.42) | 5 more per 100 (from 0 more to 13 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - lack of efficacy** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 40/1167 (3.4%) | 37/1174 (3.2%) | RR 1.09 (0.7 to 1.68) | 0 more per 100 (from 1 fewer to 2 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - lack of efficacy - paroxetine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[3] | none | 7/426 (1.6%) | 3/423 (0.7%) | RR 2.29 (0.6 to 8.78) | 1 more per 100 (from 0 fewer to 6 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - lack of efficacy - fluoxetine - no data** | | | | | | | | | | | | |
| 0 | no evidence available | | | | | none | 0/0 (0%) | 0% | not pooled | not pooled | | |
| **Leaving treatment early - lack of efficacy - escitalopram** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[3] | none | 22/411 (5.4%) | 25/414 (6%) | RR 0.88 (0.51 to 1.53) | 1 fewer per 100 (from 3 fewer to 3 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - lack of efficacy - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised | no serious | no serious | serious[2] | very | none | 11/330 | 9/337 (2.7%) | RR 1.24 (0.52 to | 1 more per 100 | ⊕OOO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | | serious[3] | | (3.3%) | | 2.95) | (from 1 fewer to 5 more) | VERY LOW | |
| **No. reporting side effects** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 1010/1274 (79.3%) | 949/1243 (76.3%) | RR 1.02 (0.98 to 1.07) | 2 more per 100 (from 2 fewer to 5 more) | ⊕⊕⊕O MODERATE | |
| **No. reporting side effects - paroxetine** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 424/601 (70.5%) | 389/599 (64.9%) | RR 1.07 (0.99 to 1.15) | 5 more per 100 (from 1 fewer to 10 more) | ⊕⊕⊕O MODERATE | |
| **No. reporting side effects - fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[5] | none | 62/70 (88.6%) | 30/33 (90.9%) | RR 0.97 (0.85 to 1.12) | 3 fewer per 100 (from 14 fewer to 11 more) | ⊕⊕OO LOW | |
| **No. reporting side effects - escitalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[5] | none | 241/273 (88.3%) | 237/274 (86.5%) | RR 1.02 (0.96 to 1.09) | 2 more per 100 (from 3 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 8 more) | | |
| **No. reporting side effects - venlafaxine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | serious[2] | no serious imprecision | none | 283/330 (85.8%) | 293/337 (86.9%) | RR 0.99 (0.88 to 1.11) | 1 fewer per 100 (from 10 fewer to 10 more) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint (sensitivity analysis) (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 1042 | 1016 | - | MD 0 higher (0.03 lower to 0.03 higher) | ⊕⊕⊕O MODERATE | |
| **Mean weight change (kg) at endpoint - paroxetine (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 422 | 412 | - | MD 0 higher (0.03 lower to 0.03 higher) | ⊕⊕⊕O MODERATE | |
| **Mean weight change (kg) at endpoint - fluoxetine (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[5] | none | 65 | 33 | - | MD 0.01 lower (0.74 lower to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 0.72 higher) | | |
| **Mean weight change (kg) at endpoint - escitalopram (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[5] | none | 273 | 274 | - | MD 0.06 higher (1.08 lower to 1.2 higher) | ⊕⊕OO LOW | |
| **Mean weight change (kg) at endpoint - venlafaxine (measured with: kg; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 282 | 297 | - | MD 0.39 higher (0.09 lower to 0.86 higher) | ⊕⊕⊕O MODERATE | |

[1] Significant heterogeneity; random effects model used
[2] Selected outpatients from multiple sites
[3] Inconsistent effect size
[4] Inconsistent effect size; single study
[5] Single study

**Is duloxetine effective as a continuation treatment following a 30% improvement in baseline (HAMD-17) symptoms of depression?**

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine | Placebo | Relative (95% CI) | Absolute | | |
| **Mean change scores from end of acute phase - 80 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[1] | none | 70 | 70 | - | MD 1 lower (2.5 lower to 0.5 higher) | ⊕⊕OO LOW | |
| **Mean change scores from end of acute phase - 120 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 80 | 70 | - | MD 0.2 lower (1.78 lower to 1.38 higher) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - for any reason - 80 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 58/71 (81.7%) | 62/71 (87.3%) | RR 0.94 (0.81 to 1.08) | 5 fewer per 100 (from 17 fewer to 7 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - for any reason - 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 62/81 (76.5%) | 62/71 (87.3%) | RR 0.88 (0.75 to 1.02) | 10 fewer per 100 (from 22 fewer to 2 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions - 80 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 7/146 (4.8%) | 6/129 (4.7%) | RR 0.96 (0.34 to 2.73) | 0 fewer per 100 (from 3 fewer to 8 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early - adverse reactions - 120 mg** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | no serious imprecision | none | 6/151 (4%) | 6/129 (4.7%) | RR 0.84 (0.28 to 2.54) | 1 fewer per 100 (from 3 fewer to 7 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early - lack of efficacy - 80 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 1/71 (1.4%) | 1/71 (1.4%) | RR 1 (0.06 to 15.68) | 0 fewer per 100 (from 1 fewer to 21 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - lack of efficacy - 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 4/81 (4.9%) | 1/71 (1.4%) | RR 3.51 (0.4 to 30.65) | 4 more per 100 (from 1 fewer to 42 more) | ⊕⊕OO LOW | |

[1] Single study

[2] Selective patients from multiple sites

**Is one dose of duloxetine more effective than another as a continuation treatment following a 30% improvement in baseline (HAMD-17) symptoms of depression?**

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine at different doses | Control | Relative (95% CI) | Absolute | Quality | |
| **Mean change scores from end of acute phase - 80 mg vs 120 mg (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 70 | 80 | - | MD 0.8 lower (2.18 lower to 0.58 higher) | ⊕⊕OO LOW | |
| **Leaving treatment early - for any reason - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 58/71 (81.7%) | 62/81 (76.5%) | RR 1.07 (0.91 to 1.26) | 5 more per 100 (from 7 fewer to 20 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 1 | randomised | no serious | no serious | serious[1] | very | none | 2/71 (2.8%) | 3/81 | RR 0.76 | 1 fewer | ⊕OOO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | | serious[3] | | | (3.7%) | (0.13 to 4.42) | per 100 (from 3 fewer to 13 more) | VERY LOW | |
| **Leaving treatment early - lack of efficacy - 80 mg vs 120 mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 1/71 (1.4%) | 4/81 (4.9%) | RR 0.29 (0.03 to 2.49) | 4 fewer per 100 (from 5 fewer to 7 more) | ⊕OOO VERY LOW | |

[1] Selected patients from multiple sites

[2] Single study

[3] Single study + inconsistent effect size

**Is duloxetine more effective than other antidepressants as a continuation treatment following a 30% improvement in baseline (HAMD-17) symptoms of depression?**

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No of patients | | Effect | | | |
| No of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Continuation phase for those with 30% improvement in baseline HAMD-17 scores: duloxetine | Other drugs | Relative (95% CI) | Absolute | Quality | |
| **Mean change scores from end of acute phase - 80 mg vs paroxetine (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 70 | 70 | - | MD 0.3 higher (1.06 lower to 1.66 higher) | ⊕⊕OO LOW | |
| **Leaving treatment early - for any reason - paroxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | serious[1] | none | 58/71 (81.7%) | 61/70 (87.1%) | RR 0.94 (0.81 to 1.08) | 5 fewer per 100 (from 17 fewer to 7 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - adverse reactions - paroxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[3] | none | 7/146 (4.8%) | 2/140 (1.4%) | RR 2.84 (0.7 to | 3 more per 100 (from | ⊕OOO VERY | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 11.6) | 0 fewer to 15 more) | LOW | |
| **Leaving treatment early - lack of efficacy - paroxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[2] | very serious[4] | none | 1/71 (1.4%) | 2/70 (2.9%) | RR 0.49 (0.05 to 5.31) | 1 fewer per 100 (from 3 fewer to 12 more) | ⊕OOO VERY LOW | |

[1] Single study
[2] Selective outpatients from multiple sites
[3] Inconsistent effect size
[4] Single study + inconsistent effect size

## Is duloxetine more effective than other antidepressants following response to acute phase treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No of patients | | Effect | | Quality | |
| No of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Continuation phase no entry criteria: duloxetine | Other drugs | Relative (95% CI) | Absolute | | |
| **Mean scores at endpoint - escitalopram (measured with: HAMD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 146 | 141 | - | MD 1.34 higher (0.25 lower to 2.93 higher) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Non-response - escitalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 49/151 (32.5%) | 40/143 (28%) | RR 1.16 (0.82 to 1.65) | 4 more per 100 (from 5 fewer to 18 more) | ⊕OOO VERY LOW | |
| **Non-remission - escitalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 39/151 (25.8%) | 28/143 (19.6%) | RR 1.32 (0.86 to 2.02) | 6 more per 100 (from 3 fewer to 20 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - any reason - escitalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | very serious[3] | none | 37/151 (24.5%) | 31/143 (21.7%) | RR 1.13 (0.74 to 1.72) | 3 more per 100 (from 6 fewer to 16 more) | ⊕OOO VERY LOW | |
| **Leaving treatment early - adverse reactions - escitalopram** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | serious[1] | serious[2] | none | 26/151 (17.2%) | 13/143 (9.1%) | RR 1.89 (1.01 to 3.54) | 8 more per 100 (from 0 more to 23 more) | ⊕⊕OO LOW | |
| **Leaving treatment early - lack of efficacy - escitalopram** | | | | | | | | | | | | |
| 1 | randomised | no serious | no serious | serious[1] | very | none | 2/151 (1.3%) | 7/143 | RR 0.27 (0.06 to | 4 fewer per 100 (from 5 | ⊕OOO VERY | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | | serious[3] | | | (4.9%) | 1.28) | fewer to 1 more) | LOW | |

[1] Selected patients from multiple sites
[2] Single study
[3] Single study + inconsistent effect size

# Light therapy

## Is bright light effective for depression with a seasonal pattern/SAD compared with waitlist control?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Bright light | Waitlist | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason (overall) (total number not completing study)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 3/42 (7.1%) | 3/40 (7.5%) | RR 0.95 (0.21 to 4.32) | 0 fewer per 100 (from 6 fewer to 25 more) | ⊕⊕OO LOW | |
| | | | | | | | | 8.7% | | 0 fewer per 100 (from 7 fewer to 29 more) | | |
| **Leaving study early due to side effects - Light box vs waitlist control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 0/16 (0%) | 0/15 (0%) | not pooled | not pooled | ⊕⊕⊕O | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 0% | | not pooled | MODERATE | |
| **Leaving study early - Light room vs waitlist control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 1/26 (3.8%) | 1/25 (4%)<br>0% | RR 0.96 (0.06 to 14.55) | 0 fewer per 100 (from 4 fewer to 54 more)<br>0 fewer per 100 (from 0 fewer to 0 more) | ⊕⊕⊕O MODERATE | |
| **Mean self rated SAD depression scores at endpoint - Light room vs waitlist control (measured with: SIGH-SAD-SR; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 24 | 24 | - | MD 12.8 lower (18.52 to 7.08 lower) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated SAD depression scores at endpoint - Light box vs waitlist control (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 16 | 15 | - | MD 10.4 lower (15.99 to 4.81 lower) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated typical depression scores at endpoint - Light box vs waitlist control (measured with: HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 16 | 15 | - | MD 6.3 lower (10.34 to 2.26 | ⊕⊕⊕⊕ HIGH | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | lower) | | |
| **Mean self-rated depression score - overall (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 40 | 39 | - | MD 1.15 lower (1.63 to 0.67 lower) | ⊕⊕⊕⊕ HIGH | |
| **Mean self rated depression scores at endpoint - Light room vs waitlist control (measured with: HRSD-21-SR; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 24 | 24 | - | MD 7.7 lower (11.58 to 3.82 lower) | ⊕⊕⊕O MODERATE | |
| **Mean self rated depression scores at endpoint - Light box vs waitlist control (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 16 | 15 | - | MD 10.9 lower (16.99 to 4.81 lower) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint - Light box vs waitlist control (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 16 | 15 | - | MD 4 lower (6.73 to 1.27 lower) | ⊕⊕⊕O MODERATE | |
| **Mean self rated atypical depression scores at endpoint - Light room vs waitlist control (measured with: SAD-SR subscale of SIGH-SAD); Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised | no serious | no serious | no serious | serious[2] | none | 24 | 24 | - | MD 5.2 lower (7.39 | ⊕⊕⊕O | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | | | | | | to 3.01 lower) | MODERATE | |
| **Non remission (SIGH-SAD-SR) (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 20/42 (47.6%) | 36/40 (90%)<br>88% | RR 0.53 (0.38 to 0.74) | 42 fewer per 100 (from 23 fewer to 56 fewer)<br>41 fewer per 100 (from 23 fewer to 55 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Non remission (SIGH-SAD-SR) - Light room vs waitlist control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 12/26 (46.2%) | 24/25 (96%)<br>96% | RR 0.48 (0.31 to 0.73) | 50 fewer per 100 (from 26 fewer to 66 fewer)<br>50 fewer per 100 (from 26 fewer to 66 fewer) | ⊕⊕⊕O MODERATE | |
| **Non remission (SIGH-SAD-SR) - Light box vs waitlist control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 8/16 (50%) | 12/15 (80%)<br>80% | RR 0.62 (0.36 to 1.08) | 30 fewer per 100 (from 51 fewer to 6 more)<br>30 fewer per | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 100 (from 51 fewer to 6 more) | | |
| **Non response (SIGH-SAD) - Light room vs waitlist control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 13/26 (50%) | 25/25 (100%) | RR 0.50 (0.34 to 0.73) | 50 fewer per 100 (from 27 fewer to 66 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 100% | | 50 fewer per 100 (from 27 fewer to 66 fewer) | | |

[1] Inconclusive effect size

[2] Single study

## Is bright light effective for depression with a seasonal pattern/SAD compared with attentional control?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Bright light | Attentional control | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason (overall)** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 18/134 (13.4%) | 18/124 (14.5%)<br>13.1% | RR 0.92 (0.51 to 1.64) | 1 fewer per 100 (from 7 fewer to 9 more)<br>1 fewer per 100 (from 6 fewer to 8 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Light box vs deactivated negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 8/41 (19.5%) | 9/40 (22.5%)<br>22.5% | RR 0.87 (0.37 to 2.02) | 3 fewer per 100 (from 14 fewer to 23 more)<br>3 fewer per 100 (from 14 fewer to 23 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Low dose (<5000lux hours/day) LED light vs negative ion generator** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 1/15 (6.7%) | 2/11 (18.2%)<br>18.2% | RR 0.37 (0.04 to 3.55) | 11 fewer per 100 (from 17 fewer to 46 more)<br>11 fewer per 100 (from 17 fewer to 46 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Light box vs high dose (>300lux) dim red light box** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 6/33 (18.2%) | 5/26 (19.2%)<br>19.2% | RR 0.95 (0.32 to 2.76) | 1 fewer per 100 (from 13 fewer to 34 more)<br>1 fewer per 100 (from 13 fewer to 34 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Light box vs low-density ionisation** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 2/23 (8.7%) | 2/25 (8%)<br>8% | RR 1.09 (0.17 to 7.1) | 1 more per 100 (from 7 fewer to 49 more)<br>1 more per 100 (from 7 fewer to 49 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Low dose (<5000lux hours/day) light box vs no light box** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 1/10 (10%) | 0/12 (0%)<br>0% | RR 3.55 (0.16 to 78.56) | 0 more per 100 (from 0 fewer to 0 more)<br>0 more per 100 (from 0 fewer to 0 more) | ⊕⊕OO LOW | |
| **Leaving study early for any reason - Low dose (<5000lux hours/day) light visor vs no light visor** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 0/12 (0%) | 0/10 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕O MODERATE | |
| **Leaving study early due to lack of efficacy - Low dose (<5000lux hours/day) LED light vs negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 0/15 (0%) | 1/11 (9.1%)<br>9.1% | RR 0.25 (0.01 to 5.62) | 7 fewer per 100 (from 9 fewer to 42 more)<br>7 fewer per 100 (from 9 fewer to 42 more) | ⊕⊕OO LOW | |
| **Reported side effects (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 25/45 (55.6%) | 21/36 (58.3%)<br>44.6% | RR 0.98 (0.73 to 1.32) | 1 fewer per 100 (from 16 fewer to 19 more)<br>1 fewer per 100 (from 12 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 14 more) | | |
| **Reported side effects - Low dose (<5000lux hours/day) LED light vs negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 2/15 (13.3%) | 1/11 (9.1%)<br>9.1% | RR 1.47 (0.15 to 14.21) | 4 more per 100 (from 8 fewer to 120 more)<br>4 more per 100 (from 8 fewer to 120 more) | ⊕⊕⊕O MODERATE | |
| **Reported side effects - Light visor vs dim light visor** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious | none | 23/30 (76.7%) | 20/25 (80%)<br>80% | RR 0.96 (0.73 to 1.27) | 3 fewer per 100 (from 22 fewer to 22 more)<br>3 fewer per 100 (from 22 fewer to 22 more) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint (overall) (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[1] | none | 139 | 131 | - | MD 2.78 lower (6.81 lower to 1.26 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - Low dose (<5000lux hours/day) LED light vs negative ion generator (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 14 | 9 | - | MD 4.7 lower (10.34 lower to 0.94 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated SAD depression scores at endpoint - Light visor vs dim light visor (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[3] | none | 64 | 58 | - | MD 0.86 higher (7.56 lower to 9.29 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - Light box vs low-density ionisation (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 40 | 42 | - | MD 8.56 lower (14.73 to 2.39 lower) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated SAD depression scores at endpoint - Low dose (<5000lux hours/day) light box vs no light box (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 9 | 12 | - | MD 1.4 higher (4.93 lower to 7.73 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - Low dose (<5000lux hours/day) light visor vs no light visor (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 12 | 10 | - | MD 0.2 lower (6.22 lower to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 5.82 higher) | | |
| **Mean clinician rated typical depression scores at endpoint (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[1] | none | 106 | 103 | - | SMD 0.07 lower (0.51 lower to 0.37 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated typical depression scores at endpoint - Light visor vs dim light visor (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[4] | none | 64 | 58 | - | SMD 0.05 higher (0.52 lower to 0.63 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated typical depression scores at endpoint - Light box vs low-density ionisation (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 21 | 23 | - | SMD 0.81 lower (1.43 to 0.19 lower) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated typical depression scores at endpoint - Low dose (<5000lux hours/day) light box vs no light box (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 9 | 12 | - | SMD 0.26 higher (0.61 lower to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 1.13 higher) | | |
| **Mean clinician rated typical depression scores at endpoint - Low dose (<5000lux hours/day) light visor vs no light visor (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 12 | 10 | - | SMD 0.2 higher (0.64 lower to 1.04 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 55 | 55 | - | MD 1.25 lower (2.77 lower to 0.27 higher) | ⊕⊕⊕⊕ HIGH | |
| **Mean clinician rated atypical depression scores at endpoint - Light visor vs dim light visor (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 34 | 33 | - | MD 2.1 lower (4.31 lower to 0.11 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint - Low dose (<5000lux hours/day) light box vs no light box (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 9 | 12 | - | MD 1.2 higher (2.48 lower to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 4.88 higher) | | |
| **Mean clinician rated atypical depression scores at endpoint - Low dose (<5000lux hours/day) light visor vs no light visor (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 12 | 10 | - | MD 1.3 lower (3.84 lower to 1.24 higher) | ⊕⊕⊕O MODERATE | |
| **Mean self rated depression scores at endpoint - Light box vs deactivated negative ion generator (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 33 | 31 | - | MD 2.6 lower (6.72 lower to 1.52 higher) | ⊕⊕⊕O MODERATE | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) (overall)** | | | | | | | | | | | | |
| 6 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[3] | none | 99/176 (56.3%) | 98/160 (61.3%)<br>70.5% | RR 0.89 (0.66 to 1.2) | 7 fewer per 100 (from 21 fewer to 12 more)<br>8 fewer per 100 (from 24 fewer to 14 more) | ⊕⊕OO LOW | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) - Low dose (<5000lux hours/day) LED light vs negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 7/15 (46.7%) | 10/11 (90.9%) | RR 0.51 (0.29 to 0.91) | 45 fewer per 100 (from 8 fewer to 65 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer) | | |
| | | | | | | | | 90.9% | | 45 fewer per 100 (from 8 fewer to 65 fewer) | | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) - Light box vs deactivated negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 21/41 (51.2%) | 30/40 (75%) | RR 0.68 (0.48 to 0.97) | 24 fewer per 100 (from 2 fewer to 39 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 75% | | 24 fewer per 100 (from 2 fewer to 39 fewer) | | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) - Light visor vs dim light visor** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[4] | none | 33/64 (51.6%) | 22/58 (37.9%) | RR 1.34 (0.79 to 2.27) | 13 more per 100 (from 8 fewer to 48 more) | ⊕⊕OO LOW | |
| | | | | | | | | 38.7% | | 13 more per 100 (from 8 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 49 more) | | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) - Light box vs high dose (>300lux) dim red light box** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 25/33 (75.8%) | 19/26 (73.1%)<br>73.1% | RR 1.04 (0.77 to 1.4) | 3 more per 100 (from 17 fewer to 29 more)<br>3 more per 100 (from 17 fewer to 29 more) | ⊕⊕OO LOW | |
| **Non remission (SIGH-SAD or SIGH-SAD-SR or HDRS) - Light box vs low-density ionisation** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 13/23 (56.5%) | 17/25 (68%)<br>68% | RR 0.83 (0.53 to 1.3) | 12 fewer per 100 (from 32 fewer to 20 more)<br>12 fewer per 100 (from 32 fewer to 20 more) | ⊕⊕OO LOW | |
| **Non response (SIGH-SAD) (overall)** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[1] | none | 83/183 (45.4%) | 92/171 (53.8%)<br>58.3% | RR 0.86 (0.64 to 1.15) | 8 fewer per 100 (from 19 fewer to 8 more)<br>8 fewer per 100 (from | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 21 fewer to 9 more) | | |
| **Non response (SIGH-SAD) - Light box vs deactivated negative ion generator** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 19/41 (46.3%) | 25/40 (62.5%)<br>62.5% | RR 0.74 (0.49 to 1.11) | 16 fewer per 100 (from 32 fewer to 7 more)<br>16 fewer per 100 (from 32 fewer to 7 more) | ⊕⊕⊕O MODERATE | |
| **Non response (SIGH-SAD) - Light visor vs dim light visor** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[4] | none | 30/64 (46.9%) | 22/58 (37.9%)<br>37.2% | RR 1.24 (0.56 to 2.75) | 9 more per 100 (from 17 fewer to 66 more)<br>9 more per 100 (from 16 fewer to 65 more) | ⊕⊕OO LOW | |
| **Non response (SIGH-SAD) - Light box vs high dose (>300lux) dim red light box** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 13/33 (39.4%) | 14/26 (53.8%) | RR 0.73 (0.42 to 1.27) | 15 fewer per 100 (from 31 fewer to 15 more) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 53.9% | | 15 fewer per 100 (from 31 fewer to 15 more) | | |
| **Non response (SIGH-SAD) - Light box vs low-density ionisation** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 9/23 (39.1%) | 18/25 (72%)<br>72% | RR 0.54 (0.31 to 0.96) | 33 fewer per 100 (from 3 fewer to 50 fewer)<br>33 fewer per 100 (from 3 fewer to 50 fewer) | ⊕⊕⊕O MODERATE | |
| **Non response (SIGH-SAD) - Low dose (<5000lux hours/day) light box vs no light box** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 7/10 (70%) | 7/12 (58.3%)<br>58.3% | RR 1.2 (0.64 to 2.25) | 12 more per 100 (from 21 fewer to 73 more)<br>12 more per 100 (from 21 fewer to 73 more) | ⊕⊕⊕O MODERATE | |
| **Non response (SIGH-SAD) - Low dose (<5000lux hours/day) light visor vs no light visor** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 5/12 (41.7%) | 6/10 (60%) | RR 0.69 (0.3 to 1.61) | 19 fewer per 100 (from 42 fewer to 37 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 60% | | 19 fewer per 100 (from 42 fewer to 37 more) | | |

[1] Inconclusive effect size
[2] Single study; inconclusive effect size
[3] Significant heterogeneity; random effects model used
[4] Single study

## Is bright light effective for depression with a seasonal pattern/SAD compared with active treatments?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Bright light | Active treatment control | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason - Light box vs group CBT** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 2/25 (8%) | 4/24 (16.7%) | RR 0.53 (0.12 to 2.31) | 8 fewer per 100 (from 15 fewer to 22 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 17.8% | | 8 fewer per 100 (from 16 fewer to 23 more) | | |
| **Leaving study early for any reason - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 12/68 (17.6%) | 8/68 (11.8%) | RR 1.5 (0.65 to 3.44) | 6 more per 100 (from 4 fewer to 29 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 9.8% | | 5 more per 100 (from 3 fewer to 24 more) | | |
| | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving study early for any reason - Light box + hypericum vs dim light + hypericum** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 0/10 (0%) | 0/10 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕⊕ HIGH | |
| **Leaving study early due to side effects - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 1/48 (2.1%) | 2/48 (4.2%)<br>4.2% | RR 0.5 (0.05 to 5.33) | 2 fewer per 100 (from 4 fewer to 18 more)<br>2 fewer per 100 (from 4 fewer to 18 more) | ⊕⊕OO LOW | |
| **Leaving study early due to side effects - Light box vs group CBT** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 0/16 (0%) | 0/15 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕O MODERATE | |
| **Leaving study early due to lack of efficacy - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 2/43 (4.7%) | 0/48 (0%)<br>0% | RR 5.57 (0.27 to 112.85) | 0 more per 100 (from 0 fewer to 0 more)<br>0 more per 100 (from 0 fewer to 0 more) | | |
| **Reported side effects - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 37/48 (77.1%) | 75% | RR 1.03 (0.82 to 1.29) | 22 more per 1000 (from 135 fewer to 217 more) | | |
| **Mean clinician rated SAD depression scores at endpoint - Light box vs group CBT (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 16 | 15 | - | MD 0.2 lower (6.5 lower to 6.1 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - Light box + placebo pill vs dim light box + fluoxetine (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 68 | 68 | - | MD 0.49 lower (3.72 lower to 2.74 higher) | ⊕⊕⊕⊕ HIGH | |
| **Mean clinician rated typical depression scores at endpoint - Light box vs group CBT (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 16 | 15 | - | SMD 0.13 lower (0.83 lower to 0.58 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated typical depression scores at endpoint - Light box + placebo pill vs dim light box + fluoxetine (measured with: HAMD-17/HRSD-21;** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 68 | 68 | - | SMD 0.04 lower (0.38 lower to 0.29 higher) | ⊕⊕⊕⊕ HIGH | |
| **Mean clinician rated typical depression scores at endpoint - Light box + hypericum vs dim light + hypericum (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 10 | 10 | - | SMD 0.32 lower (1.2 lower to 0.57 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated atypical depression scores at endpoint - Light box vs group CBT (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 16 | 15 | - | MD 0.4 higher (2.68 lower to 3.48 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint - Light box + placebo pill vs dim light box + fluoxetine (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 68 | 68 | - | MD 0.3 lower (1.75 lower to 1.15 higher) | ⊕⊕OO LOW | |
| **Mean self rated depression scores at endpoint - Light box vs group CBT (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 16 | 15 | - | MD 0.7 lower (7.16 lower to 5.76 higher) | | |
| **Mean self rated depression scores at endpoint - Light box + placebo pill vs dim light box + fluoxetine (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 48 | 48 | - | MD 1.6 lower (5.68 lower to 2.48 higher) | ⊕⊕OO LOW | |
| **Non remission - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[1] | none | 34/68 (50%) | 37/68 (54.4%)<br>60.4% | RR 0.92 (0.67 to 1.27) | 4 fewer per 100 (from 18 fewer to 15 more)<br>5 fewer per 100 (from 20 fewer to 16 more) | ⊕⊕OO LOW | |
| **Non remission - Light box vs group CBT** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 12/25 (48%) | 15/24 (62.5%)<br>63.3% | RR 0.77 (0.46 to 1.28) | 14 fewer per 100 (from 34 fewer to 17 more)<br>15 fewer per 100 (from 34 | ⊕⊕⊕⊕ HIGH | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 18 more) | | |
| **Non response - Light box + placebo pill vs dim light box + fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 22/68 (32.4%) | 23/68 (33.8%) | RR 0.96 (0.59 to 1.54) | 1 fewer per 100 (from 14 fewer to 18 more) | ⊕⊕OO LOW | |
| | | | | | | | | 34.2% | | 1 fewer per 100 (from 14 fewer to 18 more) | | |

[1] Inconclusive effect size
[2] Inconclusive effect size/single study
[3] Single study
[4] Significant heterogeneity; random effects model used

## Is bright light effective for depression with a seasonal pattern/SAD compared with a combination of bright light and CBT?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Bright light | Light + CBT combo | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 2/25 (8%) | 2/23 (8.7%)<br>9.6% | RR 0.92 (0.17 to 4.91) | 1 fewer per 100 (from 7 fewer to 34 more)<br>1 fewer per 100 (from 8 fewer to 38 more) | ⊕⊕⊕O MODERATE | |
| **Leaving study early due to side effects** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 0/16 (0%) | 1/15 (6.7%)<br>6.7% | RR 0.31 (0.01 to 7.15) | 5 fewer per 100 (from 7 fewer to 41 more)<br>5 fewer per 100 (from 7 fewer to 41 more) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean clinician rated SAD depression scores at endpoint (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 16 | 15 | - | MD 4.2 higher (0.52 lower to 8.92 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated typical depression scores at endpoint (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 16 | 15 | - | SMD 0.46 higher (0.26 lower to 1.17 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 16 | 15 | - | MD 2 higher (0.12 lower to 4.12 higher) | ⊕⊕⊕O MODERATE | |
| **Mean self rated depression scores at endpoint (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 16 | 15 | - | MD 2.3 higher (2.47 lower to 7.07 higher) | ⊕⊕OO LOW | |
| **Non remission (SIGH-SAD)** | | | | | | | | | | | | |
| 2 | randomised | no serious | no serious | no serious | no serious | none | 12/25 | 5/23 | RR 2.22 (0.92 to | 27 more per 100 (from 2 | ⊕⊕⊕⊕ | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | imprecision | | (48%) | (21.7%) | 5.32) | fewer to 94 more) | HIGH | |
| | | | | | | | | 19.6% | | 24 more per 100 (from 2 fewer to 85 more) | | |

[1] Inconclusive effect size
[2] Inconclusive effect size; single study
[3] Single study

## Does the time of day increase the effectiveness of bright light box therapy?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Morning | Afternoon/evening bright light box | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason (overall)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 8/66 (12.1%) | 8/64 (12.5%) | RR 0.98 (0.41 to 2.35) | 0 fewer per 100 (from 7 fewer to 17 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 0% | | 0 fewer per 100 (from 0 fewer to 0 more) | | |
| | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving study early for any reason - SAD** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 8/50 (16%) | 8/49 (16.3%)<br>10% | RR 0.98 (0.41 to 2.35) | 0 fewer per 100 (from 10 fewer to 22 more)<br>0 fewer per 100 (from 6 fewer to 13 more) | ⊕⊕⊕O MODERATE | |
| **Leaving study early for any reason - Subsyndromal SAD** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 0/16 (0%) | 0/15 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕O MODERATE | |
| **Leaving study early due to side effects - Subsyndromal SAD** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 0/16 (0%) | 0/15 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕O MODERATE | |
| **Reported side effects - Subsyndromal SAD** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 1/16 (6.3%) | 2/15 (13.3%) | RR 0.47 (0.05 to 4.65) | 7 fewer per 100 (from 13 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 49 more) | | |
| | | | | | | | | 13.3% | | 7 fewer per 100 (from 13 fewer to 49 more) | | |
| **Mean clinician rated SAD depression scores at endpoint (overall) (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 35 | 33 | - | MD 1.38 lower (5.49 lower to 2.73 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - Subsyndromal SAD (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 16 | 14 | - | MD 0.6 higher (3.89 lower to 5.09 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated SAD depression scores at endpoint - SAD (measured with: SIGH-SAD; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 19 | 19 | - | MD 3.6 lower (8.5 lower to 1.3 higher) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean clinician rated typical depression scores at endpoint (overall) (measured with: HAMD-17/HRSD-31; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 25 | 22 | - | SMD 0.05 lower (0.63 lower to 0.52 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated typical depression scores at endpoint - Subsyndromal SAD (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 16 | 14 | - | SMD 0.15 lower (0.87 lower to 0.57 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated typical depression scores at endpoint - SAD (HRSD-31) (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 9 | 8 | - | SMD 0.12 higher (0.83 lower to 1.07 higher) | ⊕⊕OO LOW | |
| **Mean clinician rated atypical depression scores at endpoint - Subsyndromal SAD (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 16 | 14 | - | MD 1 higher (1.72 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | lower to 3.72 higher) | | |
| **Mean self rated depression scores at endpoint - SAD (measured with: BDI; Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 33 | 32 | - | MD 0.9 lower (4.66 lower to 2.86 higher) | ⊕⊕OO LOW | |
| **Non remission - SAD** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[4] | no serious indirectness | serious[1] | none | 27/50 (54%) | 26/48 (54.2%) | RR 1.00 (0.69 to 1.45) | 0 fewer per 100 (from 17 fewer to 24 more) | ⊕⊕OO LOW | |
| | | | | | | | | 42.5% | | 0 fewer per 100 (from 13 fewer to 19 more) | | |
| **Non response (overall)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[1] | none | 29/66 (43.9%) | 27/63 (42.9%) | RR 1 (0.51 to 1.98) | 0 fewer per 100 (from 21 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 42 more) | | |
| | | | | | | | | 40% | | 0 fewer per 100 (from 20 fewer to 39 more) | | |
| **Non response - SAD** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 24/50 (48%) | 18/48 (37.5%) | RR 1.26 (0.78 to 2.01) | 10 more per 100 (from 8 fewer to 38 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 32.5% | | 8 more per 100 (from 7 fewer to 33 more) | | |
| **Non response - Subsyndromal SAD** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 5/16 (31.3%) | 9/15 (60%) | RR 0.52 (0.23 to 1.2) | 29 fewer per 100 (from 46 fewer to 12 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 60% | | 29 fewer per 100 (from 46 fewer to 12 more) | | |

[1] Inconclusive effect size
[2] Single study

[3] Inconclusive effect size; single study
[4] Significant heterogeneity; random effects model used

## Is dawn simulation effective for depression with a seasonal pattern/SAD?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Dawn simulation | Attentional control | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 2/70 (2.9%) | 10/71 (14.1%) | RR 0.33 (0.05 to 2.22) | 9 fewer per 100 (from 13 fewer to 17 more) | ⊕⊕OO LOW | |
| | | | | | | | | 19.4% | | 13 fewer per 100 (from 18 fewer to 24 more) | | |
| **Leaving study early due to side effects** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 0/31 (0%) | 1/31 (3.2%) | RR 0.33 (0.01 to 7.88) | 2 fewer per 100 (from 3 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 22 more) | | |
| | | | | | | | | 3.2% | | 2 fewer per 100 (from 3 fewer to 22 more) | | |
| **Leaving study early due to lack of efficacy** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 0/45 (0%) | 6/44 (13.6%) | RR 0.14 (0.02 to 1.1) | 12 fewer per 100 (from 13 fewer to 1 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 11.9% | | 10 fewer per 100 (from 12 fewer to 1 more) | | |
| **Reported side effects** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 6/14 (42.9%) | 1/13 (7.7%) | RR 5.57 (0.77 to 40.26) | 35 more per 100 (from 2 fewer to 302 more) | ⊕⊕OO LOW | |
| | | | | | | | | 7.7% | | 35 more per 100 (from 2 fewer to 302 more) | | |
| **Mean clinician rated typical depression scores at endpoint (measured with: HAMD-17/HRSD-21; Better indicated by lower values)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | no serious imprecision | none | 37 | 36 | - | SMD 0.53 lower (1.62 lower to 0.15 higher) | ⊕⊕⊕O MODERATE | |
| **Mean clinician rated atypical depression scores at endpoint (measured with: SAD subscale; Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | very serious[2] | none | 37 | 36 | - | MD 2.20 lower (7.52 lower to 3.11 higher) | ⊕OOO VERY LOW | |
| **Non remission (SIGH-SAD)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[1] | none | 25/56 (44.6%) | 29/58 (50%) | RR 0.9 (0.46 to 1.78) | 5 fewer per 100 (from 27 fewer to 39 more) | ⊕⊕OO LOW | |
| | | | | | | | | 49.9% | | 5 fewer per 100 (from 27 fewer to 39 more) | | |
| **Non response (SIGH-SAD)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 14/56 (25%) | 21/58 (36.2%) | RR 0.71 (34 to 1.48) | 11 fewer per 100 (from 17 more to 1195 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | more) | | |
| | | | | | | | | 36.3% | | 11 fewer per 100 (from 17 more to 1198 more) | | |

[1] Inconclusive effect size

[2] Inconclusive effect size; single study

[3] Significant heterogeneity; random effects model used

## Is dawn simulation more effective than bright light box therapy for depression with a seasonal pattern/SAD?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Bright light box | Dawn simulation | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 5/56 (8.9%) | 1/56 (1.8%) | RR 3.72 (0.62 to 22.22) | 5 more per 100 (from 1 fewer to 38 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 2% | | 5 more per 100 (from 1 fewer to 42 more) | | |
| **Leaving study early due to side effects** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 2/33 (6.1%) | 0% | RR 4.71 (0.23 to 94.31) | 0 more per 1000 (from 0 fewer to 0 more) | | |
| **Leaving study early due to lack of efficacy** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 0/31 (0%) | 0/31 (0%)<br>0% | not pooled | not pooled<br>not pooled | ⊕⊕⊕⊕ HIGH | |
| **Non remission (SIGH-SAD)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | very serious[1] | none | 30/56 (53.6%) | 25/56 (44.6%)<br>46.1% | RR 1.19 (0.7 to 2) | 8 more per 100 (from 13 fewer to 45 more)<br>9 more per 100 (from 14 fewer to 46 more) | ⊕OOO VERY LOW | |
| **Non response (SIGH-SAD)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 20/56 (35.7%) | 14/56 (25%)<br>26.1% | RR 1.45 (0.82 to 2.58) | 11 more per 100 (from 5 fewer to 39 more)<br>12 more per 100 (from 5 fewer to 41 more) | ⊕⊕⊕O MODERATE | |
| **Depression: mean endpoint scores (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 21 | 24 | - | MD 0.9 lower (4 lower to 2.2 higher) | ⊕⊕OO LOW | |
| **SAD: mean endpoint scores (Better indicated by lower values)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 21 | 24 | - | MD 1.8 lower (6.98 lower to 3.38 higher) | ⊕⊕OO LOW | |

[1] Inconclusive effect size
[2] Inconclusive effect size; single study
[3] Significant effect size - random effects model used

## Which therapy is most effective for relapse prevention of depression with a seasonal pattern/SAD?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Relapse prevention | Control | Relative (95% CI) | Absolute | | |
| **Leaving study early for any reason - Bright white light visor vs no treatment control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 4/18 (22.2%) | 1/10 (10%) | RR 2.22 (0.29 to 17.27) | 12 more per 100 (from 7 fewer to 163 more) | ⊕⊕OO LOW | |
| | | | | | | | | 10% | | 12 more per 100 (from 7 fewer to 163 more) | | |
| **Leaving study early for any reason - Bright white light visor vs dim red light visor** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 4/18 (22.2%) | 3/18 (16.7%) | RR 1.33 (0.35 to | 6 more per 100 (from 11 fewer to | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 5.13) | 69 more) | | |
| | | | | | | | | 16.7% | | 6 more per 100 (from 11 fewer to 69 more) | | |
| **Relapse during course of study (BDI>=13 for 2 consecutive wks) - Bright white light visor vs no treatment control** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 9/18 (50%) | 8/10 (80%) | RR 0.63 (0.36 to 1.09) | 30 fewer per 100 (from 51 fewer to 7 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 80% | | 30 fewer per 100 (from 51 fewer to 7 more) | | |
| **Relapse during course of study (BDI>=13 for 2 consecutive wks) - Bright white light visor vs dim red light visor** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 9/18 (50%) | 4/18 (22.2%) | RR 2.25 (0.84 to 5.99) | 28 more per 100 (from 4 fewer to 111 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 22.2% | | 28 more per 100 (from 4 fewer to 111 more) | | |

[1] Inconclusive effect size; single study

[2] Single study

# Non-light therapies for depression with a seasonal pattern/SAD

## Are antidepressants effective in depression with a seasonal pattern/SAD? (Acute phase efficacy data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Acute phase treatment: antidepressants | Control | Relative (95% CI) | Absolute | | |
| **Number not achieving =/> 50% reduction in SIGH-SAD score at endpoint (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 57/129 (44.2%) | 68/126 (54%) | RR 0.82 (0.63 to 1.05) | 10 fewer per 100 (from 20 fewer to 3 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 57.8% | | 10 fewer per 100 (from 21 fewer to 3 more) | | |
| **Number not achieving =/> 50% reduction SIGH-SAD score** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 41/93 (44.1%) | 47/94 (50%) | RR 0.88 (0.65 to 1.2) | 6 fewer per 100 (from 18 fewer to 10 more) | ⊕⊕OO LOW | |
| | | | | | | | | 50% | | 6 fewer | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 100 (from 18 fewer to 10 more) | | |
| **Number not achieving =/> 50% reduction in outcome score at endpoint - Fluoxetine vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 16/36 (44.4%) | 21/32 (65.6%) | RR 0.68 (0.43 to 1.05) | 21 fewer per 100 (from 37 fewer to 3 more) | ⊕⊕OO LOW | |
| | | | | | | | | 65.6% | | 21 fewer per 100 (from 37 fewer to 3 more) | | |
| **Mean endpoint SIGH-SAD (clinician rated) (antidepressants) (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | serious | none | 52 | 47 | - | SMD 0.11 lower (0.65 lower to 0.42 higher) | ⊕⊕OO LOW | |
| **Mean endpoint (clinician rated) (antidepressants) - Moclobemide vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 16 | 15 | - | SMD 0.23 higher (0.48 lower to 0.94 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | higher) | | |
| **Mean endpoint (clinician rated) (antidepressants) - Fluoxetine vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 36 | 32 | - | SMD 0.33 lower (0.81 lower to 0.15 higher) | ⊕⊕OO LOW | |
| **Mean endpoint BDI (self rated) - Fluoxetine vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 36 | 32 | - | MD 1.7 lower (6.53 lower to 3.13 higher) | ⊕⊕OO LOW | |
| **Mean change (clinician rated) - Sertraline vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 93 | 93 | - | MD 4.51 lower (8.23 to 0.79 lower) | ⊕⊕⊕O MODERATE | |
| **Relapse Prevention - Number of patients experiencing a recurrence** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 92/542 (17%) | 153/519 (29.5%) | RR 0.58 (0.46 to 0.72) | 12 fewer per 100 (from 8 fewer to | ⊕⊕⊕⊕ HIGH | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 16 fewer) | | |
| | | | | | | | | 31.9% | | 13 fewer per 100 (from 9 fewer to 17 fewer) | | |

[1] Single study; inconclusive effect size
[2] Significant heterogeneity - random effects model used
[3] Single study

## Are antidepressants effective in depression with a seasonal pattern/SAD? (Acute phase acceptability/tolerability data)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Acute phase acceptability and tolerability (antidepressants) | Placebo | Relative (95% CI) | Absolute | | |
| **Number leaving the study early for any reason (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | very serious[2] | none | 20/109 (18.3%) | 23/112 (20.5%) | RR 0.7 (0.16 to 3.05) | 6 fewer per 100 (from 17 fewer to 42 more) | ⊕OOO VERY LOW | |
| | | | | | | | | 19% | | 6 fewer per 100 (from 16 fewer to 39 more) | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number leaving the study early for any reason - Sertraline vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 20/93 (21.5%) | 20/94 (21.3%)<br>21.3% | RR 1.01 (0.58 to 1.75) | 0 more per 100 (from 9 fewer to 16 more)<br>0 more per 100 (from 9 fewer to 16 more) | ⊕⊕OO LOW | |
| **Number leaving the study early for any reason - Moclobemide vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 0/16 (0%) | 3/18 (16.7%)<br>16.7% | RR 0.16 (0.01 to 2.87) | 14 fewer per 100 (from 17 fewer to 31 more)<br>14 fewer per 100 (from 17 fewer to 31 more) | ⊕⊕OO LOW | |
| **Number leaving the study early due to side effects** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 12/145 (8.3%) | 8/144 (5.6%)<br>5.3% | RR 1.48 (0.63 to 3.47) | 3 more per 100 (from 2 fewer to 14 more)<br>3 more | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 100 (from 2 fewer to 13 more) | | |
| **Number leaving the study early due to side effects - Sertraline vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 10/93 (10.8%) | 5/94 (5.3%) | RR 2.02 (0.72 to 5.69) | 5 more per 100 (from 1 fewer to 25 more) | ⊕⊕OO LOW | |
| | | | | | | | | 5.3% | | 5 more per 100 (from 1 fewer to 25 more) | | |
| **Number leaving the study early due to side effects - Moclobemide vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 0/16 (0%) | 2/18 (11.1%) | RR 0.22 (0.01 to 4.34) | 9 fewer per 100 (from 11 fewer to 37 more) | ⊕⊕OO LOW | |
| | | | | | | | | 11.1% | | 9 fewer per 100 (from 11 fewer to 37 more) | | |
| **Number leaving the study early due to side effects - Fluoxetine vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 2/36 (5.6%) | 1/32 (3.1%) | RR 1.78 (0.17 to | 2 more per 100 (from 3 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 18.69) | fewer to 55 more) | | |
| | | | | | | | | 3.1% | | 2 more per 100 (from 3 fewer to 55 more) | | |
| **Number reporting side effects - Sertraline vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 76/93 (81.7%) | 47/94 (50%) | RR 1.63 (1.31 to 2.04) | 31 more per 100 (from 15 more to 52 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 50% | | 31 more per 100 (from 15 more to 52 more) | | |
| **Number reporting side effects - Fluoxetine vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 35/36 (97.2%) | 29/32 (90.6%) | RR 1.07 (0.95 to 1.21) | 6 more per 100 (from 5 fewer to 19 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 90.6% | | 6 more per 100 (from 5 fewer to 19 more) | | |

[1] Significant heterogeneity - random effects model used
[2] Inconclusive effect size
[3] Single study; inconclusive effect size
[4] Single study

## Which antidepressant is more effective in depression with a seasonal pattern/SAD?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Acute phase treatment: antidepressants | Active control | Relative (95% CI) | Absolute | | |
| **Number not achieving =/> 50% reduction in SIGH-SAD score at endpoint - High ion density vs Low ion density** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 5/12 (41.7%) | 11/13 (84.6%) | RR 0.49 (0.24 to 1) | 43 fewer per 100 (from 64 fewer to 0 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 84.6% | | 43 fewer per 100 (from 64 fewer to 0 more) | | |
| **Mean endpoint SIGH-SAD (clinician rated) - Moclobemide vs Fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 11 | 18 | - | MD 1.6 lower | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | (7.01 lower to 3.81 higher) | | |

[1] Single study; inconclusive effect size

## Is continuation treatment effective for depression with a seasonal pattern/SAD?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Continuation treatment | Control | Relative (95% CI) | Absolute | | |
| **Mean endpoint HAMD-21 (clinician-rated) - Propanolol vs Placebo (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 12 | 11 | - | MD 7 lower (11.24 to 2.76 lower) | ⊕⊕⊕O MODERATE | |
| **Number leaving the study early for any reason - Propanolol vs Placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 1/13 (7.7%) | 0/11 (0%)<br>0% | RR 2.57 (0.12 to 57.44) | 0 more per 100 (from 0 fewer to 0 more)<br>0 more per 100 (from 0 fewer to 0 more) | ⊕⊕OO LOW | |

[1] Single study
[2] Single study; inconclusive effect size

Is relapse prevention effective for depression with a seasonal pattern/SAD? (Buspirone versus placebo)

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Buspirone-preven-tion | Placebo | Relative (95% CI) | Absolute | | |
| **Relapse Prevention - Number of patients experiencing a recurrence** | | | | | | | | | | | | |
| 3 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 92/542 (17%) | 153/519 (29.5%) | RR 0.58 (0.46 to 0.72) | 12 fewer per 100 (from 8 fewer to -16 fewer) | ⊕⊕⊕⊕HIGH | |
| | | | | | | | | 31.9% | | 13 fewer per 100 | | |

# Next-step treatments

## Is dose escalation effective for depression that has not adequately responded to treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Dose escalation | Control | Relative (95% CI) | Absolute | | |
| **Mean depression scores (overall) (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 228 | 215 | - | SMD 0.11 lower (0.29 lower to 0.08 higher) | ⊕⊕⊕⊕ HIGH | |
| **Mean depression scores - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 130 | 118 | - | SMD 0.01 lower (0.26 lower to 0.24 higher) | ⊕⊕⊕O MODERATE | |
| **Mean depression scores - Same-dose sertraline (100mg) vs high-dose sertraline (200mg) (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 98 | 97 | - | SMD 0.22 lower (0.51 lower to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 0.06 higher) | | |
| **Number not achieving remission (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 154/230 (67%) | 158/222 (71.2%)<br>71.2% | RR 0.94 (0.83 to 1.06) | 4 fewer per 100 (from 12 fewer to 4 more)<br>4 fewer per 100 (from 12 fewer to 4 more) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving remission - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 92/131 (70.2%) | 88/124 (71%)<br>71% | RR 0.99 (0.84 to 1.16) | 1 fewer per 100 (from 11 fewer to 11 more)<br>1 fewer per 100 (from 11 fewer to 11 more) | ⊕⊕⊕O MODERATE | |
| **Number not achieving remission - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 62/99 (62.6%) | 70/98 (71.4%)<br>71.4% | RR 0.88 (0.72 to 1.07) | 9 fewer per 100 (from 20 fewer to 5 more)<br>9 fewer per 100 (from 20 fewer to 5 more) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number not achieving response (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[4] | none | 103/230 (44.8%) | 121/222 (54.5%)<br>53.6% | RR 0.8 (0.59 to 1.1) | 11 fewer per 100 (from 22 fewer to 5 more)<br>11 fewer per 100 (from 22 fewer to 5 more) | ⊕⊕OO LOW | |
| **Number not achieving response - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 73/131 (55.7%) | 76/124 (61.3%)<br>61.3% | RR 0.91 (0.74 to 1.12) | 6 fewer per 100 (from 16 fewer to 7 more)<br>6 fewer per 100 (from 16 fewer to 7 more) | ⊕⊕OO LOW | |
| **Number not achieving response - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 30/99 (30.3%) | 45/98 (45.9%)<br>45.9% | RR 0.66 (0.46 to 0.95) | 16 fewer per 100 (from 2 fewer to 25 fewer)<br>16 fewer per 100 (from 2 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 25 fewer) | | |
| **Leaving treatment early for any reason (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 36/230 (15.7%) | 49/222 (22.1%)<br>21.4% | RR 0.7 (0.48 to 1.04) | 7 fewer per 100 (from 11 fewer to 1 more)<br>6 fewer per 100 (from 11 fewer to 1 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early for any reason - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 26/131 (19.8%) | 34/124 (27.4%)<br>27.4% | RR 0.72 (0.46 to 1.13) | 8 fewer per 100 (from 15 fewer to 4 more)<br>8 fewer per 100 (from 15 fewer to 4 more) | ⊕⊕⊕O MODERATE | |
| **Leaving treatment early for any reason - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 10/99 (10.1%) | 15/98 (15.3%)<br>15.3% | RR 0.66 (0.31 to 1.4) | 5 fewer per 100 (from 11 fewer to 6 more)<br>5 fewer per 100 (from 11 fewer to 6 more) | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving treatment early due to side effects (overall)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 12/230 (5.2%) | 12/223 (5.4%)<br>5.4% | RR 0.97 (0.45 to 2.11) | 0 fewer per 100 (from 3 fewer to 6 more)<br>0 fewer per 100 (from 3 fewer to 6 more) | ⊕⊕OO LOW | |
| **Leaving treatment early due to side effects - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 6/131 (4.6%) | 7/124 (5.6%)<br>5.7% | RR 0.81 (0.28 to 2.35) | 1 fewer per 100 (from 4 fewer to 8 more)<br>1 fewer per 100 (from 4 fewer to 8 more) | ⊕⊕OO LOW | |
| **Leaving treatment early due to side effects - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 6/99 (6.1%) | 5/99 (5.1%)<br>5.1% | RR 1.2 (0.38 to 3.8) | 1 more per 100 (from 3 fewer to 14 more)<br>1 more per 100 (from 3 fewer to 14 more) | ⊕⊕OO LOW | |
| **Leaving treatment early due to lack of efficacy - Same or increased-dose duloxetine 60mg vs high-dose duloxetine 120mg** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 5/131 (3.8%) | 10/124 (8.1%)<br>8.1% | RR 0.47 (0.17 to 1.35) | 4 fewer per 100 (from 7 fewer to 3 more)<br>4 fewer per 100 (from 7 fewer to 3 more) | ⊕⊕OO LOW | |
| **Number reporting side effects - Same-dose sertraline (100mg) vs high-dose sertraline (200mg)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 45/99 (45.5%) | 54/98 (55.1%)<br>55.1% | RR 0.82 (0.62 to 1.09) | 10 fewer per 100 (from 21 fewer to 5 more)<br>10 fewer per 100 (from 21 fewer to 5 more) | ⊕⊕OO LOW | |

[1] Single study
[2] Significant heterogeneity - random effects model used
[3] Inconclusive effect size
[4] Single study; inconclusive effect size

## Is switching antidepressants effective for depression that has not adequately responded to treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other | Switching: | Switching | Relative | Absolute | | |

| studies | | | | | | considerations | continuing AD | | (95% CI) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number not achieving response - Nortriptyline vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 21/68 (30.9%) | 41/142 (28.9%)<br>28.9% | RR 1.07 (0.69 to 1.66) | 2 more per 100 (from 9 fewer to 19 more)<br>2 more per 100 (from 9 fewer to 19 more) | ⊕⊕OO LOW | |
| **Number not achieving response - Fluoxetine vs mianserin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 24/38 (63.2%) | 18/34 (52.9%)<br>52.9% | RR 1.19 (0.8 to 1.78) | 10 more per 100 (from 11 fewer to 41 more)<br>10 more per 100 (from 11 fewer to 41 more) | ⊕⊕OO LOW | |
| **Number not achieving response - Venlafaxine vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[1] | none | 46/59 (78%) | 50/60 (83.3%) | RR 0.94 (0.78 to 1.12) | 5 fewer per 100 (from 18 fewer to 10 more) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 83.3% | | 5 fewer per 100 (from 18 fewer to 10 more) | | |
| **Number not achieving remission - Nortriptyline vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 12/68 (17.6%) | 19/142 (13.4%) | RR 1.32 (0.68 to 2.56) | 4 more per 100 (from 4 fewer to 21 more) | ⊕⊕OO LOW | |
| | | | | | | | | 13.4% | | 4 more per 100 (from 4 fewer to 21 more) | | |
| **Number not achieving remission - Fluoxetine vs mianserin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 31/38 (81.6%) | 22/34 (64.7%) | RR 1.26 (0.94 to 1.69) | 17 more per 100 (from 4 fewer to 45 more) | ⊕⊕OO LOW | |
| | | | | | | | | 64.7% | | 17 more per 100 (from 4 fewer to 45 more) | | |
| **Number not achieving remission - Venlafaxine vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 30/59 (50.8%) | 41/60 (68.3%) | RR 0.74 (0.55 to 1.01) | 18 fewer per 100 (from 31 fewer to 1 | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | more) | | |
| | | | | | | | | 68.3% | | 18 fewer per 100 (from 31 fewer to 1 more) | | |
| **Other comparisons: mean endpoint scores (self-rated) - Nortriptyline vs fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 68 | 142 | - | MD 1.05 higher (1.31 lower to 3.41 higher) | ⊕⊕⊕O MODERATE | |
| **Other comparisons: mean endpoint scores (self-rated) - Fluoxetine vs mianserin (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 38 | 33 | - | MD 1.8 higher (1.63 lower to 5.23 higher) | ⊕⊕OO LOW | |
| **Other comparisons: mean endpoint scores (self-rated) - Venlafaxine vs fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 59 | 60 | - | MD 2.03 lower (5.22 lower to 1.16 higher) | ⊕⊕OO LOW | |
| **Other comparisons: number leaving treatment early for any reason - Nortriptyline vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised | no serious | no serious | no serious | very | none | 8/68 | 28/142 | RR 0.6 | 8 fewer per | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | serious[1] | | (11.8%) | (19.7%)<br><br>19.7% | (0.29 to 1.24) | 100 (from 14 fewer to 5 more)<br><br>8 fewer per 100 (from 14 fewer to 5 more) | LOW | |
| **Other comparisons: number leaving treatment early for any reason - Venlafaxine versus fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 15/59 (25.4%) | 12/60 (20%)<br><br>20% | RR 1.27 (0.65 to 2.48) | 5 more per 100 (from 7 fewer to 30 more)<br><br>5 more per 100 (from 7 fewer to 30 more) | ⊕⊕OO LOW | |
| **Other comparisons: number leaving treatment early because of side effects - Nortriptyline vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 2/68 (2.9%) | 4/142 (2.8%)<br><br>2.9% | RR 1.04 (0.2 to 5.56) | 0 more per 100 (from 2 fewer to 13 more)<br><br>0 more per 100 (from 2 fewer to 13 more) | ⊕⊕OO LOW | |
| **Other comparisons: number leaving treatment early because of side effects - Fluoxetine continuation vs mianserin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 7/38 (18.4%) | 12/34 (35.3%) | RR 0.52 (0.23 to | 17 fewer per 100 | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.17) | (from 27 fewer to 6 more) | LOW | |
| | | | | | | | | 35.3% | | 17 fewer per 100 (from 27 fewer to 6 more) | | |
| **Other comparisons: number leaving treatment early because of side effects - Venlafaxine vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 1/59 (1.7%) | 3/60 (5%) | RR 0.34 (0.04 to 3.17) | 3 fewer per 100 (from 5 fewer to 11 more) | ⊕⊕OO LOW | |
| | | | | | | | | 5% | | 3 fewer per 100 (from 5 fewer to 11 more) | | |
| **Other comparisons: number reporting side effects - Nortriptyline vs fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 58/68 (85.3%) | 119/142 (83.8%) | RR 0.98 (0.87 to 1.11) | 2 fewer per 100 (from 11 fewer to 9 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 85.3% | | 2 fewer per 100 (from 11 fewer to 9 more) | | |

[1] Single study; inconclusive effect size

[2] Single study

## Which switching regimen is most effective – switching to single or combination drugs?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Switching: switching to single or combination drugs | Control | Relative (95% CI) | Absolute | | |
| **Switch to venlafaxine vs switch to another antidepressant (efficacy) - Non-response** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 157/255 (61.6%) | 173/264 (65.5%) | RR 0.91 (0.73 to 1.14) | 6 fewer per 100 (from 18 fewer to 9 more) | ⊕⊕OO LOW | |
| | | | | | | | | 67.4% | | 6 fewer per 100 (from 18 fewer to 9 more) | | |
| **Switch to venlafaxine vs switch to another antidepressant (efficacy) - Non-remission** | | | | | | | | | | | | |
| 2 | randomised | no serious | serious[1] | no serious | serious[2] | none | 133/255 | 144/264 | RR 0.91 | 5 fewer | ⊕⊕OO | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | | indirectness | | | (52.2%) | (54.5%) | (0.67 to 1.24) | per 100 (from 18 fewer to 13 more) | LOW | |
| | | | | | | | | 64.2% | | 6 fewer per 100 (from 21 fewer to 15 more) | | |
| **Switch to venlafaxine vs switch to another antidepressant (efficacy) - versus SSRI (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 194 | 202 | - | MD 0.5 lower (2.09 lower to 1.09 higher) | ⊕⊕⊕O MODERATE | |
| **Switch to venlafaxine vs switch to another antidepressant (acceptability/tolerability) - Number reporting side effects** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 157/260 (60.4%) | 169/266 (63.5%) | RR 0.95 (0.83 to 1.09) | 3 fewer per 100 (from 11 fewer to 6 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 63.7% | | 3 fewer per 100 (from 11 fewer to 6 more) | | |
| **Switch to venlafaxine vs switch to another antidepressant (acceptability/tolerability) - Leaving treatment early for any reason** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 58/261 (22.2%) | 50/268 (18.7%)<br>16.1% | RR 1.19 (0.85 to 1.67) | 4 more per 100 (from 3 fewer to 13 more)<br>3 more per 100 (from 2 fewer to 11 more) | ⊕⊕OO LOW | |
| **Switch to venlafaxine vs switch to another antidepressant (acceptability/tolerability) - Leaving treatment early due to side effects** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 16/261 (6.1%) | 14/268 (5.2%)<br>5.1% | RR 1.17 (0.58 to 2.36) | 1 more per 100 (from 2 fewer to 7 more)<br>1 more per 100 (from 2 fewer to 7 more) | ⊕⊕OO LOW | |
| **Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine - non-response** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 183/389 (47%) | 82/202 (40.6%)<br>48.6% | RR 0.88 (0.74 to 1.05) | 5 fewer per 100 (from 11 fewer to 2 more)<br>6 fewer per 100 (from 13 fewer to 2 more) | ⊕⊕⊕O MODERATE | |
| **Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine - non-remission** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | very serious[2] | none | 209/389 (53.7%) | 69/202 (34.2%)<br><br>48.4% | RR 1 (0.69 to 1.47) | 0 fewer per 100 (from 11 fewer to 16 more)<br><br>0 fewer per 100 (from 15 fewer to 23 more) | ⊕OOO VERY LOW | |
| **Switch to augmentation strategy vs switch to single drug: efficacy outcomes - Fluoxetine + olanzapine vs fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 389 | 202 | - | MD 1.13 lower (3.22 lower to 0.97 higher) | ⊕⊕OO LOW | |
| **Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - leaving treatment early for any reason** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 90/389 (23.1%) | 40/202 (19.8%)<br><br>19.9% | RR 1.12 (0.79 to 1.59) | 2 more per 100 (from 4 fewer to 12 more)<br><br>2 more per 100 (from 4 fewer to 12 more) | ⊕⊕OO LOW | |
| **Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - leaving treatment early due to** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **side effects** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 39/389 (10%) | 7/202 (3.5%)<br>3.9% | RR 2.41 (1.07 to 5.43) | 5 more per 100 (from 0 more to 15 more)<br>5 more per 100 (from 0 more to 17 more) | ⊕⊕⊕⊕ HIGH | |
| **Switch to augmentation strategy vs switch to single drug: acceptability/tolerability - Fluoxetine + olanzapine vs fluoxetine - number reporting side effects** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 129/146 (88.4%) | 119/142 (83.8%)<br>83.8% | RR 1.05 (0.96 to 1.16) | 4 more per 100 (from 3 fewer to 13 more)<br>4 more per 100 (from 3 fewer to 13 more) | ⊕⊕⊕O MODERATE | |

[1] Significant heterogeneity - random effects model used
[2] Inconclusive effect size
[3] Single study

## Should SSRIs or TCAs be used as first- or second-line treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Switching: switching to single drug (randomised first-step drug) | Control | Relative (95% CI) | Absolute | Quality | Importance |
| **Switching strategies: Number of people not achieving at least 50% reduction in depression score - Sertraline to imipramine vs imipramine to sertraline** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 65/117 (55.6%) | 21/51 (41.2%) | RR 1.35 (0.94 to 1.95) | 14 more per 100 (from 2 fewer to 39 more) | ⊕⊕OO LOW | |
| | | | | | | | | 41.2% | | 14 more per 100 (from 2 fewer to 39 more) | | |
| **Switching strategies: Mean endpoint scores - Sertraline to imipramine vs imipramine to sertraline (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[1] | none | 117 | 50 | - | MD 2.5 higher (0.38 lower to 5.38 higher) | ⊕⊕OO LOW | |

| Switching strategies: Leaving the study early - Sertraline to imipramine vs imipramine to sertraline | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 29/117 (24.8%) | 5/51 (9.8%) | RR 2.53 (1.04 to 6.16) | 15 more per 100 (from 0 more to 51 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 9.8% | | 15 more per 100 (from 0 more to 51 more) | | |

[1] Single study; inconclusive effect size

[2] Single study

## Is augmenting existing antidepressant treatment with another antidepressant effective for depression that has not adequately responded to treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Augmentation: Antidepressant +Antidepressant | Antidepressant + (placebo or nothing) | Relative (95% CI) | Absolute | | |
| **Number not achieving response - SSRIs + Mianserin** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 49/141 (34.8%) | 65/149 (43.6%) | RR 0.71 (0.44 to 1.17) | 13 fewer per 100 (from 24 fewer to 7 more) | ⊕⊕OO LOW | |
| | | | | | | | | 63.2% | | 18 fewer per 100 (from 35 fewer to 11 more) | | |
| **Number not achieving response - Sertraline + mianserin vs high dose sertraline + placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 32/98 (32.7%) | 45/98 (45.9%) | RR 0.71 (0.5 to 1.02) | 13 fewer per 100 (from 23 fewer to 1 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 45.9% | | 13 fewer per 100 (from 23 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | fewer to 1 more) | | |
| **Number not achieving response - Antidepressants + Mirtazapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 4/11 (36.4%) | 12/15 (80%) | RR 0.45 (0.2 to 1.03) | 44 fewer per 100 (from 64 fewer to 2 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 80% | | 44 fewer per 100 (from 64 fewer to 2 more) | | |
| **Number not achieving remission - SSRIs + Mianserin** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 73/130 (56.2%) | 93/137 (67.9%) | RR 0.81 (0.62 to 1.04) | 13 fewer per 100 (from 26 fewer to 3 more) | ⊕⊕OO LOW | |
| | | | | | | | | 72.1% | | 14 fewer per 100 (from 27 fewer to 3 more) | | |
| **Number not achieving remission - Antidepressants + Mirtazapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[4] | none | 6/11 (54.5%) | 13/15 (86.7%) | RR 0.63 (0.35 to 1.12) | 32 fewer per 100 (from 56 fewer to | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 10 more) | | |
| | | | | | | | | 86.7% | | 32 fewer per 100 (from 56 fewer to 10 more) | | |
| **Number not achieving remission - Sertraline + mianserin vs high dose sertraline + placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 55/98 (56.1%) | 70/98 (71.4%) | RR 0.79 (0.63 to 0.97) | 15 fewer per 100 (from 2 fewer to 26 fewer) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 71.4% | | 15 fewer per 100 (from 2 fewer to 26 fewer) | | |
| **Number not achieving remission - Fluoxetine + desipramine vs high dose fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 33/46 (71.7%) | 26/48 (54.2%) | RR 1.32 (0.96 to 1.81) | 17 more per 100 (from 2 fewer to 44 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 52.1% | | 17 more per 100 (from 2 fewer to 42 more) | | |
| | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean endpoint or change scores - SSRIs + Mianserin (Better indicated by lower values)** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 141 | 147 | - | SMD 0.46 lower (1.07 lower to 0.15 higher) | ⊕⊕OO LOW | |
| **Mean endpoint or change scores - Fluoxetine + desipramine vs high dose fluoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | serious[2] | none | 46 | 48 | - | SMD 0.67 higher (0.05 to 1.28 higher) | ⊕⊕OO LOW | |
| **Mean endpoint or change scores - Antidepressants + Mirtazapine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 11 | 15 | - | SMD 0.83 lower (1.64 to 0.01 lower) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint or change scores - Amitriptyline + Moclobemide (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 20 | 19 | - | SMD 0.63 lower (1.28 lower to 0.01 higher) | ⊕⊕⊕O MODERATE | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean endpoint or change scores - Antidepressant + atomoxetine (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 70 | 71 | - | SMD 0.23 lower (0.56 lower to 0.1 higher) | ⊕⊕⊕O MODERATE | |
| **Leaving the study early - SSRIs + Mianserin** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 23/130 (17.7%) | 17/137 (12.4%) | RR 1.44 (0.81 to 2.58) | 5 more per 100 (from 2 fewer to 20 more) | ⊕⊕OO LOW | |
| | | | | | | | | 14.3% | | 6 more per 100 (from 3 fewer to 23 more) | | |
| **Leaving the study early - Fluoxetine + desipramine vs high dose fluoxetine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 8/46 (17.4%) | 5/48 (10.4%) | RR 1.71 (0.61 to 4.83) | 7 more per 100 (from 4 fewer to 40 more) | ⊕⊕OO LOW | |
| | | | | | | | | 11.2% | | 8 more per 100 (from 4 fewer to 43 more) | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Leaving the study early - Antidepressants + Mirtazapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 1/11 (9.1%) | 2/15 (13.3%)<br>13.3% | RR 0.68 (0.07 to 6.61) | 4 fewer per 100 (from 12 fewer to 75 more)<br>4 fewer per 100 (from 12 fewer to 75 more) | ⊕⊕OO LOW | |
| **Leaving the study early - Antidepressant + buspirone** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 7/54 (13%) | 9/54 (16.7%)<br>16.7% | RR 0.78 (0.31 to 1.94) | 4 fewer per 100 (from 12 fewer to 16 more)<br>4 fewer per 100 (from 12 fewer to 16 more) | ⊕⊕OO LOW | |
| **Leaving the study early - Sertraline + mianserin vs high dose sertraline + placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 17/98 (17.3%) | 15/98 (15.3%)<br>15.3% | RR 1.13 (0.6 to 2.14) | 2 more per 100 (from 6 fewer to 17 more)<br>2 more | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | per 100 (from 6 fewer to 17 more) | | |
| **Leaving the study early - Antidepressant + atomoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 13/72 (18.1%) | 13/74 (17.6%) | RR 1.03 (0.51 to 2.06) | 1 more per 100 (from 9 fewer to 19 more) | ⊕⊕OO LOW | |
| | | | | | | | | 17.6% | | 1 more per 100 (from 9 fewer to 19 more) | | |
| **Leaving the study early due to side effects - SSRIs + Mianserin** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 9/130 (6.9%) | 6/137 (4.4%) | RR 1.52 (0.58 to 3.96) | 2 more per 100 (from 2 fewer to 13 more) | ⊕⊕OO LOW | |
| | | | | | | | | 3% | | 2 more per 100 (from 1 fewer to 9 more) | | |
| **Leaving the study early due to side effects - Fluoxetine + desipramine vs high dose fluoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 2/12 (16.7%) | 0/15 (0%) | RR 6.15 (0.32 to | 0 more per 100 (from 0 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 117.21) | fewer to 0 more) | | |
| | | | | | | | | 0% | | 0 more per 100 (from 0 fewer to 0 more) | | |
| **Leaving the study early due to side effects - Antidepressant + atomoxetine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[4] | none | 7/72 (9.7%) | 4/74 (5.4%) | RR 1.8 (0.55 to 5.88) | 4 more per 100 (from 2 fewer to 26 more) | ⊕⊕OO LOW | |
| | | | | | | | | 5.4% | | 4 more per 100 (from 2 fewer to 26 more) | | |
| **Patients reporting side effects - SSRIs + Mianserin** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[3] | none | 75/98 (76.5%) | 45/99 (45.5%) | RR 1.68 (1.32 to 2.14) | 31 more per 100 (from 15 more to 52 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 45.5% | | 31 more per 100 (from 15 more to 52 more) | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Patients reporting side effects - Sertraline + mianserin vs high dose sertraline + placebo** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 75/98 (76.5%) | 54/98 (55.1%) | RR 1.39 (1.13 to 1.71) | 21 more per 100 (from 7 more to 39 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 55.1% | | 21 more per 100 (from 7 more to 39 more) | | |

[1] Significant heterogeneity - random effects model used
[2] Inconclusive effect size
[3] Single study
[4] Single study; inconclusive effect size

## Is augmenting existing antidepressant treatment with an antipsychotic effective for depression that has not adequately responded to treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Augmentation: Antidepressant + Antipsychotic | Antidepressant + (placebo or nothing) | Relative (95% CI) | Absolute | | |
| **Number not achieving response** | | | | | | | | | | | | |
| 9 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 557/866 (64.3%) | 72.4% | RR 0.88 (0.82 to 0.95) | 87 fewer per 1000 (from 36 fewer to 130 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving response - Aripiprazole** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | no serious imprecision | none | 251/372 (67.5%) | 71.8% | RR 0.94 (0.81 to 1.1) | 43 fewer per 1000 (from 136 fewer to 72 more) | ⊕⊕⊕O MODERATE | |
| **Number not achieving response - Olanzapine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 124/210 (59%) | 71.2% | RR 0.81 (0.67 to 1) | 135 fewer per 1000 (from 235 fewer to 0 | ⊕⊕OO LOW | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | more) | | |
| **Number not achieving response - Risperidone** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 167/255 (65.5%) | 75.2% | RR 0.86 (0.77 to 0.97) | 105 fewer per 1000 (from 23 fewer to 173 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving response - Quetiapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[3] | none | 15/29 (51.7%) | 72.4% | RR 0.71 (0.47 to 1.08) | 210 fewer per 1000 (from 384 fewer to 58 more) | ⊕⊕OO LOW | |
| **Number not achieving remission** | | | | | | | | | | | | |
| 8 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 640/857 (74.7%) | 84.2% | RR 0.88 (0.84 to 0.92) | 101 fewer per 1000 (from 67 fewer to 135 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving remission - Aripiprazole** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 278/372 (74.7%) | 84.8% | RR 0.88 (0.82 to 0.95) | 102 fewer per 1000 (from 42 fewer to | ⊕⊕⊕⊕ HIGH | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 153 fewer) | | |
| **Number not achieving remission - Olanzapine** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 146/200 (73%) | 83.5% | RR 0.87 (0.79 to 0.97) | 109 fewer per 1000 (from 25 fewer to 175 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving remission - Risperidone** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 196/256 (76.6%) | 84% | RR 0.88 (0.81 to 0.96) | 101 fewer per 1000 (from 34 fewer to 160 fewer) | ⊕⊕⊕⊕ HIGH | |
| **Number not achieving remission - Quetiapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 20/29 (69%) | 82.8% | RR 0.83 (0.62 to 1.12) | 141 fewer per 1000 (from 315 fewer to 99 more) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint (Better indicated by lower values)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 568 | 578 | - | SMD 0.45 lower (0.62 to 0.28 lower) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint - Aripiprazole (Better indicated by lower values)** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 185 | 184 | - | SMD 0.32 lower (0.53 to 0.12 lower) | ⊕⊕⊕O MODERATE | |
| **Mean endpoint - Olanzapine (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[3] | no serious indirectness | serious[2] | none | 198 | 203 | - | SMD 0.35 lower (0.77 lower to 0.07 higher) | ⊕⊕OO LOW | |
| **Mean endpoint - Risperidone (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 156 | 162 | - | SMD 0.56 lower (0.78 to 0.33 lower) | ⊕⊕⊕⊕ HIGH | |
| **Mean endpoint - Quetiapine (Better indicated by lower values)** | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 29 | 29 | - | SMD 0.77 lower (1.3 to 0.23 lower) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 121/626 (19.3%) | 18.6% | RR 1.19 (0.93 to 1.51) | 35 more per 1000 (from 13 fewer to 95 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason - Aripiprazole** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 22/182 (12.1%) | 9.3% | RR 1.3 (0.71 to 2.39) | 28 more per 1000 (from 27 fewer to 129 more) | ⊕⊕OO LOW | |
| **Number leaving treatment early for any reason - Olanzapine** | | | | | | | | | | | | |
| 3 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 53/210 (25.2%) | 20.2% | RR 1.29 (0.9 to 1.84) | 59 more per 1000 (from 20 fewer to 170 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early for any reason - Risperidone** | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | no serious limitations | serious[2] | no serious indirectness | very serious[2] | none | 35/205 (17.1%) | 15.1% | RR 1.21 (0.64 to 2.29) | 32 more per 1000 (from 54 fewer to 195 more) | ⊕OOO VERY LOW | |
| **Number leaving treatment early for any reason - Quetiapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 11/29 (37.9%) | 48.3% | RR 0.79 (0.43 to 1.43) | 101 fewer per 1000 (from 275 fewer to 208 more) | ⊕⊕OO LOW | |
| **Number leaving treatment early due to side effects** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | serious[2] | no serious indirectness | no serious imprecision | none | 64/807 (7.9%) | 2.3% | RR 2.43 (1.18 to 5.03) | 33 more per 1000 (from 4 more to 93 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early due to side effects - Aripiprazole** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 13/373 (3.5%) | 1.7% | RR 2.01 (0.76 to 5.33) | 17 more per 1000 (from 4 fewer to 74 more) | ⊕⊕⊕O MODERATE | |
| **Number leaving treatment early due to side effects - Olanzapine** | | | | | | | | | | | | |
| 2 | randomised | no serious | no serious | no serious | no serious | none | 27/200 (13.5%) | 2.4% | RR 5.53 (2.17 to | 109 more per 1000 | ⊕⊕⊕⊕ | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | limitations | inconsistency | indirectness | imprecision | | | | 14.08) | (from 28 more to 314 more) | HIGH | |
| **Number leaving treatment early due to side effects - Risperidone** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | serious[2] | none | 16/205 (7.8%) | 11.7% | RR 1.13 (0.27 to 4.74) | 15 more per 1000 (from 85 fewer to 438 more) | ⊕⊕OO LOW | |
| **Number leaving treatment early due to side effects - Quetiapine** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 8/29 (27.6%) | 6.9% | RR 4 (0.93 to 17.25) | 207 more per 1000 (from 5 fewer to 1121 more) | ⊕⊕OO LOW | |
| **Number reporting side effects - Aripiprazole** | | | | | | | | | | | | |
| 1 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 19/30 (63.3%) | 56.7% | RR 1.12 (0.74 to 1.69) | 68 more per 1000 (from 147 fewer to 391 more) | ⊕⊕OO LOW | |
| **Number reporting side effects - Risperidone** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | very serious[2] | none | 129/199 (64.8%) | 67.9% | RR 1.11 (0.94 to | 75 more per 1000 (from 41 | ⊕⊕OO LOW | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 1.31) | fewer to 210 more) | | |

[1] Significant heterogeneity - random effects model used

[2] Inconclusive effect size

[3] Single study

Is augmenting existing antidepressant treatment with another psychotropic drug effective for depression that has not adequately responded to treatment?

| Quality assessment | | | | | | | Summary of findings | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Augmentation: AD + other psychotropic drug | AD + (placebo or nothing) | Relative (95% CI) | Absolute | Quality | Importance |
| **Number not achieving response - Antidpressants + lithium** | | | | | | | | | | | | |
| 6 | randomised trial | no serious limitations | serious[1] | no serious indirectness | no serious imprecision[2] | none | 56/87 (64.4%) | 68/86 (79.1%)<br>81.8% | RR 0.83 (0.66 to 1.03) | 13 fewer per 100 (from 27 fewer to 2 more)<br>13 fewer per 100 | ⊕⊕⊕OMODERATE | |
| **Number not achieving remission - Antidepressants + lithium** | | | | | | | | | | | | |
| 3 | randomised trial | no serious limitations | serious2 | no serious indirectness | serious3 | none | 57/107 (53.3%) | 53/109 (48.6%)<br>53.3% | RR 1.26 (0.72 to 2.17) | 13 more per 100 (from 14 fewer to 57 more)<br>13 more per 100 | ⊕⊕OOLOW | |
| **Number not achieving remission - Antidepressants + atomoxetine** | | | | | | | | | | | | |
| 1 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | very serious4 | none | 43/72 (59.7%) | 36/74 (48.6%)<br>48.7% | RR 1.23 (0.91 to 1.66) | 11 more per 100 (from -4 fewer to 32 more)<br>11 more per 100 | ⊕⊕OOLOW | |
| **Mean endpoint or change scores - Antidepressants + lithium (range of scores: Better indicated by less)** | | | | | | | | | | | | |
| 7 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 135 | 138 | - | SMD -0.32 (-0.56 to -0.08) | ⊕⊕⊕⊕HIGH | |
| **Mean endpoint or change scores - Antidepressants + atomoxetine (range of scores: Better indicated by less)** | | | | | | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | very serious4 | none | 70 | 71 | - | SMD -0.23 (-0.56 to 0.1) | ⊕⊕OOLOW |
| **Leaving the study early - Antidepressants + lithium** | | | | | | | | | | | |
| 8 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 55/178 (30.9%) | 31/178 (17.4%)<br>9.8% | RR 1.79 (1.23 to 2.6) | 14 more per 100 (from 4 more to 28 more)<br>7 more per 100 | ⊕⊕⊕⊕HIGH |
| **Leaving the study early - Antidepressants + atomoxetine** | | | | | | | | | | | |
| 1 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | very serious4 | none | 13/72 (18.1%) | 13/74 (17.6%)<br>17.6% | RR 1.03 (0.51 to 2.06) | 1 more per 100 (from -9 fewer to 19 more)<br>0 more per 100 | ⊕⊕OOLOW |
| **Leaving the study early due to side effects - Antidepressants + atomoxetine** | | | | | | | | | | | |
| 1 | randomised trial | no serious limitations | no serious inconsistency | no serious indirectness | very serious4 | none | 7/72 (9.7%) | 4/74 (5.4%)<br>5.4% | RR 1.8 (0.55 to 5.88) | 4 more per 100 (from -2 fewer to 26 more)<br>4 more per 100 | ⊕⊕OOLOW |

[1] Significant heterogeneity - random effects model used [2] Not needed 3 Inconclusive effect size 4 Single study; inconclusive effect size

# Electroconvulsive therapy (ECT)

## Is ECT effective in severe depression?

| Quality assessment | | | | | | | Summary of findings | | | | | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of patients | | Effect | | Quality | |
| No. of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Other considerations | Comparisons involving ECT | Control | Relative (95% CI) | Absolute | | |
| **Low-dose bilateral ECT vs low-dose unilateral ECT - non-responders** | | | | | | | | | | | | |
| 4 | randomised trials | no serious limitations | serious[1] | no serious indirectness | very serious[2] | none | 51/98 (52%) | 83/119 (69.7%) | RR 0.65 (0.35 to 1.21) | 24 fewer per 100 (from 45 fewer to 15 more) | ⊕OOO VERY LOW | |
| | | | | | | | | 67.9% | | 24 fewer per 100 (from 44 fewer to 14 more) | | |
| **Low-dose bilateral ECT vs low-dose unilateral ECT - non-remission** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 43/67 (64.2%) | 46/67 (68.7%) | RR 0.93 (0.77 to 1.14) | 5 fewer per 100 (from 16 fewer to 10 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 57.8% | | 4 fewer per | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 100 (from 13 fewer to 8 more) | | |
| **Low-dose bilateral vs low-dose unilateral - mean endpoint depression scores (Better indicated by lower values)** | | | | | | | | | | | | |
| 2 | randomised trials | no serious limitations | serious[1] | no serious indirectness | very serious[2] | none | 49 | 42 | - | SMD 0.46 lower (1.69 lower to 0.76 higher) | ⊕OOO VERY LOW | |
| **Low-dose bilateral ECT vs high-dose unilateral ECT - non-responders** | | | | | | | | | | | | |
| 7 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | no serious imprecision | none | 63/179 (35.2%) | 66/183 (36.1%) | RR 0.98 (0.74 to 1.29) | 1 fewer per 100 (from 9 fewer to 10 more) | ⊕⊕⊕⊕ HIGH | |
| | | | | | | | | 38.5% | | 1 fewer per 100 (from 10 fewer to 11 more) | | |
| **Low-dose bilateral ECT vs high-dose unilateral ECT - non-remission** | | | | | | | | | | | | |
| 5 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 62/118 (52.5%) | 51/119 (42.9%) | RR 1.24 (0.97 to 1.6) | 10 more per 100 (from 1 fewer to 26 more) | ⊕⊕⊕O MODERATE | |
| | | | | | | | | 31.8% | | 8 more per 100 (from 1 fewer to 19 more) | | |

| Bilateral ECT (low dose) vs high-dose unilateral ECT - mean endpoint scores (Better indicated by lower values) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4 | randomised trials | no serious limitations | no serious inconsistency | no serious indirectness | serious[2] | none | 107 | 97 | - | SMD 0.01 higher (0.27 lower to 0.29 higher) | ⊕⊕⊕O MODERATE | |

[1] Significant heterogeneity - random effects model used

[2] Inconclusive effect size