Appendix 19d: Clinical evidence forest plots for the management of subthreshold depressive symptoms

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### Pharmacological interventions

#### Pharm subthreshold 01 Efficacy: active treatment versus placebo

01.01 Non-response at endpoint

#### Review:
Depression Update Subthreshold: Pharm

#### Comparison:
01 Overall efficacy (versus placebo)

#### Outcome:
01 Number of people not achieving at least 50% reduction in depression score

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
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<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
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<tr>
<td><strong>01 SSRIs: dysthymia only</strong></td>
<td></td>
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<tr>
<td>BARRETT99D Px(Pst)*C</td>
<td>51/111</td>
<td>66/112</td>
<td>28.36</td>
<td>0.78</td>
<td>[0.60, 1.01]</td>
<td>0</td>
</tr>
<tr>
<td>HELLERSTEIN93 Fix°C</td>
<td>9/19</td>
<td>13/16</td>
<td>6.09</td>
<td>0.58</td>
<td>[0.34, 0.99]</td>
<td>0</td>
</tr>
<tr>
<td>RAVINDRAN2000 St</td>
<td>76/158</td>
<td>101/152</td>
<td>44.43</td>
<td>0.72</td>
<td>[0.59, 0.88]</td>
<td>0</td>
</tr>
<tr>
<td>RAVINDRAN99St(cbt)*C</td>
<td>10/22</td>
<td>18/26</td>
<td>7.12</td>
<td>0.66</td>
<td>[0.39, 1.11]</td>
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<tr>
<td>VANELLE1997 Fix</td>
<td>30/72</td>
<td>25/39</td>
<td>14.00</td>
<td>0.65</td>
<td>[0.45, 0.93]</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>382</td>
<td>345</td>
<td>100.00</td>
<td>0.72</td>
<td>[0.63, 0.82]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 176 (Treatment), 223 (Control)

Test for heterogeneity: Ch² = 1.40, df = 4 (P = 0.84), I² = 0%

Test for overall effect: Z = 4.90 (P < 0.00001)

| **02 SSRIs: minor depression only** |           |         |            |        |            |       |
|                                   | n/N       | n/N     | 95% CI     | %      | 95% CI     |       |
| BARRETT99M Px(Pst)*C              | 55/106    | 57/109  | 100.00     | 0.99   | [0.77, 1.28]| 0     |

Subtotal (95% CI) 106 109

Total events: 55 (Treatment), 57 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 0.66 (P = 0.995)

| **03 TCAs: dysthymia only**       |           |         |            |        |            |       |
|                                   | n/N       | n/N     | 95% CI     | %      | 95% CI     |       |
| VERSIANI97mP(Mcl)*C               | 25/68     | 54/76   | 100.00     | 0.52   | [0.37, 0.73]| 0     |

Subtotal (95% CI) 68 76

Total events: 25 (Treatment), 54 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 3.76 (P = 0.0002)

| **04 MAOIs: dysthymia only**      |           |         |            |        |            |       |
|                                   | n/N       | n/N     | 95% CI     | %      | 95% CI     |       |
| VERSIANI97mP(Mcl)*C               | 25/70     | 54/76   | 100.00     | 0.50   | [0.36, 0.71]| 0     |

Subtotal (95% CI) 70 76

Total events: 25 (Treatment), 54 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 3.90 (P < 0.0001)

---

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control
01.02 Non-remission at endpoint

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random)</th>
<th>Weight</th>
<th>Control</th>
<th>RR (random)</th>
<th>Order</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
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</tr>
<tr>
<td>01 SSRIs: dysthymia only</td>
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<td></td>
</tr>
<tr>
<td>BARRETT99D Px(Pst)*C</td>
<td>56/111</td>
<td>70/112</td>
<td>0.81 [0.64, 1.02]</td>
<td>0.33</td>
<td>0.78</td>
<td>[0.64, 0.95]</td>
<td>0</td>
</tr>
<tr>
<td>THASE1996A Stl (Imp)</td>
<td>71/134</td>
<td>95/140</td>
<td>0.78 [0.64, 0.95]</td>
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<tr>
<td>VANELLE1997 Fix</td>
<td>40/72</td>
<td>29/39</td>
<td>0.75 [0.57, 0.99]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>17/191</td>
<td>29/39</td>
<td>0.78 [0.68, 0.89]</td>
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<tr>
<td>Total events: 167 (Treatment), 194 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chi² = 0.18, df = 2 (P = 0.92), F = 0%</td>
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<tr>
<td>Test for overall effect: Z = 3.66 (P = 0.0002)</td>
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</tr>
<tr>
<td>02 SSRIs: minor depression only</td>
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</tr>
<tr>
<td>BARRETT99M Px(Pst)*C</td>
<td>62/106</td>
<td>60/109</td>
<td>1.06 [0.84, 1.34]</td>
<td>100.00</td>
<td>1.06</td>
<td>[0.84, 1.34]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>106</td>
<td>109</td>
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<tr>
<td>Total events: 62 (Treatment), 60 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 0.51 (P = 0.61)</td>
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<tr>
<td>03 TCAs: dysthymia only</td>
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<td></td>
</tr>
<tr>
<td>THASE1996A Imp (Stl)</td>
<td>83/136</td>
<td>95/140</td>
<td>0.90 [0.75, 1.07]</td>
<td>57.98</td>
<td>0.90</td>
<td>[0.75, 1.07]</td>
<td>0</td>
</tr>
<tr>
<td>VERSIANI97Imp(Mcl)*C</td>
<td>37/68</td>
<td>59/76</td>
<td>0.70 [0.55, 0.90]</td>
<td>42.02</td>
<td>0.70</td>
<td>[0.55, 0.90]</td>
<td>0</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>204</td>
<td>216</td>
<td>0.81 [0.63, 1.03]</td>
<td>100.00</td>
<td>0.81</td>
<td>[0.63, 1.03]</td>
<td></td>
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<tr>
<td>Total events: 120 (Treatment), 154 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chi² = 2.57, df = 1 (P = 0.11), F = 61.1%</td>
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<tr>
<td>Test for overall effect: Z = 1.74 (P = 0.08)</td>
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<tr>
<td>04 MAOIs: dysthymia only</td>
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</tr>
<tr>
<td>VERSIANI97Mcl(Imp)*C</td>
<td>34/70</td>
<td>59/76</td>
<td>0.63 [0.48, 0.82]</td>
<td>100.00</td>
<td>0.63</td>
<td>[0.48, 0.82]</td>
<td>0</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>70</td>
<td>76</td>
<td>0.63 [0.48, 0.82]</td>
<td>100.00</td>
<td>0.63</td>
<td>[0.48, 0.82]</td>
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<tr>
<td>Total events: 34 (Treatment), 59 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 3.41 (P = 0.0007)</td>
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Favours treatment Favours control
### 01.03 Mean endpoint (clinician-rated)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
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<tbody>
<tr>
<td><strong>Overall efficacy</strong></td>
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<tr>
<td><strong>01 SSRIs: dysthymia only</strong></td>
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<td></td>
</tr>
<tr>
<td>BARRETT99D Px(Pst)*C</td>
<td>88</td>
<td>5.80 (4.50)</td>
<td>99</td>
<td>8.30 (5.10)</td>
<td>86.16</td>
<td>-0.52 [-0.81, -0.22]</td>
</tr>
<tr>
<td>HELLERSTEIN93 Flx *C</td>
<td>16</td>
<td>9.67 (4.85)</td>
<td>16</td>
<td>14.63 (6.29)</td>
<td>13.84</td>
<td>-0.86 [-1.59, -0.13]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>104</td>
<td>115</td>
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<td>100.00</td>
<td>-0.96 [-0.83, -0.29]</td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 4.08 (P &lt; 0.0001)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>02 SSRIs: minor depression only</strong></td>
<td></td>
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</tr>
<tr>
<td>BARRETT99M Px(Pst)*C</td>
<td>77</td>
<td>5.98 (4.10)</td>
<td>88</td>
<td>6.60 (4.70)</td>
<td>51.16</td>
<td>-0.18 [-0.49, 0.13]</td>
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<tr>
<td>JUDD2004 Flx</td>
<td>78</td>
<td>7.10 (5.00)</td>
<td>79</td>
<td>8.10 (5.00)</td>
<td>48.84</td>
<td>-0.20 [-0.51, 0.11]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
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<td>167</td>
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<td></td>
<td>100.00</td>
<td>-0.19 [-0.41, 0.03]</td>
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<tr>
<td><strong>Test for overall effect:</strong> Z = 1.69 (P = 0.09)</td>
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<tr>
<td><strong>03 TCAs: dysthymia only</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOYER1999 Amt (Ams)</td>
<td>107</td>
<td>9.60 (7.20)</td>
<td>105</td>
<td>14.10 (7.20)</td>
<td>100.00</td>
<td>-0.62 [-0.90, -0.35]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>107</td>
<td>105</td>
<td></td>
<td></td>
<td>100.00</td>
<td>-0.62 [-0.90, -0.35]</td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 4.43 (P &lt; 0.00001)</td>
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<tr>
<td><strong>04 APs: dysthymia only</strong></td>
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<tr>
<td>BOYER1999 Ams (Amm)</td>
<td>101</td>
<td>9.30 (7.20)</td>
<td>105</td>
<td>14.10 (7.20)</td>
<td>100.00</td>
<td>-0.66 [-0.94, -0.38]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>101</td>
<td>105</td>
<td></td>
<td></td>
<td>100.00</td>
<td>-0.66 [-0.94, -0.38]</td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 4.64 (P &lt; 0.00001)</td>
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</table>
### 01.04 Mean endpoint (self-rated)

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 01 Overall efficacy (versus placebo)  
**Outcome:** 04 Mean endpoint scores (self rated)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
</table>
| 01 SSRIs: minor depression only  
JUDD2004 Flx | 73 8.60 (8.50) | 74 12.00 (8.50) | -0.40 [-0.72, -0.07] | 100.00 | -0.40 [-0.72, -0.07] | 0 |

**Subtotal (95% CI)**  
73  
74  
100.00  
-0.40 [-0.72, -0.07]  

Test for heterogeneity: not applicable  
Test for overall effect: Z = 2.39 (P = 0.02)
## 01.05 Mean change at endpoint (clinician-rated)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (random)</th>
<th>Weight</th>
<th>SMD (random)</th>
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<tr>
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<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 SSRIs: dysthymia only</td>
<td>THASE1996A Stl (Imp)</td>
<td>134</td>
<td>-5.60(6.10)</td>
<td>140</td>
<td>-3.90(5.10)</td>
</tr>
<tr>
<td></td>
<td>VANELLE1997 Flx</td>
<td>72</td>
<td>-10.20(7.30)</td>
<td>39</td>
<td>-7.70(7.60)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>216</td>
<td>179</td>
<td>100.00</td>
<td>-0.31</td>
<td>[-0.51, -0.11]</td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Test for overall effect: Z = 2.99 (P = 0.003)</td>
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<td></td>
</tr>
<tr>
<td>02 TCAs: dysthymia only</td>
<td>BOYER1999 Amt (Amt)</td>
<td>107</td>
<td>-8.20(7.24)</td>
<td>105</td>
<td>-3.80(7.17)</td>
</tr>
<tr>
<td></td>
<td>THASE1996A Imp (Stl)</td>
<td>136</td>
<td>-5.90(5.80)</td>
<td>140</td>
<td>-3.90(5.10)</td>
</tr>
<tr>
<td></td>
<td>VERSIANI97Imp/Mcl(C)</td>
<td>63</td>
<td>-11.10(5.60)</td>
<td>72</td>
<td>-5.60(6.30)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>306</td>
<td>317</td>
<td>100.00</td>
<td>-0.61</td>
<td>[-0.90, -0.31]</td>
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<tr>
<td></td>
<td>Test for heterogeneity: Chi² = 6.49, df = 2 (P = 0.04), I² = 69.2%</td>
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<tr>
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<td>Test for overall effect: Z = 3.99 (P &lt; 0.0001)</td>
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<td></td>
</tr>
<tr>
<td>03 APs: dysthymia only</td>
<td>BOYER1999 Ams (Amt)</td>
<td>101</td>
<td>-8.60(7.03)</td>
<td>105</td>
<td>-3.80(7.17)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>101</td>
<td>105</td>
<td>100.00</td>
<td>-0.67</td>
<td>[-0.95, -0.39]</td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: not applicable</td>
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<td></td>
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<tr>
<td></td>
<td>Test for overall effect: Z = 4.70 (P &lt; 0.00001)</td>
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</tr>
<tr>
<td>04 MAOIs: dysthymia only</td>
<td>VERSIANI97Mcl(Imp)/C</td>
<td>67</td>
<td>-11.80(6.40)</td>
<td>72</td>
<td>-5.60(6.30)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>67</td>
<td>72</td>
<td>100.00</td>
<td>-0.97</td>
<td>[-1.32, -0.62]</td>
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<tr>
<td></td>
<td>Test for heterogeneity: not applicable</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 5.40 (P &lt; 0.00001)</td>
<td></td>
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</tbody>
</table>

-10  -5  0  5  10
Favours treatment  Favours control
Pharm subthreshold 02 Acceptability and tolerability: active treatment versus placebo

02.01 Dropout at endpoint for any reason

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random) 95% CI</th>
<th>Weight</th>
<th>RR (random) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 SSRIs: dysthymia only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT990 Pe/Pr*C</td>
<td>29/111</td>
<td>21/112</td>
<td>24.59</td>
<td>1.35 [0.82, 2.22]</td>
<td>0.95</td>
<td>1.09</td>
</tr>
<tr>
<td>HELLERSTEIN93 Fix*C</td>
<td>3/19</td>
<td>0/16</td>
<td>1.09</td>
<td>0.94 [0.61, 1.39]</td>
<td>0.94</td>
<td>1.02</td>
</tr>
<tr>
<td>RAVIDAN9200009 Stl</td>
<td>37/158</td>
<td>38/152</td>
<td>33.00</td>
<td>25.16</td>
<td>0.65 [0.40, 1.05]</td>
<td>0</td>
</tr>
<tr>
<td>RAVIDAN99099St(cbt)*C</td>
<td>0/22</td>
<td>2/26</td>
<td>1.02</td>
<td>0.23 [0.01, 4.45]</td>
<td>0.23</td>
<td>0.83 [0.08, 10.83]</td>
</tr>
<tr>
<td>THASE1996St (Imp)</td>
<td>21/134</td>
<td>34/140</td>
<td>25.16</td>
<td>0.65</td>
<td>0.40 [0.25, 1.00]</td>
<td>0</td>
</tr>
<tr>
<td>VANELLE1997 Fx</td>
<td>12/92</td>
<td>13/49</td>
<td>1.02</td>
<td>0.31</td>
<td>0.25 [0.06, 0.99]</td>
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</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>935</td>
<td>495</td>
<td>100.00</td>
<td>0.84</td>
<td>0.57 [0.34, 0.95]</td>
<td>0</td>
</tr>
</tbody>
</table>

Total events: 101 (Treatment), 108 (Control)
Test for heterogeneity: Chi² = 9.34, df = 5 (P = 0.10), I² = 46.5%
Test for overall effect: Z = 0.87 (P = 0.38)

| **02 SSRIs: minor depression** |           |         |                   |        |                   |       |
| BARRETT99M Pe/Pr*C | 37/106 | 28/109 | 56.29 | 1.36 [0.90, 2.05] | 0.90 | 56.29 | 1.36 [0.90, 2.05] | 0 |
| JUDD2000 Fx | 22/81 | 22/81 | 56.29 | 1.36 [0.90, 2.05] | 0.90 | 56.29 | 1.36 [0.90, 2.05] | 0 |
| **Subtotal (95% CI)** | 187 | 190 | 100.00 | 1.20 | 0.87 [1.65] | 0 |

Total events: 59 (Treatment), 50 (Control)
Test for heterogeneity: Chi² = 0.85, df = 1 (P = 0.36), P < 0.1%
Test for overall effect: Z = 1.13 (P = 0.26)

| **03 TCAs: dysthymia only** |           |         |                   |        |                   |       |
| BAKISH1993 Imp (Rts) | 5/16 | 7/16 | 11.65 | 0.71 [0.29, 1.78] | 0.29 | 11.65 | 0.71 [0.29, 1.78] | 0 |
| BOYER1999 Amt (Ams) | 20/111 | 22/108 | 26.58 | 0.89 | 0.51 [1.52] | 0 |
| THASE1996Amp (lmt) | 49/136 | 34/140 | 41.86 | 1.36 | 0.39 [0.93, 1.99] | 0 |
| VERSIAN97Imp(lmt)*C | 15/103 | 15/104 | 19.91 | 1.01 | 0.52 [0.96] | 0 |
| **Subtotal (95% CI)** | 366 | 368 | 100.00 | 1.10 | 0.84 [1.44] | 0 |

Total events: 85 (Treatment), 78 (Control)
Test for heterogeneity: Chi² = 2.77, df = 3 (P = 0.43), P = 0%
Test for overall effect: Z = 1.32 (P = 0.19)

| **04 MAOIs: dysthymia only** |           |         |                   |        |                   |       |
| VERSIAN97Mlmp(lmt)*C | 13/108 | 15/104 | 100.00 | 0.83 | 0.42 [1.67] | 0 |
| **Subtotal (95% CI)** | 108 | 104 | 100.00 | 0.83 | 0.42 [1.67] | 0 |

Total events: 15 (Treatment), 15 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 0.51 (P = 0.61)

| **05 APs: dysthymia only** |           |         |                   |        |                   |       |
| BOYER1999 Ams (Ams) | 14/104 | 22/108 | 100.00 | 0.66 | 0.36 [1.22] | 0 |
| **Subtotal (95% CI)** | 104 | 108 | 100.00 | 0.66 | 0.36 [1.22] | 0 |

Total events: 14 (Treatment), 22 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 1.32 (P = 0.19)
## 02.02 Dropout at endpoint due to side effects

**Review:** Depression Update Subthreshold: Pharm

**Comparison:** 02 Overall acceptability and tolerability (versus placebo)

**Outcome:** 02 Leaving the study early due to side effects

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
<th>Order</th>
</tr>
</thead>
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<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 SSRIs: dysthymia only</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>BARRETT99 D Px(Pst)*C</td>
<td>4/111</td>
<td>2/112</td>
<td>29.78</td>
<td>2.02</td>
<td>(0.38, 10.79)</td>
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<tr>
<td>THASE1996A SNI (mp)</td>
<td>8/134</td>
<td>5/140</td>
<td>70.22</td>
<td>1.67</td>
<td>(0.56, 4.98)</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>245</td>
<td>252</td>
<td>100.00</td>
<td>1.77</td>
<td>(0.71, 4.41)</td>
<td></td>
</tr>
<tr>
<td>Total events: 12 (Treatment), 7 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: Chi² = 0.03, df = 1 (P = 0.85), I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 1.22 (P = 0.22)</td>
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</tr>
<tr>
<td>02 SSRIs: minor depression only</td>
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</tr>
<tr>
<td>BARRETT99M Px(Pst)*C</td>
<td>14/106</td>
<td>6/109</td>
<td>71.79</td>
<td>2.40</td>
<td>(0.96, 6.01)</td>
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<tr>
<td>JUD2004 Fx</td>
<td>3/81</td>
<td>4/81</td>
<td>28.21</td>
<td>0.75</td>
<td>(0.17, 3.25)</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>187</td>
<td>190</td>
<td>100.00</td>
<td>1.55</td>
<td>(0.51, 4.68)</td>
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<tr>
<td>Total events: 17 (Treatment), 10 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chi² = 1.74, df = 1 (P = 0.19), I² = 42.5%</td>
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<tr>
<td>Test for overall effect: Z = 0.78 (P = 0.43)</td>
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<tr>
<td>03 TCAs: dysthymia only</td>
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</tr>
<tr>
<td>BAKISH1993 Imp (Pts)</td>
<td>3/16</td>
<td>0/17</td>
<td>6.13</td>
<td>7.41</td>
<td>(0.41, 133.11)</td>
<td>0</td>
</tr>
<tr>
<td>BOYER1999 Amt (Amst)</td>
<td>6/111</td>
<td>1/108</td>
<td>11.59</td>
<td>5.84</td>
<td>(0.71, 47.69)</td>
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<tr>
<td>THASE1996A Imp (Stl)</td>
<td>25/136</td>
<td>5/140</td>
<td>59.01</td>
<td>5.15</td>
<td>(2.03, 13.05)</td>
<td>0</td>
</tr>
<tr>
<td>THASE1996A Imp (Stl)</td>
<td>25/136</td>
<td>5/140</td>
<td>59.01</td>
<td>5.15</td>
<td>(2.03, 13.05)</td>
<td>0</td>
</tr>
<tr>
<td>VERSIANI97 Imp (Mc)*C</td>
<td>11/103</td>
<td>2/104</td>
<td>23.28</td>
<td>5.55</td>
<td>(1.26, 24.44)</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>366</td>
<td>369</td>
<td>100.00</td>
<td>5.44</td>
<td>(2.66, 11.11)</td>
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<tr>
<td>Total events: 45 (Treatment), 8 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chi² = 0.06, df = 3 (P = 1.00), I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 4.64 (P &lt; 0.00001)</td>
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<tr>
<td>04 MAOs: dysthymia only</td>
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</tr>
<tr>
<td>VERSIANI97 Mcl (Imp)*C</td>
<td>7/108</td>
<td>2/104</td>
<td>100.00</td>
<td>3.37</td>
<td>(0.72, 15.85)</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>108</td>
<td>104</td>
<td>100.00</td>
<td>3.37</td>
<td>(0.72, 15.85)</td>
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<tr>
<td>Total events: 7 (Treatment), 2 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 1.54 (P = 0.12)</td>
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<tr>
<td>05 APs: dysthymia only</td>
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</tr>
<tr>
<td>BOYER1999 Amst (Amst)</td>
<td>3/104</td>
<td>1/108</td>
<td>100.00</td>
<td>3.12</td>
<td>(0.35, 29.47)</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>104</td>
<td>108</td>
<td>100.00</td>
<td>3.12</td>
<td>(0.35, 29.47)</td>
<td></td>
</tr>
<tr>
<td>Total events: 3 (Treatment), 1 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.99 (P = 0.32)</td>
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</tbody>
</table>

0.1  0.2  0.5  1  2  5  10
Favours treatment  Favours control
### 02.03 Number reporting side effects at endpoint

**Review:** Depression Update Subthreshold: Pharm

**Comparison:** 02 Overall acceptability and tolerability (versus placebo)

**Outcome:** 03 Patients reporting side effects

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
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<tbody>
<tr>
<td><strong>01 SSRIs: dysthymia only</strong></td>
<td></td>
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</tr>
<tr>
<td>BARRETT99D Px(Pst)°C</td>
<td>34/111</td>
<td>33/112</td>
<td>20.36</td>
<td>1.04 [0.70, 1.55]</td>
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<tr>
<td>RAIVINDRAN2000 Stl</td>
<td>119/158</td>
<td>98/152</td>
<td>61.91</td>
<td>1.17 [1.01, 1.35]</td>
<td>0</td>
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<tr>
<td>VANELLE1997 Flx</td>
<td>35/91</td>
<td>22/49</td>
<td>17.73</td>
<td>0.86 [0.57, 1.28]</td>
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<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>360</td>
<td>313</td>
<td>100.00</td>
<td>1.09 [0.95, 1.25]</td>
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<tr>
<td>Total events: 188 (Treatment), 153 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chi² = 2.29, df = 2 (P = 0.32), I² = 12.7%</td>
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<tr>
<td>Test for overall effect: Z = 1.17 (P = 0.24)</td>
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</tr>
<tr>
<td><strong>02 SSRIs: minor depression only</strong></td>
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</tr>
<tr>
<td>BARRETT99M Px(Pst)°C</td>
<td>25/106</td>
<td>34/109</td>
<td>100.00</td>
<td>0.76 [0.49, 1.18]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>106</td>
<td>109</td>
<td>100.00</td>
<td>0.76 [0.49, 1.18]</td>
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<tr>
<td>Total events: 25 (Treatment), 34 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 1.24 (P = 0.21)</td>
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<tr>
<td><strong>03 TCAs: dysthymia only</strong></td>
<td></td>
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</tr>
<tr>
<td>BOYER1999 Amt (Ams)</td>
<td>69/111</td>
<td>48/108</td>
<td>100.00</td>
<td>1.40 [1.08, 1.81]</td>
<td>0</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>111</td>
<td>108</td>
<td>100.00</td>
<td>1.40 [1.08, 1.81]</td>
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<td></td>
</tr>
<tr>
<td>Total events: 69 (Treatment), 48 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 2.57 (P = 0.01)</td>
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<tr>
<td><strong>05 APs: dysthymia only</strong></td>
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<tr>
<td>BOYER1999 Ams (Amt)</td>
<td>57/104</td>
<td>48/108</td>
<td>100.00</td>
<td>1.23 [0.94, 1.62]</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>104</td>
<td>108</td>
<td>100.00</td>
<td>1.23 [0.94, 1.62]</td>
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<td></td>
</tr>
<tr>
<td>Total events: 57 (Treatment), 48 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.50 (P = 0.13)</td>
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</tr>
</tbody>
</table>

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0.1 0.2 0.5 1 2 5 10

Favours treatment  Favours control
Pharm subthreshold 03 Efficacy: active treatment versus active treatment

03.01 Non-response at endpoint: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 01 Number of people not achieving at least 50% reduction in depression score: SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
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</tr>
<tr>
<td><strong>Dysthymia =&gt; 50% (v AD)</strong></td>
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</tr>
<tr>
<td>DEJONGHE1991 Fvx/Mpt</td>
<td>18/24</td>
<td>18/24</td>
<td>1.00 [0.72, 1.39]</td>
<td>0.00</td>
<td>1.00 [0.72, 1.39]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>24</td>
<td>24</td>
<td>100.00</td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Total events: 18 (Treatment), 18 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.00 (P = 1.00)</td>
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</tr>
<tr>
<td><strong>Dysthymia =&gt; 50% (v AP)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMORE2001 Srt/Ams</td>
<td>37/156</td>
<td>26/157</td>
<td>1.43 [0.91, 2.25]</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>SMERALDI1996 Flx/Ams</td>
<td>52/139</td>
<td>39/142</td>
<td>1.36 [0.97, 1.92]</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>295</td>
<td>299</td>
<td>100.00</td>
<td>1.39</td>
<td>1.06, 1.83</td>
<td>0</td>
</tr>
<tr>
<td>Total events: 89 (Treatment), 65 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 0.03, df = 1 (P = 0.86), P = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.36 (P = 0.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Minor depression only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SZEGEDI1997 Prx/Mpt</td>
<td>30/126</td>
<td>39/119</td>
<td>0.73 [0.48, 1.09]</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>126</td>
<td>119</td>
<td>100.00</td>
<td>0.73</td>
<td>0.48, 1.09</td>
<td>0</td>
</tr>
<tr>
<td>Total events: 30 (Treatment), 39 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.55 (P = 0.12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>0.1</th>
<th>0.2</th>
<th>0.5</th>
<th>1.0</th>
<th>2.0</th>
<th>5.0</th>
<th>10.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favor treatment</td>
<td>Favor control</td>
<td>Favor treatment</td>
<td>Favor control</td>
<td>Favor treatment</td>
<td>Favor control</td>
<td>Favor treatment</td>
</tr>
</tbody>
</table>

0.1 0.2 0.5 1 2 5 10
Favours treatment Favours control
### 03.02 Non-response at endpoint: TCA

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 02 Number of people not achieving at least 50% reduction in depression score: TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALZMANN95 Imp/Mnp*C</td>
<td>21/34</td>
<td>18/33</td>
<td>42.58</td>
<td>1.13</td>
<td>[0.75, 1.70]</td>
<td>0</td>
</tr>
<tr>
<td>VERSIANI97Imp(Mcl)*C</td>
<td>25/68</td>
<td>25/70</td>
<td>57.42</td>
<td>1.03</td>
<td>[0.66, 1.60]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>102</td>
<td>103</td>
<td>100.00</td>
<td>1.07</td>
<td>[0.79, 1.46]</td>
<td></td>
</tr>
<tr>
<td>Total events:</td>
<td>46 (Treatment), 43 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity:</td>
<td>Chi² = 0.10, df = 1 (P = 0.75), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect:</td>
<td>Z = 0.45 (P = 0.65)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 02 Dysthymia => 50%  |              |             |                   |          |                  |       |
| RAVIZZA1999 Amt/Ams  | 34/87        | 67/166      | 100.00            | 0.97     | [0.70, 1.33]     | 0     |
| Subtotal (95% CI)    | 87           | 166         | 100.00            | 0.97     | [0.70, 1.33]     |       |
| Total events:        | 34 (Treatment), 67 (Control) |              |                   |          |                  |       |
| Test for heterogeneity: | not applicable | | | | |
| Test for overall effect: | Z = 0.20 (P = 0.84) | | | | |

- 0.1  0.2  0.5  1  2  5  10
- Favours treatment  Favours control
### 03.03 Non-remission at endpoint: SSRI

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 03 Number of people not achieving remission: SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Dysthymia only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THASE1996A Stl (Imp)</td>
<td>71/134</td>
<td>83/136</td>
<td>-</td>
<td>100.00</td>
<td>0.87 [0.70, 1.07]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>134</td>
<td>136</td>
<td></td>
<td>100.00</td>
<td>0.87 [0.70, 1.07]</td>
<td></td>
</tr>
<tr>
<td>Total events: 71 (Treatment), 83 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.33 (P = 0.18) |
| **02 Dysthymia \(\geq 50\)%** |             |             |                   |          |                   |       |
| AMORE2001 Srt/Ams     | 54/156        | 42/157      | -                 | 100.00   | 1.29 [0.92, 1.81] | 0     |
| Subtotal (95% CI)     | 156           | 157         |                   | 100.00   | 1.29 [0.92, 1.81] |       |
| Total events: 54 (Treatment), 42 (Control) |            |             |                   |          |                   |       |
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.50 (P = 0.13) |
| **03 Minor depression and subsyndromal depressive symptomatology (49% v 51%)** | | | | | | |
| ROCCA2005 Stl/Ctp     | 42/72         | 31/66       | -                 | 100.00   | 1.24 [0.90, 1.71] | 0     |
| Subtotal (95% CI)     | 72            | 66          |                   | 100.00   | 1.24 [0.90, 1.71] |       |
| Total events: 42 (Treatment), 31 (Control) |            |             |                   |          |                   |       |
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.32 (P = 0.19) |

### 03.04 Non-remission at endpoint: TCA

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 04 Number of people not achieving remission: TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Dysthymia only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VERSIAN97 Imp(Mcl)*C</td>
<td>37/68</td>
<td>34/70</td>
<td>-</td>
<td>100.00</td>
<td>1.12 [0.81, 1.55]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>68</td>
<td>70</td>
<td></td>
<td>100.00</td>
<td>1.12 [0.81, 1.55]</td>
<td></td>
</tr>
<tr>
<td>Total events: 37 (Treatment), 34 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 0.69 (P = 0.49) |
03.05 Mean endpoint (clinician-rated): SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 05 Mean endpoint scores (clinician rated): SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Dysthymia =&gt; 50% (v AD)</td>
<td>21</td>
<td>13.60 (6.10)</td>
<td>21</td>
<td>13.70 (7.80)</td>
<td>-0.01 [-0.62, 0.59]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>21</td>
<td>13.60 (6.10)</td>
<td>21</td>
<td>13.70 (7.80)</td>
<td>-0.01 [-0.62, 0.59]</td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.05 (P = 0.96)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Dysthymia =&gt; 50% (v AP)</td>
<td>150</td>
<td>6.10 (6.20)</td>
<td>156</td>
<td>5.20 (5.70)</td>
<td>0.15 [-0.07, 0.38]</td>
</tr>
<tr>
<td>AMORE2001 Srt/Ams</td>
<td>129</td>
<td>9.50 (9.10)</td>
<td>139</td>
<td>8.10 (7.10)</td>
<td>0.17 [-0.07, 0.41]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>279</td>
<td>8.80 (8.10)</td>
<td>295</td>
<td>8.10 (7.10)</td>
<td>0.16 [0.00, 0.32]</td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.92 (P = 0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 03.06 Mean endpoint (clinician-rated): TCA

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 06 Mean endpoint scores (clinician rated): TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (Mean (SD))</td>
<td>N (Mean (SD))</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td>24 (14.50(7.15))</td>
<td>27 (13.67(9.07))</td>
<td>63.06</td>
<td>0.11 [-0.44, 0.66]</td>
<td></td>
</tr>
<tr>
<td>SALZMANN95 Imp/Mnp*C</td>
<td>16 (10.44(5.10))</td>
<td>16 (7.25(3.17))</td>
<td>36.84</td>
<td>0.73 [0.01, 1.45]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>40</td>
<td>43</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Dysthymia only (v AP)</td>
<td>107 (9.60(7.20))</td>
<td>101 (9.30(7.20))</td>
<td>100.00</td>
<td>0.04 [-0.23, 0.31]</td>
<td></td>
</tr>
<tr>
<td>BOYER1999 Amt (Ams)</td>
<td>107</td>
<td>101</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>04 Dysthymia -&gt; 50% (v AP)</td>
<td>85 (10.10(8.50))</td>
<td>165 (10.20(8.30))</td>
<td>100.00</td>
<td>-0.01 [-0.27, 0.25]</td>
<td></td>
</tr>
<tr>
<td>RAVIZZA1999 Amt/Ams</td>
<td>85</td>
<td>165</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 1.83, df = 1 (P = 0.18), I² = 45.5%  
Test for overall effect: Z = 1.52 (P = 0.13)  
Test for heterogeneity: not applicable  
Test for overall effect: Z = 0.09 (P = 0.93)
### 03.07 Mean endpoint (clinician-rated): antipsychotic

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 07 Mean endpoint scores (clinician rated): AP

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N</th>
<th>Treatment Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>SMD (fixed) 95% CI</th>
<th>Weight %</th>
<th>SMD (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEISLER1992 Flp/Rts</td>
<td>36</td>
<td>11.00 (4.21)</td>
<td>31</td>
<td>12.10 (4.21)</td>
<td>100.00</td>
<td>-0.26 [-0.74, 0.22]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>36</td>
<td></td>
<td>31</td>
<td></td>
<td>100.00</td>
<td>-0.26 [-0.74, 0.22]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.05 (P = 0.29)

### 03.08 Mean change at endpoint (clinician-rated): SSRI

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 03 Overall efficacy (head to head)  
**Outcome:** 08 Mean change (clinician rated): SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N</th>
<th>Treatment Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>SMD (fixed) 95% CI</th>
<th>Weight %</th>
<th>SMD (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THASE1996A Stl (Imp)</td>
<td>134</td>
<td>-5.60 (6.10)</td>
<td>136</td>
<td>-5.90 (5.80)</td>
<td>100.00</td>
<td>0.05 [-0.19, 0.29]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>134</td>
<td></td>
<td>136</td>
<td></td>
<td>100.00</td>
<td>0.05 [-0.19, 0.29]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable  
Test for overall effect: Z = 0.41 (P = 0.68)
## 03.09 Mean change at endpoint (clinician-rated): TCA

### Review:
Depression Update Subthreshold: Pharm

### Comparison:
03 Overall efficacy (head to head)

### Outcome:
09 Mean change (clinician rated): TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td>VERSIANI97Imp(Mcl)*C</td>
<td>63 -11.10(5.60)</td>
<td>67 -11.80(6.40)</td>
<td>100.00</td>
<td>0.12 [−0.23, 0.46]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>63</td>
<td>67</td>
<td>100.00</td>
<td>0.12 [−0.23, 0.46]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable
Test for overall effect: Z = 0.66 (P = 0.51)

| 02 Dysthymia only (v AP) | BOYER1999 Amt (Ams) | 107 -8.20(7.24) | 101 -8.60(7.03) | 100.00 | 0.06 [−0.22, 0.33] | 0 |
| Subtotal (95% CI) | 107 | 101 | 100.00 | 0.06 [−0.22, 0.33] | |

Test for heterogeneity: not applicable
Test for overall effect: Z = 0.40 (P = 0.69)
Pharm subthreshold 04 Acceptability versus tolerability: active treatment versus active treatment

04.01 Dropout at endpoint for any reason: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 01 Leaning the study early: SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THASE1996A Stl (Imp)</td>
<td>21/134</td>
<td>45/136</td>
<td>100.00</td>
<td>0.47</td>
<td>[0.30, 0.75]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>134</td>
<td>136</td>
<td>100.00</td>
<td>0.47</td>
<td>[0.30, 0.75]</td>
<td></td>
</tr>
<tr>
<td>Total events: 21 (Treatment), 45 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.19 (P = 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Dysthymia =/&gt; 50% (v AD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEJONGHE1991 Fvx/Mpt</td>
<td>4/24</td>
<td>6/24</td>
<td>100.00</td>
<td>0.67</td>
<td>[0.22, 2.07]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>24</td>
<td>24</td>
<td>100.00</td>
<td>0.67</td>
<td>[0.22, 2.07]</td>
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</tr>
<tr>
<td>Total events: 4 (Treatment), 6 (Control)</td>
<td></td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.70 (P = 0.48)</td>
<td></td>
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</tr>
<tr>
<td>03 Dysthymia =/&gt; 50% (v AP)</td>
<td></td>
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</tr>
<tr>
<td>AMORE2001 Srt/Ams</td>
<td>27/156</td>
<td>18/157</td>
<td>36.17</td>
<td>1.51</td>
<td>[0.87, 2.63]</td>
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</tr>
<tr>
<td>SMERALDI1996 Flx/Ams</td>
<td>40/139</td>
<td>32/142</td>
<td>63.83</td>
<td>1.28</td>
<td>[0.86, 1.91]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>295</td>
<td>299</td>
<td>100.00</td>
<td>1.36</td>
<td>[0.98, 1.89]</td>
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<tr>
<td>Total events: 67 (Treatment), 50 (Control)</td>
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<tr>
<td>Test for heterogeneity: Chisq = 0.23, df = 1 (P = 0.63), I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 1.85 (P = 0.06)</td>
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</tr>
<tr>
<td>04 Minor depression and subsyndromal depressive symptomatology (49% v 51%)</td>
<td></td>
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</tr>
<tr>
<td>ROCCA2005 St/Ctp</td>
<td>20/72</td>
<td>18/66</td>
<td>100.00</td>
<td>1.02</td>
<td>[0.59, 1.75]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>72</td>
<td>66</td>
<td>100.00</td>
<td>1.02</td>
<td>[0.59, 1.75]</td>
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</tr>
<tr>
<td>Total events: 20 (Treatment), 18 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.07 (P = 0.95)</td>
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</table>
### 04.02 Dropout at endpoint for any reason: TCA

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 04 Overall acceptability and tolerability (head to head)  
**Outcome:** 02 Leaving the study early: TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td>VERSIANI97Imp(Mcl)*C</td>
<td>15/103</td>
<td>13/108</td>
<td>100.00</td>
<td>1.21 [0.61, 2.42]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>103</td>
<td>108</td>
<td>100.00</td>
<td>1.21 [0.61, 2.42]</td>
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</tr>
<tr>
<td>Total events: 15 (Treatment), 13 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.54 (P = 0.59)</td>
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</tr>
<tr>
<td>02 Dysthymia only (v AP)</td>
<td>BOYER1999 Amt (Ams)</td>
<td>20/111</td>
<td>14/104</td>
<td>100.00</td>
<td>1.34 [0.71, 2.51]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>111</td>
<td>104</td>
<td>100.00</td>
<td>1.34 [0.71, 2.51]</td>
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<td></td>
</tr>
<tr>
<td>Total events: 20 (Treatment), 14 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.91 (P = 0.36)</td>
<td></td>
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</tr>
<tr>
<td>03 Dysthymia &gt;50% (AD)</td>
<td>VALLEJO87 Imp/Phz *C</td>
<td>5/37</td>
<td>4/36</td>
<td>100.00</td>
<td>1.22 [0.35, 4.17]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>37</td>
<td>36</td>
<td>100.00</td>
<td>1.22 [0.35, 4.17]</td>
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<tr>
<td>Total events: 5 (Treatment), 4 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.31 (P = 0.76)</td>
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<tr>
<td>04 Dysthymia &gt;50% (v AP)</td>
<td>RAVIZZAI999 Amts/Ams</td>
<td>41/87</td>
<td>73/166</td>
<td>100.00</td>
<td>1.07 [0.81, 1.42]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>87</td>
<td>166</td>
<td>100.00</td>
<td>1.07 [0.81, 1.42]</td>
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<tr>
<td>Total events: 41 (Treatment), 73 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 0.48 (P = 0.63)</td>
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## 04.03 Dropout at endpoint for any reason: antipsychotic

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 04 Overall acceptability and tolerability (head to head)  
**Outcome:** 03 Leaving the study early: AP

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>GEISLER1992 Flp/Rts</td>
<td>3/36</td>
<td>2/31</td>
<td></td>
<td>100.00</td>
<td>1.29 [0.23, 7.24]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>36</td>
<td>31</td>
<td></td>
<td>100.00</td>
<td>1.29 [0.23, 7.24]</td>
<td></td>
</tr>
<tr>
<td>Total events:</td>
<td>3 (Treatment), 2 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.29 (P = 0.77)</td>
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</tbody>
</table>

## 04.04 Dropout at endpoint due to side effects: SSRI

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 04 Overall acceptability and tolerability (head to head)  
**Outcome:** 04 Leaving the study early due to side effects: SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td></td>
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</tr>
<tr>
<td>THASE1996A Stl (Imp)</td>
<td>8/134</td>
<td>25/136</td>
<td></td>
<td>100.00</td>
<td>0.32 [0.15, 0.69]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>134</td>
<td>136</td>
<td></td>
<td>100.00</td>
<td>0.32 [0.15, 0.69]</td>
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</tr>
<tr>
<td>Total events:</td>
<td>8 (Treatment), 25 (Control)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 2.90 (P = 0.004)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>02 Dysthymia =/&gt; 50% (v AP)</td>
<td></td>
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</tr>
<tr>
<td>AMORE2001 Srt/Ams</td>
<td>12/156</td>
<td>10/157</td>
<td></td>
<td>43.66</td>
<td>1.21 [0.54, 2.71]</td>
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</tr>
<tr>
<td>SMERALDI1996 Flx/Ams</td>
<td>10/139</td>
<td>13/142</td>
<td></td>
<td>56.34</td>
<td>0.79 [0.36, 1.73]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>235</td>
<td>299</td>
<td></td>
<td>100.00</td>
<td>0.97 [0.55, 1.70]</td>
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</tr>
<tr>
<td>Total events:</td>
<td>22 (Treatment), 23 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: CH² = 0.55, df = 1 (P = 0.46), P = 0%</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.11 (P = 0.92)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>03 Minor depression and subsyndromal depressive symptomatology (49% v 51%) (v AD)</td>
<td></td>
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</tr>
<tr>
<td>ROCCA2005 Stl/Ctp</td>
<td>8/32</td>
<td>10/66</td>
<td></td>
<td>100.00</td>
<td>0.73 [0.31, 1.75]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>72</td>
<td>66</td>
<td></td>
<td>100.00</td>
<td>0.73 [0.31, 1.75]</td>
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</tr>
<tr>
<td>Total events:</td>
<td>8 (Treatment), 10 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.70 (P = 0.48)</td>
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</tbody>
</table>
04.05 Dropout at endpoint due to side effects: TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 05 Leaving the study early due to side effects: TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td></td>
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</tr>
<tr>
<td>SALZMANN95 Imp/Mnp*C</td>
<td>4/34</td>
<td>3/33</td>
<td>30.82</td>
<td>1.29</td>
<td>0.31, 5.34</td>
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<tr>
<td>VERSANI97Imp(Mnp)/C</td>
<td>11/103</td>
<td>7/108</td>
<td>69.18</td>
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<td>0.66, 4.09</td>
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<tr>
<td>Subtotal (95% CI)</td>
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<td>141</td>
<td>100.00</td>
<td>1.94</td>
<td>0.72, 3.30</td>
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<td>Total events: 15 (Treatment), 10 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: Ch² = 0.08, df = 1 (P = 0.78), I² = 0%</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.11 (P = 0.27)</td>
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</tr>
<tr>
<td>02 Dysthymia only (v AP)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>BOYER1999 Amt (Ams)</td>
<td>6/111</td>
<td>3/104</td>
<td>100.00</td>
<td>1.87</td>
<td>0.48, 7.30</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>111</td>
<td>104</td>
<td>100.00</td>
<td>1.87</td>
<td>0.48, 7.30</td>
</tr>
<tr>
<td>Total events: 6 (Treatment), 3 (Control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.91 (P = 0.37)</td>
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</tr>
<tr>
<td>03 Dysthymia =/&gt; 50% (v AP)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>RAVIZZA1999 Amt/Ams</td>
<td>11/87</td>
<td>23/166</td>
<td>100.00</td>
<td>0.91</td>
<td>0.47, 1.78</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>87</td>
<td>166</td>
<td>100.00</td>
<td>0.91</td>
<td>0.47, 1.78</td>
</tr>
<tr>
<td>Total events: 11 (Treatment), 23 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.27 (P = 0.79)</td>
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</table>

0.1 0.2 0.5 1 2 5 10
Favours treatment Favours control
04.06 Dropout at endpoint due to side effects: antipsychotic

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 06 Leaving the study early due to side effects: AP

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>95% CI</td>
<td>n/N</td>
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</tr>
<tr>
<td>01 Dysthymia only</td>
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</tr>
<tr>
<td>GEISLER1992 Flp/Rts</td>
<td>2/36</td>
<td>100.00</td>
<td>2/33</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>100.00</td>
<td>33</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>04 Overall acceptability and tolerability (head to head)</td>
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</tr>
</tbody>
</table>

Total events: 2 (Treatment), 2 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 0.09 (P = 0.93)

04.07 Number reporting side effects at endpoint: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 07 Patients reporting side effects: SSRI

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
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<td></td>
<td>n/N</td>
<td>95% CI</td>
<td>n/N</td>
<td></td>
</tr>
<tr>
<td>01 Dysthymia =&gt;50% (&gt; AP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMORE2001 Srt/Ams</td>
<td>74/156</td>
<td>51.38</td>
<td>70/157</td>
<td>1.06</td>
</tr>
<tr>
<td></td>
<td>299</td>
<td>100.00</td>
<td>298</td>
<td></td>
</tr>
<tr>
<td>SMERALDI1996 Flx/Ams</td>
<td>56/137</td>
<td>48.62</td>
<td>67/141</td>
<td>0.86</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>07 Patients reporting side effects: SSRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 130 (Treatment), 137 (Control)
Test for heterogeneity: Chi² = 1.35, df = 1 (P = 0.24), I² = 26.1%
Test for overall effect: Z = 0.39 (P = 0.69)
### 04.08 Number reporting side effects at endpoint: TCA

**Review:** Depression Update Subthreshold: Pharm  
**Comparison:** 04 Overall acceptability and tolerability (head to head)  
**Outcome:** 08 Patients reporting side effects: TCA

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Dysthymia only (v AD)</td>
<td>SALZMANN95 Imp/Mnp°C</td>
<td>20/34</td>
<td>14/33</td>
<td>100.00</td>
<td>1.39 [0.85, 2.26]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>34</td>
<td>33</td>
<td>100.00</td>
<td>1.39 [0.85, 2.26]</td>
<td></td>
</tr>
<tr>
<td>Total events:</td>
<td>20 (Treatment), 14 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.32 (P = 0.19) |
| 02 Dysthymia only (v AP) | BOYER1999 Amt (Ams) | 69/111 | 57/104 | 100.00 | 1.13 [0.90, 1.42] | 0 |
|                      | Subtotal (95% CI) | 111    | 104 | 100.00 | 1.13 [0.90, 1.42] |       |
| Total events:        | 69 (Treatment), 57 (Control) |        |     |        |                 |       |
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.09 (P = 0.28) |
| 03 Dysthymia \( \geq 50\% \) (v AP) | RAVIZZA1999 Amt/Ams | 62/85 | 106/165 | 100.00 | 1.14 [0.96, 1.35] | 0 |
|                      | Subtotal (95% CI) | 85     | 165 | 100.00 | 1.14 [0.96, 1.35] |       |
| Total events:        | 62 (Treatment), 106 (Control) |        |     |        |                 |       |
| Test for heterogeneity: not applicable  
Test for overall effect: Z = 1.44 (P = 0.15) |

Favours treatment Favours control
04.09 Number reporting side effects at endpoint: antipsychotic

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 Dysthymia only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEISLER1992 Flp/Rts</td>
<td>16/36</td>
<td>15/33</td>
<td>100.00</td>
<td>0.98</td>
<td>[0.58, 1.65]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>36</td>
<td>33</td>
<td>100.00</td>
<td>0.98</td>
<td>[0.58, 1.65]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 16 (Treatment), 15 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 0.08 (P = 0.93)

Pharm subthreshold 05 Relapse prevention: active treatment versus placebo
05.01 Recurrence at endpoint

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 TCAs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MILLER2001 A Dsp/Plb</td>
<td>0/14</td>
<td>6/13</td>
<td>0.07</td>
<td>0.07</td>
<td>[0.00, 1.16]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>14</td>
<td>13</td>
<td>100.00</td>
<td>0.07</td>
<td>[0.00, 1.16]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 0 (Treatment), 6 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 1.86 (P = 0.06)
**Psychological interventions**

**Psych sub-thresh 01 Psychological therapies versus control**

**01.01 Dichotomous outcomes at endpoint and follow-up**

Review: Depression Update Subthreshold: Psych  
Comparison: 01 Psychological therapies vs control  
Outcome: 01 Efficacy data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Number not responding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT99 D Px/Ps/Pb</td>
<td>56/115</td>
<td>66/112</td>
<td>71.14</td>
<td>0.83 [0.65, 1.05]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>16/24</td>
<td>18/26</td>
<td>28.86</td>
<td>0.96 [0.66, 1.41]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>139</td>
<td>138</td>
<td>100.00</td>
<td>0.86 [0.78, 1.06]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total events: 72 (Treatment), 84 (Control)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 0.45, df = 1 (P = 0.50), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.40 (P = 0.16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>02 Number not achieving remission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT99 D Px/Ps/Pb</td>
<td>62/115</td>
<td>70/112</td>
<td>100.00</td>
<td>0.86 [0.69, 1.08]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>115</td>
<td>112</td>
<td>100.00</td>
<td>0.86 [0.69, 1.08]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total events: 62 (Treatment), 70 (Control)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.31 (P = 0.19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

0.1  0.2  0.5  1  2  5  10  
Favours treatment  Favours control
### 01.02 Continuous outcomes at endpoint and follow-up

**Review:** Depression Update Subthreshold: Psych
**Comparison:** Psychological therapies vs control
**Outcome:** Efficacy data (continuous)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (random)</th>
<th>Weight</th>
<th>SMD (random)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>95% CI</td>
<td>%</td>
</tr>
<tr>
<td>01 Clinician-rated endpoint scores</td>
<td>97</td>
<td>6.90(5.10)</td>
<td>99</td>
<td>8.30(5.10)</td>
<td></td>
<td>100.00</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>97</td>
<td></td>
<td>99</td>
<td></td>
<td>100.00</td>
<td>-0.27</td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable
Test for overall effect: Z = 1.90 (P = 0.06)

### 01.03 Dropout at endpoint

**Review:** Depression Update Subthreshold: Psych
**Comparison:** Psychological therapies vs control
**Outcome:** Acceptability and tolerability data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>RR (fixed)</td>
<td>%</td>
<td>RR (fixed)</td>
<td></td>
</tr>
<tr>
<td>01 Leaving treatment early for any reason</td>
<td>20/115</td>
<td>21/112</td>
<td>89.85</td>
<td>0.93</td>
<td>0.53</td>
<td>1.61</td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>0/24</td>
<td>2/26</td>
<td>10.15</td>
<td>0.22</td>
<td>0.01</td>
<td>4.28</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>139</td>
<td>138</td>
<td>100.00</td>
<td>0.86</td>
<td>0.50</td>
<td>1.47</td>
</tr>
</tbody>
</table>

Total events: 20 (Treatment), 23 (Control)
Test for heterogeneity: Chi² = 0.90, df = 1 (P = 0.34), I² = 0%
Test for overall effect: Z = 0.57 (P = 0.57)
### Psych sub-thresh 02 Psychological therapies versus antidepressants

#### 02.01 Dichotomous outcomes at endpoint

**Review:** Depression Update Subthreshold: Psych  
**Comparison:** 02 Psychological therapies vs antidepressants  
**Outcome:** 01 Efficacy data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random) 95% CI</th>
<th>Weight</th>
<th>RR (random) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Number not responding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT99 D Px/Ps/Pb</td>
<td>56/115</td>
<td>51/111</td>
<td>38.57</td>
<td>1.06 [0.80, 1.40]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MARKOWITZ05 Ip/St/BS</td>
<td>20/23</td>
<td>20/24</td>
<td>51.31</td>
<td>1.04 [0.82, 1.33]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>16/24</td>
<td>10/22</td>
<td>10.11</td>
<td>1.47 [0.86, 2.51]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>162</td>
<td>157</td>
<td>100.00</td>
<td>1.09 [0.92, 1.29]</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 1.38, df = 2 (P = 0.50), I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random) 95% CI</th>
<th>Weight</th>
<th>RR (random) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>02 Number not remitting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT99 D Px/Ps/Pb</td>
<td>62/115</td>
<td>56/111</td>
<td>71.99</td>
<td>1.07 [0.83, 1.37]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MARKOWITZ05 Ip/St/BS</td>
<td>18/23</td>
<td>14/24</td>
<td>28.01</td>
<td>1.34 [0.90, 2.00]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>138</td>
<td>135</td>
<td>100.00</td>
<td>1.14 [0.92, 1.41]</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 0.91, df = 1 (P = 0.34), I² = 0%
Test for overall effect: Z = 1.20 (P = 0.23)
### 02.02 Continuous outcomes at endpoint and follow-up

**Review:** Depression Update Subthreshold: Psych
**Comparison:** Psychological therapies vs antidepressants
**Outcome:** Efficacy data (continuous)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment Mean (SD)</td>
<td>Control Mean (SD)</td>
<td>SMD (95% CI)</td>
<td></td>
<td>SMD (95% CI)</td>
<td></td>
</tr>
<tr>
<td>01 Clinician-rated mean endpoint</td>
<td>97  6.90(5.10)</td>
<td>88  5.80(4.50)</td>
<td>29.68 0.23 [-0.06, 0.52]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BROWN02 IPT/St/Comb</td>
<td>178  16.80(10.60)</td>
<td>196  14.30(9.80)</td>
<td>59.94 0.24 [0.04, 0.45]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUNNER1996 CT/Flx</td>
<td>10  10.80(5.50)</td>
<td>12  6.90(5.50)</td>
<td>3.30 0.68 [-0.19, 1.55]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARKOWITZ05 Ip/St/BS</td>
<td>23  12.50(5.90)</td>
<td>24  8.30(5.40)</td>
<td>7.09 0.73 [0.14, 1.32]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>308</td>
<td>320</td>
<td>100.00</td>
<td>0.29 [0.13, 0.45]</td>
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</tr>
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</table>

Test for heterogeneity: Chi² = 3.28, df = 3 (P = 0.35), I² = 8.6%
Test for overall effect: Z = 3.59 (P = 0.0003)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment Mean (SD)</td>
<td>Control Mean (SD)</td>
<td>SMD (95% CI)</td>
<td></td>
<td>SMD (95% CI)</td>
<td></td>
</tr>
<tr>
<td>02 Clinician-rated mean endpoint 6-month follow-up</td>
<td>167  15.30(10.60)</td>
<td>186  13.40(9.80)</td>
<td>100.00 0.19 [-0.02, 0.40]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>167</td>
<td>186</td>
<td>100.00</td>
<td>0.19 [-0.02, 0.40]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable
Test for overall effect: Z = 1.74 (P = 0.08)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment Mean (SD)</td>
<td>Control Mean (SD)</td>
<td>SMD (95% CI)</td>
<td></td>
<td>SMD (95% CI)</td>
<td></td>
</tr>
<tr>
<td>03 Clinician-rated mean endpoint 18-month follow-up</td>
<td>156  14.30(10.00)</td>
<td>179  11.70(9.70)</td>
<td>100.00 0.26 [0.05, 0.48]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>156</td>
<td>179</td>
<td>100.00</td>
<td>0.26 [0.05, 0.48]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: not applicable
Test for overall effect: Z = 2.40 (P = 0.02)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment Mean (SD)</td>
<td>Control Mean (SD)</td>
<td>SMD (95% CI)</td>
<td></td>
<td>SMD (95% CI)</td>
<td></td>
</tr>
<tr>
<td>04 Self-rated mean endpoint</td>
<td>9  9.10(5.20)</td>
<td>11  9.10(9.70)</td>
<td>30.46 0.00 [-0.88, 0.88]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUNNER1996 CT/Flx</td>
<td>23  12.80(8.90)</td>
<td>24  8.30(7.60)</td>
<td>69.54 0.54 [-0.05, 1.12]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>32</td>
<td>35</td>
<td>100.00</td>
<td>0.37 [-0.11, 0.86]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 0.99, df = 1 (P = 0.32), I² = 0%
Test for overall effect: Z = 1.50 (P = 0.13)
## 02.03 Dropout at endpoint

### Review: Depression Update Subthreshold: Psych
### Comparison: 02 Psychological therapies vs antidepressants
### Outcome: 03 Acceptability and tolerability data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Leaving treatment early for any reason</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARRETT99 D PxPsPb</td>
<td>20/115</td>
<td>28/111</td>
<td>79.86</td>
<td>0.69 [0.41, 1.15]</td>
<td>0</td>
</tr>
<tr>
<td>DUNNER1996 CT/Flx</td>
<td>1/13</td>
<td>6/18</td>
<td>5.25</td>
<td>0.23 [0.05, 1.69]</td>
<td>0</td>
</tr>
<tr>
<td>MARKowitz1995 p/S/BS</td>
<td>4/23</td>
<td>5/24</td>
<td>14.89</td>
<td>0.83 [0.26, 2.73]</td>
<td>0</td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>0/24</td>
<td>0/22</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>175</td>
<td>175</td>
<td>100.00</td>
<td>0.67 [0.42, 1.06]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 25 (Treatment), 39 (Control)
Test for heterogeneity: Chi² = 1.26, df = 2 (P = 0.53), I² = 0%
Test for overall effect: Z = 1.72 (P = 0.09)

### 02 Leaving treatment early due to side effects

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>DUNNER1996 CT/Flx</td>
<td>0/13</td>
<td>1/18</td>
<td>100.00</td>
<td>0.45 [0.02, 10.30]</td>
<td>0</td>
</tr>
</tbody>
</table>

Subtotal (95% CI): 13 18

Total events: 0 (Treatment), 1 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 0.50 (P = 0.62)

---

0.1 0.2 0.5 1 2 5 10
Favours treatment  Favours control
Psych sub-thresh 03 Psychological therapies + antidepressants versus antidepressants
03.01 Dichotomous outcomes at endpoint

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Number not responding</td>
<td>MARKOWITZ05 Ip/St/BS 20/21</td>
<td>20/24</td>
<td>70.87 1.14 [0.93, 1.40]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAVINDRAN1999 CBT/St 8/25</td>
<td>10/22</td>
<td>29.13 0.70 [0.34, 1.46]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI) 46</td>
<td>46</td>
<td>100.00 0.96 [0.52, 1.79]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total events: 28 (Treatment), 30 (Control)</td>
<td></td>
<td>Test for heterogeneity: Chi² = 2.90, df = 1 (P = 0.09), I² = 65.6%</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 0.12 (P = 0.91)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Number not remitting</td>
<td>MARKOWITZ05 Ip/St/BS 10/21</td>
<td>14/24</td>
<td>100.00 0.82 [0.47, 1.43]</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI) 21</td>
<td>24</td>
<td>100.00 0.82 [0.47, 1.43]</td>
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</tr>
<tr>
<td></td>
<td>Total events: 10 (Treatment), 14 (Control)</td>
<td></td>
<td>Test for heterogeneity: not applicable</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 0.71 (P = 0.48)</td>
<td></td>
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</tr>
</tbody>
</table>
### 03.02 Continuous outcomes at endpoint and follow-up

**Review:** Depression Update Subthreshold: Psych

**Comparison:** 03 Psychological therapies + antidepressants vs antidepressants

**Outcome:** 02 Efficacy data (continuous)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment N</th>
<th>Control N</th>
<th>SMD (fixed)</th>
<th>Weight %</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Clinician-rated mean endpoint</td>
<td>BROWNE02 IPT/Stl/Cmb 212</td>
<td>196</td>
<td>15.00(10.40)</td>
<td>14.30(9.80)</td>
<td>90.17</td>
<td>0.07 [-0.13, 0.26]</td>
</tr>
<tr>
<td></td>
<td>MARKOWITZ05 Ip/Stl/BS 21</td>
<td>24</td>
<td>9.90(6.30)</td>
<td>8.30(5.40)</td>
<td>9.83</td>
<td>0.27 [-0.32, 0.86]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>233</td>
<td>220</td>
<td>100.00</td>
<td>0.09 [-0.10, 0.27]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: $\chi^2 = 0.40$, df = 1 ($P = 0.53$), $I^2 = 0%$</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: $Z = 0.94$ ($P = 0.35$)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>02 Clinician-rated mean endpoint at 6-month follow-up</td>
<td>BROWNE02 IPT/Stl/Cmb 196</td>
<td>186</td>
<td>13.50(9.90)</td>
<td>13.40(9.80)</td>
<td>100.00</td>
<td>0.01 [-0.19, 0.21]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>196</td>
<td>186</td>
<td>100.00</td>
<td>0.01 [-0.19, 0.21]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: $Z = 0.10$ ($P = 0.92$)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>03 Clinician-rated mean endpoint at 18-month follow-up</td>
<td>BROWNE02 IPT/Stl/Cmb 190</td>
<td>179</td>
<td>12.30(9.90)</td>
<td>11.70(9.70)</td>
<td>100.00</td>
<td>0.06 [-0.14, 0.27]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>190</td>
<td>179</td>
<td>100.00</td>
<td>0.06 [-0.14, 0.27]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Test for overall effect: $Z = 0.59$ ($P = 0.56$)</td>
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</tbody>
</table>

Favours treatment  Favours control
### 03.03 Dropout at endpoint

**Review:** Depression Update Subthreshold: Psych  
**Comparison:** 03 Psychological therapies + antidepressants vs antidepressants  
**Outcome:** 03 Acceptability and tolerability data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 Leaving treatment early for any reason</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARKOWITZ05 Ip/St/BS</td>
<td>4/21</td>
<td>5/24</td>
<td>89.79</td>
<td>0.91</td>
<td>[0.28, 2.97]</td>
<td>0</td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>1/25</td>
<td>0/22</td>
<td>10.21</td>
<td>2.65</td>
<td>[0.11, 62.00]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>100.00</td>
<td>1.09</td>
<td>[0.37, 3.25]</td>
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</tr>
<tr>
<td>Total events: 5 (Treatment), 5 (Control)</td>
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</tr>
<tr>
<td>Test for heterogeneity:</td>
<td>Chi² = 0.39, df = 1 (P = 0.53),</td>
<td></td>
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<tr>
<td>Test for overall effect:</td>
<td>Z = 0.16 (P = 0.87)</td>
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</tbody>
</table>

**Psych sub-thresh 04 Psychological therapies + antidepressants versus psychological therapies**

**04.01 Dichotomous outcomes at endpoint**

**Review:** Depression Update Subthreshold: Psych  
**Comparison:** 04 Psychological therapies + antidepressants vs psychological therapies  
**Outcome:** 01 Efficacy data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
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<tr>
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<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 Number not responding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAVINDRAN1999 CBT/St</td>
<td>8/25</td>
<td>16/24</td>
<td>100.00</td>
<td>0.48</td>
<td>[0.25, 0.91]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>100.00</td>
<td>0.48</td>
<td>[0.25, 0.91]</td>
<td></td>
</tr>
<tr>
<td>Total events: 8 (Treatment), 16 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect:</td>
<td>Z = 2.26 (P = 0.02)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Favours treatment  
Favours control
## 04.02 Continuous outcomes at endpoint and follow-up

**Review:** Depression Update Subthreshold: Psych

**Comparison:** 04 Psychological therapies + antidepressants vs psychological therapies

**Outcome:** 02 Efficacy data (continuous)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Clinician-rated mean endpoint data</td>
<td>212</td>
<td>15.00 (10.40)</td>
<td>178</td>
<td>16.80 (10.60)</td>
<td>100.00</td>
<td>-0.17</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>212</td>
<td>178</td>
<td>100.00</td>
<td>-0.17</td>
<td>[-0.37, 0.03]</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 1.68 (P = 0.09)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Clinician-rated mean endpoint data 6-month follow-up</td>
<td>196</td>
<td>13.50 (9.90)</td>
<td>167</td>
<td>15.30 (10.60)</td>
<td>100.00</td>
<td>-0.18</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>196</td>
<td>167</td>
<td>100.00</td>
<td>-0.18</td>
<td>[-0.38, 0.03]</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 1.66 (P = 0.10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>03 Clinician-rated mean endpoint data 18-month follow-up</td>
<td>190</td>
<td>12.30 (9.90)</td>
<td>156</td>
<td>14.30 (10.00)</td>
<td>100.00</td>
<td>-0.20</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>190</td>
<td>156</td>
<td>100.00</td>
<td>-0.20</td>
<td>[-0.41, 0.01]</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 1.85 (P = 0.06)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Favours treatment Favours control
04.03 Dropout at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 04 Psychological therapies + antidepressants vs psychological therapies
Outcome: 03 Acceptability and tolerability data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>01 Leaving treatment early for any reason</td>
<td>RAVINDRAN1999 CBT/St</td>
<td>1/25</td>
<td>0/24</td>
<td>100.00</td>
<td>2.88 [0.12, 67.53]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>25</td>
<td>24</td>
<td>100.00</td>
<td>2.88 [0.12, 67.53]</td>
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<td></td>
</tr>
</tbody>
</table>

Total events: 1 (Treatment), 0 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 0.66 (P = 0.51)

Psych sub-thresh 05 Short psychodynamic verbal therapy versus short psychodynamic art therapy
05.01 Continuous outcomes at endpoint and follow-up

Review: Depression Update Subthreshold: Psych
Comparison: 05 Short Psychodynamic Verbal v Short Psychodynamic Art
Outcome: 01 Efficacy data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N Treatment</th>
<th>N Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
<td>Mean (SD)</td>
<td>95% CI</td>
<td>%</td>
</tr>
<tr>
<td>01 Self-rated mean endpoint</td>
<td>THYME07 vrbl v art/C</td>
<td>21</td>
<td>13.38(11.03)</td>
<td>18</td>
<td>14.44(7.35)</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>21</td>
<td>18</td>
<td>100.00</td>
<td>-0.11 [-0.74, 0.52]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Test for heterogeneity: not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N Treatment</th>
<th>N Control</th>
<th>SMD (fixed)</th>
<th>Weight</th>
<th>SMD (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
<td>Mean (SD)</td>
<td>95% CI</td>
<td>%</td>
</tr>
<tr>
<td>02 Self-rated mean endpoint at 3-month follow-up</td>
<td>THYME07 vrbl v art/C</td>
<td>21</td>
<td>10.67(7.20)</td>
<td>18</td>
<td>12.89(9.40)</td>
<td>100.00</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>21</td>
<td>18</td>
<td>100.00</td>
<td>-0.26 [-0.90, 0.37]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Test for heterogeneity: not applicable
Test for overall effect: Z = 0.81 (P = 0.42)

-10 -5 0 5 10
Favours treatment Favours control

-10 -5 0 5 10
Favours treatment Favours control
## 05.02 Dropout at endpoint

**Review:** Depression Update Subthreshold: Psych

**Comparison:** 07 Short Psychodynamic Verbal v Short Psychodynamic Art

**Outcome:** 02 Acceptability and tolerability data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
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<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Leaving treatment early for any reason</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THYME07 vrbl v art'C</td>
<td>1/22</td>
<td>3/21</td>
<td>100.00</td>
<td>0.32</td>
<td>[0.04, 2.82]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
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<td>21</td>
<td>100.00</td>
<td>0.32</td>
<td>[0.04, 2.82]</td>
</tr>
</tbody>
</table>

Total events: 1 (Treatment), 3 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 1.03 (P = 0.30)
### Psych sub-thresh 06 Partial responders: psychological therapy + SSRI versus SSRI

#### 06.01 Dichotomous outcomes at endpoint

**Review:** Depression Update Subthreshold: Psych  
**Comparison:** 08 Partial responders: Psych/SSRI combo v SSRI  
**Outcome:** 01 Efficacy data

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Number not responding</strong></td>
<td>Hellerstein01CBT/Fl</td>
<td>4/20</td>
<td>7/20</td>
<td>100.00</td>
<td>0.57 [0.20, 1.65]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>20</td>
<td>20</td>
<td>100.00</td>
<td>0.57 [0.20, 1.65]</td>
<td></td>
</tr>
<tr>
<td>Total events: 4 (Treatment), 7 (Control)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.03 (P = 0.30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>02 Number not responding at 12-week follow-up</strong></td>
<td>Hellerstein01CBT/Fl</td>
<td>9/20</td>
<td>14/20</td>
<td>100.00</td>
<td>0.64 [0.37, 1.13]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>20</td>
<td>20</td>
<td>100.00</td>
<td>0.64 [0.37, 1.13]</td>
<td></td>
</tr>
<tr>
<td>Total events: 9 (Treatment), 14 (Control)</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.54 (P = 0.12)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>03 Number not achieving remission</strong></td>
<td>Hellerstein01CBT/Fl</td>
<td>6/20</td>
<td>10/20</td>
<td>100.00</td>
<td>0.60 [0.27, 1.34]</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>20</td>
<td>20</td>
<td>100.00</td>
<td>0.60 [0.27, 1.34]</td>
<td></td>
</tr>
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<td>Total events: 6 (Treatment), 10 (Control)</td>
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<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.25 (P = 0.21)</td>
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<tr>
<td><strong>04 Number not achieving remission at 12-week follow-up</strong></td>
<td>Hellerstein01CBT/Fl</td>
<td>16/20</td>
<td>14/20</td>
<td>100.00</td>
<td>1.14 [0.80, 1.64]</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
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<td>20</td>
<td>20</td>
<td>100.00</td>
<td>1.14 [0.80, 1.64]</td>
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</tr>
<tr>
<td>Total events: 16 (Treatment), 14 (Control)</td>
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<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.72 (P = 0.47)</td>
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</tbody>
</table>
## 06.02 Dropout at endpoint

### Review:
**Depression Update Subthreshold: Psych**

### Comparison:
**Partial responders: Psych/SSRI combo v SSRI**

### Outcome:
**Acceptability and tolerability data**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td><strong>01 Leaving study early for any reason</strong></td>
<td>2/20</td>
<td>3/20</td>
<td>100.00</td>
<td>0.67 [0.12, 3.57]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hellerstein01CBT/RT</td>
<td>20</td>
<td>20</td>
<td>100.00</td>
<td>0.67 [0.12, 3.57]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>20</td>
<td>20</td>
<td></td>
<td></td>
<td>0.67 [0.12, 3.57]</td>
<td></td>
</tr>
</tbody>
</table>

**Total events:** 2 (Treatment), 3 (Control)

Test for heterogeneity: not applicable

Test for overall effect: $Z = 0.47$ ($P = 0.64$)

![Graph showing dropout at endpoint](image_url)