

<b>Combined</b>	-0.11 (-0.66 to 0.42)	-0.30 (-0.94 to 0.35)	-0.34 (-1.02 to 0.34)	-0.38 (-0.93 to 0.17)	-0.39 (-0.84 to 0.06)	-0.44 (-1.09 to 0.21)	-0.44 (-1.13 to 0.24)	-0.49 (-1.11 to 0.14)	-0.50 (-1.38 to 0.39)	-0.55 (-1.20 to 0.10)	-0.67 (-1.13 to -0.21)	-0.68 (-1.19 to -0.17)	-0.83 (-1.23 to -0.43)	-0.94 (-1.56 to -0.32)	-0.94 (-1.98 to 0.09)	-1.30 (-1.73 to -0.88)
1.09 (0.60 to 2.29)	<b>Individual CBT</b>	-0.18 (-0.83 to 0.47)	-0.22 (-0.92 to 0.47)	-0.27 (-0.81 to 0.28)	-0.27 (-0.72 to 0.19)	-0.32 (-0.94 to 0.30)	-0.33 (-0.99 to 0.33)	-0.37 (-1.00 to 0.27)	-0.38 (-1.27 to 0.51)	-0.43 (-1.05 to 0.19)	-0.56 (-1.00 to -0.11)	-0.56 (-1.03 to -0.11)	-0.72 (-1.13 to -0.30)	-0.82 (-1.41 to -0.24)	-0.83 (-1.85 to 0.19)	-1.19 (-1.56 to -0.81)
1.32 (0.68 to 3.93)	1.19 (0.58 to 3.44)	<b>MAOI</b>	-0.04 (-0.82 to 0.73)	-0.09 (-0.75 to 0.57)	-0.09 (-0.66 to 0.48)	-0.14 (-0.88 to 0.60)	-0.15 (-0.92 to 0.63)	-0.19 (-0.91 to 0.52)	-0.20 (-1.14 to 0.75)	-0.25 (-0.99 to 0.21)	-0.37 (-0.95 to 0.21)	-0.38 (-1.01 to 0.24)	-0.53 (-1.06 to 0.01)	-0.64 (-1.36 to 0.07)	-0.65 (-1.74 to 0.44)	-1.00 (-1.56 to -0.45)
1.39 (0.70 to 4.50)	1.25 (0.58 to 4.01)	1.04 (0.36 to 3.30)	<b>Benzodiazepines</b>	-0.05 (-0.74 to 0.66)	-0.05 (-0.67 to 0.58)	-0.10 (-0.87 to 0.68)	-0.11 (-0.91 to 0.70)	-0.15 (-0.90 to 0.62)	-0.16 (-1.13 to 0.83)	-0.21 (-0.98 to 0.56)	-0.33 (-0.95 to 0.30)	-0.34 (-1.00 to 0.33)	-0.49 (-1.08 to 0.10)	-0.60 (-1.34 to 0.15)	-0.61 (-1.72 to 0.50)	-0.96 (-1.56 to -0.36)
1.48 (0.83 to 3.85)	1.32 (0.72 to 3.29)	1.09 (0.42 to 2.81)	1.05 (0.37 to 2.76)	<b>Group CBT</b>	-0.00 (-0.48 to 0.47)	-0.05 (-0.69 to 0.58)	-0.06 (-0.74 to 0.61)	-0.10 (-0.75 to 0.54)	-0.11 (-1.00 to 0.79)	-0.17 (-0.80 to 0.47)	-0.29 (-0.72 to 0.14)	-0.30 (-0.80 to 0.20)	-0.45 (-0.88 to -0.03)	-0.55 (-1.17 to 0.06)	-0.56 (-1.59 to 0.46)	-0.92 (-1.33 to -0.51)
1.49 (0.93 to 3.29)	1.33 (0.79 to 2.85)	1.10 (0.48 to 2.43)	1.05 (0.40 to 2.42)	1.00 (0.49 to 1.97)	<b>SSRIs and SNRIs</b>	-0.05 (-0.63 to 0.53)	-0.06 (-0.68 to 0.57)	-0.10 (-0.63 to 0.44)	-0.11 (-0.93 to 0.71)	-0.16 (-0.74 to 0.42)	-0.28 (-0.64 to 0.07)	-0.29 (-0.71 to 0.12)	-0.44 (-0.67 to -0.22)	-0.55 (-1.09 to -0.01)	-0.56 (-1.55 to 0.43)	-0.91 (-1.23 to -0.60)
1.58 (0.80 to 4.97)	1.42 (0.71 to 4.20)	1.16 (0.42 to 3.63)	1.11 (0.36 to 3.51)	1.06 (0.44 to 2.92)	1.06 (0.49 to 2.69)	<b>SHWS</b>	-0.01 (-0.75 to 0.74)	-0.05 (-0.77 to 0.68)	-0.06 (-1.01 to 0.90)	-0.11 (-0.79 to 0.57)	-0.23 (-0.79 to 0.33)	-0.24 (-0.83 to 0.34)	-0.39 (-0.93 to 0.15)	-0.50 (-1.19 to 0.19)	-0.51 (-1.59 to 0.56)	-0.86 (-1.36 to -0.36)
1.59 (0.77 to 5.48)	1.43 (0.68 to 4.60)	1.18 (0.41 to 3.94)	1.12 (0.36 to 3.84)	1.07 (0.43 to 3.16)	1.07 (0.47 to 2.98)	1.01 (0.34 to 3.15)	<b>EXPO</b>	-0.04 (-0.80 to 0.73)	-0.05 (-1.03 to 0.93)	-0.10 (-0.85 to 0.64)	-0.23 (-0.82 to 0.37)	-0.24 (-0.87 to 0.39)	-0.39 (-0.98 to 0.20)	-0.49 (-1.23 to 0.24)	-0.50 (-1.60 to 0.60)	-0.86 (-1.42 to -0.29)
1.69 (0.86 to 5.47)	1.51 (0.74 to 4.79)	1.24 (0.47 to 3.87)	1.18 (0.40 to 3.83)	1.12 (0.47 to 3.25)	1.12 (0.56 to 2.81)	1.06 (0.36 to 3.30)	1.05 (0.33 to 3.38)	<b>Anti-convulsants</b>	-0.01 (-0.93 to 0.92)	-0.06 (-0.79 to 0.66)	-0.19 (-0.81 to 0.37)	-0.19 (-0.81 to 0.41)	-0.34 (-0.84 to 0.14)	-0.45 (-1.16 to 0.25)	-0.46 (-1.54 to 0.62)	-0.81 (-1.36 to -0.28)
1.70 (0.68 to 9.03)	1.53 (0.58 to 7.86)	1.25 (0.37 to 6.30)	1.19 (0.33 to 6.12)	1.14 (0.36 to 5.38)	1.14 (0.41 to 4.87)	1.07 (0.29 to 5.29)	1.06 (0.27 to 5.41)	1.01 (0.28 to 4.67)	<b>NSSA</b>	-0.05 (-1.01 to 0.90)	-0.17 (-1.02 to 0.66)	-0.18 (-1.06 to 0.68)	-0.34 (-1.13 to 0.45)	-0.44 (-1.38 to 0.49)	-0.45 (-1.70 to 0.79)	-0.80 (-1.64 to 0.01)
1.85 (0.90 to 6.24)	1.65 (0.81 to 5.21)	1.34 (0.49 to 4.47)	1.28 (0.43 to 4.47)	1.22 (0.51 to 3.57)	1.22 (0.56 to 3.33)	1.14 (0.42 to 3.41)	1.13 (0.37 to 3.62)	1.08 (0.36 to 3.42)	1.06 (0.22 to 4.26)	<b>SHNS</b>	-0.12 (-0.68 to 0.43)	-0.13 (-0.71 to 0.45)	-0.28 (-0.83 to 0.26)	-0.39 (-1.08 to 0.68)	-0.40 (-1.47 to 0.68)	-0.75 (-1.25 to -0.26)
2.26 (1.18 to 5.73)	2.02 (1.11 to 4.83)	1.61 (0.72 to 4.15)	1.52 (0.62 to 4.12)	1.46 (0.81 to 3.12)	1.46 (0.91 to 2.85)	1.36 (0.59 to 3.36)	1.34 (0.55 to 3.44)	1.27 (0.54 to 3.15)	1.25 (0.31 to 4.18)	1.18 (0.48 to 2.85)	<b>PSYP</b>	-0.01 (-0.38 to 0.36)	-0.16 (-0.45 to 0.13)	-0.27 (-0.80 to 0.26)	-0.27 (-1.26 to 0.70)	-0.63 (-0.90 to -0.36)
2.28 (1.15 to 6.30)	2.04 (1.10 to 5.09)	1.62 (0.69 to 4.57)	1.54 (0.60 to 4.49)	1.48 (0.74 to 3.55)	1.48 (0.84 to 3.23)	1.37 (0.58 to 3.60)	1.36 (0.52 to 3.75)	1.29 (0.51 to 3.45)	1.26 (0.31 to 4.51)	1.19 (0.47 to 3.01)	1.01 (0.55 to 1.89)	<b>PDPT</b>	-0.15 (-0.52 to 0.21)	-0.26 (-0.81 to 0.29)	-0.26 (-1.27 to 0.73)	-0.62 (-0.93 to -0.31)
3.00 (1.37 to 7.25)	2.64 (1.29 to 6.30)	2.08 (1.01 to 5.26)	1.96 (0.85 to 5.29)	1.89 (1.04 to 4.20)	1.93 (1.23 to 3.18)	1.74 (0.79 to 4.44)	1.72 (0.72 to 4.65)	1.63 (0.79 to 3.80)	1.59 (0.45 to 5.24)	1.50 (0.65 to 3.77)	1.27 (0.81 to 2.17)	1.25 (0.70 to 2.43)	<b>Placebo pill</b>	-0.11 (-0.62 to 0.40)	-0.11 (-1.09 to 0.85)	-0.47 (-0.71 to -0.23)
3.52 (1.30 to 13.47)	3.14 (1.24 to 11.13)	2.48 (0.91 to 9.60)	2.34 (0.79 to 9.60)	2.25 (0.93 to 7.62)	2.26 (1.01 to 7.06)	2.08 (0.75 to 7.54)	2.05 (0.69 to 7.54)	1.94 (0.67 to 7.20)	1.88 (0.43 to 8.95)	1.79 (0.62 to 6.41)	1.51 (0.67 to 4.32)	1.49 (0.63 to 4.38)	1.19 (0.52 to 3.13)	<b>OTHER</b>	-0.01 (-0.99 to 0.98)	-0.36 (-0.84 to 0.12)
3.51 (0.92 to 30.53)	3.13 (0.83 to 26.07)	2.49 (0.57 to 21.32)	2.37 (0.51 to 20.38)	2.26 (0.56 to 17.79)	2.27 (0.60 to 17.25)	2.10 (0.46 to 17.07)	2.07 (0.44 to 17.35)	1.97 (0.42 to 16.21)	1.89 (0.30 to 18.27)	1.82 (0.38 to 14.32)	1.53 (0.37 to 10.66)	1.51 (0.36 to 10.82)	1.20 (0.29 to 8.02)	1.01 (0.21 to 6.52)	<b>EXER</b>	-0.36 (-1.32 to 0.61)
7.07 (2.27 to 19.54)	6.32 (2.21 to 15.60)	4.86 (1.82 to 14.13)	4.57 (1.68 to 13.83)	4.44 (1.90 to 10.66)	4.49 (2.01 to 9.54)	4.06 (1.68 to 10.64)	3.98 (1.56 to 11.35)	3.76 (1.53 to 10.52)	3.60 (0.97 to 14.26)	3.47 (1.49 to 8.97)	2.96 (1.66 to 5.45)	2.90 (1.58 to 5.64)	2.28 (1.43 to 3.87)	1.88 (0.79 to 4.57)	1.84 (0.30 to 8.63)	<b>Waitlist</b>

Figure 4: Efficacy of classes of interventions

Classes of interventions are ordered according to efficacy ranking from largest mean effect (top, left) to smallest mean effect (bottom, right). Data in blue represent the effects on symptoms of social anxiety (SMD [95% CrI]); SMD less than 0 favours the intervention in the row. Data in green represent the effects on recovery (RR [95% CrI]); RR greater than 1 favours the intervention in the column. Significant results are shaded dark blue and dark green. CBT=cognitive-behavioural therapy. CrI=credible interval. EXER=promotion of exercise. EXPO=exposure and social skills. MAOI=monoamine oxidase inhibitors. NSSA=noradrenergic and specific serotonergic antidepressants. OTHER=other psychological therapy. PDPT=psychodynamic psychotherapy. PSYP=psychological placebo. RR=risk ratio. SHNS=self-help without support. SHWS=self-help with support. SMD=standardised mean difference. SNRI=serotonin-norepinephrine reuptake inhibitors. SSRI=selective serotonin-reuptake inhibitor.

-1.73 to -0.88; table; figure 4), but the quality of the evidence was poor. Five different combinations of psychological and pharmacological interventions were assessed in one trial each; all reported large effects, but only 156 participants received combined interventions across all five trials. There was no evidence that combined interventions had greater effects than the leading monotherapies (table).

### Discussion

To our knowledge, this is the first time that psychological and pharmacological interventions for a mental health problem have been compared in network meta-analysis.<sup>16</sup> The findings confirm that social anxiety disorder responds well to treatment, although many people continue to experience some symptoms after the end of the acute treatment phase.

Several classes of pharmacological and psychological intervention had greater effects on outcomes than did waitlist. Individual CBT and the class including SSRIs and SNRIs also had greater effects on outcomes than appropriate placebos, suggesting that they have specific effects. Psychological and pill placebo had greater effects than waitlist; investigation of these effects suggests that non-specific factors might account for about half the total

effects of individual CBT and SSRIs. Comparisons between psychological interventions revealed some evidence of differential effects. In particular, individual CBT had a greater effect than psychodynamic psychotherapy and other psychological therapies (interpersonal psychotherapy, mindfulness, and supportive therapy). Many of the psychological treatments with large effects were versions of CBT (individual, group, or self-help), suggesting that CBT might be efficacious in a range of formats. Psychodynamic psychotherapy was also effective, although its effects were similar to psychological placebo.

Because pharmacological and psychological interventions were both efficacious, a logical question to ask is whether combined interventions might be more helpful than either intervention alone. Although large effect sizes were noted with combined treatments, only a few small studies were included, and there was no evidence that any combination was more efficacious than the leading pharmacological or psychological monotherapy in that combination.

There was little evidence of differential efficacy within or between classes of drugs. In the case of SSRIs and SNRIs, this finding is consistent with data from a previous network analysis, which showed no differences in efficacy but differences in tolerability.<sup>17</sup>

In the absence of convincing evidence for differential efficacy, differences in tolerability and side-effects are particularly important in the choice of treatment. SSRIs and SNRIs with a short half-life (eg, paroxetine and venlafaxine) are associated with the greatest risk of discontinuation effects, including effects during the treatment period and after the end of treatment.<sup>18,19</sup> Some side-effects such as increased agitation<sup>18</sup> and sexual dysfunction<sup>20</sup> can be especially distressing for people with social anxiety disorder, particularly if these effects are unexpected or if they reinforce existing worries. These issues should be discussed with patients before starting drug treatment.

We were not able to investigate whether immediate treatment effects persist or diminish in the long term because most trials stopped at the end of treatment. Findings from studies that have addressed this issue<sup>21,22</sup> suggest that most people who respond to a SSRI will relapse within a few months if the drug is discontinued after acute treatment, and about 25% of people who respond to SSRI treatment and continue drug treatment will relapse within 6 months. By contrast, the effects of psychological interventions are generally well maintained at follow-up,<sup>23</sup> and participants can continue to apply new skills and make further gains after the end of acute treatment.<sup>24</sup> For this reason, and because of the lower risk of side-effects, psychological interventions should be preferred over pharmacological interventions for initial treatment.<sup>25</sup>

This study has several limitations. There were only a few studies of moderate size for several included interventions, and some have only been tested by one or two research groups. We included a broad range of interventions, which varied in duration, and there might be unknown differences among participants in different trials. However, we did not identify any systematic differences in participant demographics or initial symptom severity. Direct and indirect results were consistent, which provides further support to the pooled results. Control conditions were heterogeneous and rarely described in detail. Future trials should more clearly describe what was intended and what was actually received by people in control conditions.<sup>26,27</sup> Statistical power might have been limited because we used scores after treatment rather than the change in scores and because we calculated effects conservatively, estimating effects accounting for dropout (eg, using last-observation-carried-forward) where possible. Conversely, pairwise analyses of small studies sometimes overestimate effects compared with large studies.<sup>28,29</sup> Uncertainty in mean effects (ie, large CrIs) suggests that more research would improve our understanding of how these treatments compare. Specifically, large trials that compare active interventions and independent replications would improve the precision of these estimates and increase confidence in their external validity. We included only outcomes at the end of treatment; trials comparing active interventions with controlled long-term follow-up would provide better evidence of sustained effects.

Data for cost-effectiveness and side-effects both affect choices, and a cost-effectiveness analysis will be reported elsewhere. Taking these factors into account, NICE recently concluded that individual CBT should be offered as the treatment of choice for social anxiety disorder. For individuals who decline individual CBT, a SSRI is recommended for people who would prefer drug treatment and CBT-based supported self-help is recommended for people who prefer another psychological intervention. Psychodynamic psychotherapy is recommended as a third-line option, and other drugs are recommended only for people who do not respond to initial treatments.<sup>25,30</sup> Thus, NICE recommendations are consistent with the results of this study, which suggests that increased access to treatment would reduce disability and improve quality of life for people with social anxiety disorder.

#### Contributors

EM-W drafted the protocol with all authors. EM-W and KK assessed the eligibility of the studies for inclusion, extracted data, and assessed risk of bias. SD and AEA developed the statistical code with EM-W and IM, and SD did the analysis. All authors contributed to the interpretation of the findings. EM-W drafted the manuscript, to which all authors contributed. SP obtained funding.

#### Declaration of interests

DMC is the developer of one of the versions of individual CBT that was shown to be efficacious. All other authors declare no competing interests.

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