the identification and management of social anxiety disorder. NICE also approved funding for the Technical Support Unit to support NCCMH in undertaking a network meta-analysis of intervention studies.

The funder of the study had no further role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between 1988 and Sept 13, 2013, we identified 168 potentially eligible studies, 12 of which were excluded: four were ongoing studies and for eight studies we could not identify a complete study report. We assessed 156 studies for eligibility (figure 1). 55 studies were excluded (appendix A) because they did not include an eligible intervention (n=29), reported no usable data (n=20), included no intervention already in the analysis and thus were not connected to this network (n=2), reported implausible outcomes (n=2), included a different population (n=1), or were not a randomised trial (n=1). 101 studies were included in the network analysis (appendix A).

14 229 participants were randomly assigned in the trials, and 13 164 were included in the analysis because some trials did not report outcomes for all participants. There were 18–839 participants per study. Trials assessed 41 interventions or control conditions, which were grouped into 17 classes. Most trials included two groups (n=64), but some included three (n=28), four (n=7), or five groups (n=2). The median and mean duration of treatment was 12 weeks (range 2–28 weeks). Few studies provided controlled results for long-term follow-up, and so long-term follow-up data were not included in our analyses.

Participants had severe and longstanding social anxiety; of 65 studies reporting baseline Liebowitz Social Anxiety Scale[13] scores, the median of means was 78 (appendix A). The median of means age was 36 years and the median of percentages of participants who were white was 80%. About half of the included participants were women (52% median of means). Most psychological studies did not exclude participants receiving drug treatment, but trials of psychological interventions generally required participants to be on a stable dose of drug treatment for several months before random allocation. Participants were not receiving drug treatment in 44 trials. In 27 trials, 27% of participants (median of means) were receiving drug treatment at randomisation. The demographic characteristics of participants were similar across comparisons (appendix A), and there were no obvious differences in the initial severity of social anxiety symptoms; variation in severity was limited because studies had similar inclusion criteria.

We assessed all included trials for risk of bias (appendix A). Sequence generation and allocation concealment were adequately described in 74 and 69 trials, respectively (appendix A). Trials of psychological interventions were regarded as at high risk of bias for participant and provider masking per se, although treatment effects and side-effects could also make maintenance of masking difficult in pharmacological trials. Most reported outcomes were self-rated, and assessors were aware of treatment assignment in five trials. For incomplete outcome data, 26 trials were at high risk of bias (eg, those that reported only completer analyses and those with lots of missing data), and how missing data were handled was unclear in four trials.

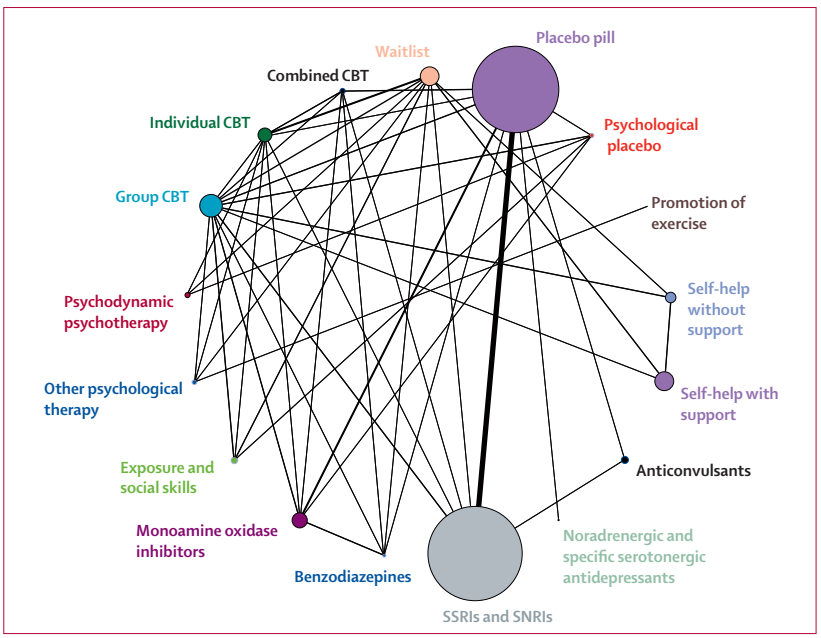

Figure 2: **Network diagram representing direct comparisons among classes**
The width of lines represents the number of trials in which each direct comparison is made. The size of each circle represents the number of people who received each treatment. CBT=cognitive–behavioural therapy. SNRI=serotonin–norepinephrine reuptake inhibitor. SSRI=selective serotonin-reuptake inhibitor.

Most included trials were not registered; only 37 trials were at low risk of selective outcome reporting bias (appendix A). In addition to risk of selective outcome reporting for included studies, there is risk of reporting bias because we could not locate a full report for eight studies, 20 studies reported no usable data, and two studies reported implausible outcomes. Results can be overestimated as a result of publication bias, particularly for interventions developed before mandatory trial registration. Unpublished information was obtained from trial investigators for 34 studies, including unpublished outcomes for 22 trials.

Excluding masking of participants and providers, which was impossible in studies of psychological interventions and difficult to maintain in studies of pharmacological interventions, only 28 trials were at low risk of bias for all other domains assessed by the Cochrane risk of bias assessment (appendix A).

Figure 2 shows the network of comparisons among classes. Of 820 possible comparisons among

	Trials	Participants	Class effect SMD (95% CrI)	Individual effect SMD (95% CrI)
Controls				
Waitlist	28	802	Reference	Reference
Placebo pill	42	3623	−0·47 (−0·71 to −0·23)	..
Psychological placebo	6	145	−0·63 (−0·90 to −0·36)	..
Pharmacological interventions				
Anticonvulsants	5	242	−0·81 (−1·36 to −0·28)	..
Gabapentin	1	34	..	−0·89 (−1·42 to −0·37)
Levetiracetam	1	9	..	−0·83 (−1·50 to −0·18)
Pregabalin	3	199	..	−0·72 (−1·07 to −0·37)
Benzodiazepines	5	112	−0·96 (−1·56 to −0·36)	..
Alprazolam	1	12	..	−0·85 (−1·40 to −0·30)
Clonazepam	4	100	..	−1·07 (−1·44 to −0·70)
Monoamine oxidase inhibitors	11	615	−1·01 (−1·56 to −0·45)	..
Moclobemide	6	490	..	−0·74 (−1·03 to −0·44)
Phenelzine	5	125	..	−1·28 (−1·57 to −0·98)
Noradrenergic and specific serotonergic antidepressants (mirtazapine)	1	30	−0·80 (−1·64 to 0·01)	−0·81 (−1·45 to −0·16)
SSRIs and SNRIs	32	4043	−0·91 (−1·23 to −0·60)	..
Citalopram	2	18	..	−0·83 (−1·28 to −0·39)
Escitalopram	2	675	..	−0·88 (−1·20 to −0·56)
Fluoxetine	3	107	..	−0·87 (−1·16 to −0·57)
Fluvoxamine	5	500	..	−0·94 (−1·25 to −0·63)
Paroxetine	12	1449	..	−0·99 (−1·26 to −0·73)
Sertraline	3	535	..	−0·92 (−1·23 to −0·61)
Venlafaxine	5	759	..	−0·96 (−1·25 to −0·67)
Psychological and behavioural interventions				
Exercise promotion	1	18	−0·36 (−1·32 to 0·61)	−0·36 (−1·07 to 0·36)
Exposure and social skills	10	227	−0·86 (−1·42 to −0·29)	..
Exposure in vivo	9	199	..	−0·83 (−1·07 to −0·59)
Social skills training	1	28	..	−0·88 (−1·38 to −0·38)
Group CBT	28	984	−0·92 (−1·33 to −0·51)	..
Heimberg model	11	338	..	−0·80 (−1·02 to −0·58)
Other (no model specified)	16	583	..	−0·85 (−1·04 to −0·68)
Enhanced CBT	1	63	..	−1·10 (−1·49 to −0·71)
Individual CBT	15	562	−1·19 (−1·56 to −0·81)	..
Hope, Heimberg, and Turk model	2	53	..	−1·02 (−1·42 to −0·62)
Other (no model specified)	6	163	..	−1·19 (−1·48 to −0·89)
Clark and Wells cognitive therapy model	3	97	..	−1·56 (−1·85 to −1·27)
Clark and Wells cognitive therapy shortened sessions	4	249	..	−0·97 (−1·21 to −0·74)
Other psychological therapy	7	182	−0·36 (−0·84 to 0·12)	..
Interpersonal psychotherapy	2	64	..	−0·43 (−0·83 to 0·04)
Mindfulness training	3	64	..	−0·39 (−0·82 to 0·03)
Supportive therapy	2	54	..	−0·26 (−0·72 to 0·20)
Psychodynamic psychotherapy	3	185	−0·62 (−0·93 to −0·31)	..
Self-help with support	16	748	−0·86 (−1·36 to −0·36)	..
Book with support	3	52	..	−0·85 (−1·17 to −0·53)
Internet with support	13	696	..	−0·88 (−1·04 to −0·71)

(Table continues on next page)

41 intervention or control conditions, 84 were studied directly (appendix A). 76 studies compared interventions with a control group; most drugs were compared with placebo, and most psychological interventions were compared with waitlist or with psychological placebo. The network also included 58 studies that compared active interventions, including four studies that compared psychological with pharmacological interventions.

25 trials also reported recovery (appendix A), and we compared effects for continuous measures and loss of diagnosis for these studies, which suggested that continuous values provide lower treatment effects compared with odds ratios of recovery.

There was potential for inconsistency in nine of the 44 loops in the network—others were formed by multi-arm trials that are consistent by definition. There were no substantial differences in magnitude and direction between the results of the network meta-analysis and the results of pairwise comparisons. The posterior mean of the residual deviance was 165·3 in the standard network meta-analysis model compared with 176·3 in the independent-effect model that compares favourably with the number of treatment groups (n=148), suggesting the network better estimates treatment effects than pairwise analyses alone with no evidence of inconsistency.[9]

The random-effects class model was a good fit to the data compared with the individual-effects model (deviance information criterion 364·8 *vs* 371·0; lower values suggest a better fit), although the between-trials SD for heterogeneity had a posterior median of 0·19 (95% CrI 0·14–0·25). That is, there was some variability between classes that might be attributable to differences among the individual treatments beyond the within-class variability. For classes with few members, there was little information about within-class variability and the prior for within-class variability led to increased uncertainty in the estimated class effects.

All pharmacological interventions apart from noradrenergic and specific serotonergic antidepressants had greater effects on outcomes compared with waitlist (table; figure 3). Mirtazapine, a noradrenergic and sepcific serotonergic antidepressant, was the only pharmacological intervention in a class by itself; its effect was not greater than that for waitlist (class effect SMD −0·80, 95% CrI −1·64 to 0·01), but only 30 people received the intervention. The largest effects were for MAOIs (class effect SMD −1·01, 95% CrI −1·56 to −0·45) and benzodiazepines (−0·96, −1·56 to −0·36), but the evidence for these effects was limited compared with evidence for SSRIs and SNRIs (−0·91, −1·23 to −0·60); more people received SSRIs and SNRIs (n=4043) than all other pharmacological interventions (n=999) or all psychological interventions (n=3312).

All psychological interventions apart from promotion of exercise and other psychological therapies (supportive therapy, mindfulness, and interpersonal psychotherapy) had greater effects on outcomes than did waitlist (table;

figure 3). In decreasing order of effect size, these were individual cognitive–behavioural therapy (CBT; class effect SMD –1·19, 95% CrI –1·56 to –0·81), group CBT (–0·92, –1·33 to –0·51), exposure and social skills (–0·86, –1·42 to –0·29), self-help with support (–0·86, –1·36 to –0·36), self-help without support (–0·75, –1·25 to –0·26), and psychodynamic psychotherapy (–0·62, –0·93 to –0·31).

Compared with pill placebo, MAOIs (SMD –0·53, 95% CrI –1·06 to –0·01) and SSRIs and SNRIs (–0·44, –0·67 to –0·22) had greater effects on outcomes, and pill placebo itself had a greater effect than waitlist (–0·47, –0·71 to –0·23; figure 4). Of the psychological interventions, only individual CBT had a greater effect on outcomes than psychological placebo (SMD –0·56, 95% CrI –1·00 to –0·11). Individual CBT also had a greater effect than pill placebo (SMD –0·72, 95% CrI –1·13 to –0·30), psychodynamic psychotherapy (–0·56, –1·00 to –0·11), and other therapies (–0·82, –1·41 to –0·24; figure 4). Figure 4 also expresses these treatment effects on the probability of recovery (ie, no longer meeting criteria for diagnosis).

Of the pharmacological interventions, there were greater individual effects compared with waitlist for all SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) and the SNRI venlafaxine. Effects of SSRIs and SNRIs were measured in 32 studies, and they were similar in magnitude within the class except for citalopram, which was assessed in two small studies; all individual SMDs were within 0·08 of the class SMD. Compared with waitlist, the effects of the MOAIs phenelzine (SMD –1·28, –1·57 to –0·98) and moclobemide (–0·74, –1·03 to –0·44) were also greater; however, only 125 people received phenelzine across five trials and the results might be overestimated. The large effect for phenelzine was dissimilar to the small effect for moclobemide (appendix B), which was the only other MAOI included in the analysis.

The most efficacious psychological interventions were individual CBT—following the Clark and Wells model (SMD –1·56, 95% CrI –1·85 to –1·27),[14] the Hope, Heimberg and Turk model (–1·02, –1·42 to –0·62),[15] and CBT not following a named manual (–1·19, –1·48 to –0·89)—and group enhanced CBT (–1·10, –1·49 to –0·71; table). Supported self-help was efficacious when provided via the internet (SMD –0·88, 95% CrI –1·04 to –0·71) or by book (–0·85, –1·17 to –0·53). Psychological placebo also had a greater effect than waitlist (SMD –0·63, 95% CrI –0·90 to –0·36), and its effect was comparable to psychodynamic psychotherapy (–0·62, –0·93 to –0·31).

Several drugs had greater effects on outcomes compared with pill placebo: clonazepam, escitalopram, fluoxetine, fluvoxamine, moclobemide, paroxetine, phenelzine, sertraline, and venlafaxine (appendix B). Citalopram was the only included SSRI that did not have a greater effect than placebo. Of the psychological interventions, only Clark and Wells cognitive therapy model, Clark and Wells cognitive therapy model with shortened sessions, individual CBT, and group enhanced CBT had greater effects than psychological placebo. There was no consistent evidence of differential efficacy within pharmacotherapies. There was some evidence of differential efficacy within the psychological interventions. Individual CBT according to the Clark and Wells manual showed the most consistent evidence of greater effects, as suggested by non-overlapping 95% CrIs between this intervention and most other psychological intervention (table).

Combined interventions had greater effects on outcomes than waitlist overall (SMD –1·30, 95% CrI

	Trials	Participants	Class effect SMD (95% CrI)	Individual effect SMD (95% CrI)
(Continued from previous page)				
Self-help without support	9	406	–0·75 (–1·25 to –0·26)	..
Book without support	4	136	..	–0·84 (–1·08 to –0·60)
Internet without support	5	270	..	–0·66 (–0·94 to –0·39)
Combined interventions				
Combined	5	156	–1·30 (–1·73 to –0·88)	..
Group CBT and moclobemide	1	22	..	–1·23 (–1·72 to –0·74)
Group CBT and fluoxetine	1	59	..	–0·95 (–1·34 to –0·58)
Group CBT and phenelzine	1	32	..	–1·69 (–2·10 to –1·27)
Psychodynamic and clonazepam	1	29	..	–1·28 (–1·82 to –0·74)
Paroxetine and clonazepam	1	14	..	–1·35 (–1·93 to –0·79)

CBT=cognitive–behavioural therapy. CrI=credible interval. SMD=standardised mean difference. SNRI=serotonin–norepinephrine reuptake inhibitor. SSRI=selective serotonin-reuptake inhibitor.

Table: **Summary of treatment effects compared with waitlist**

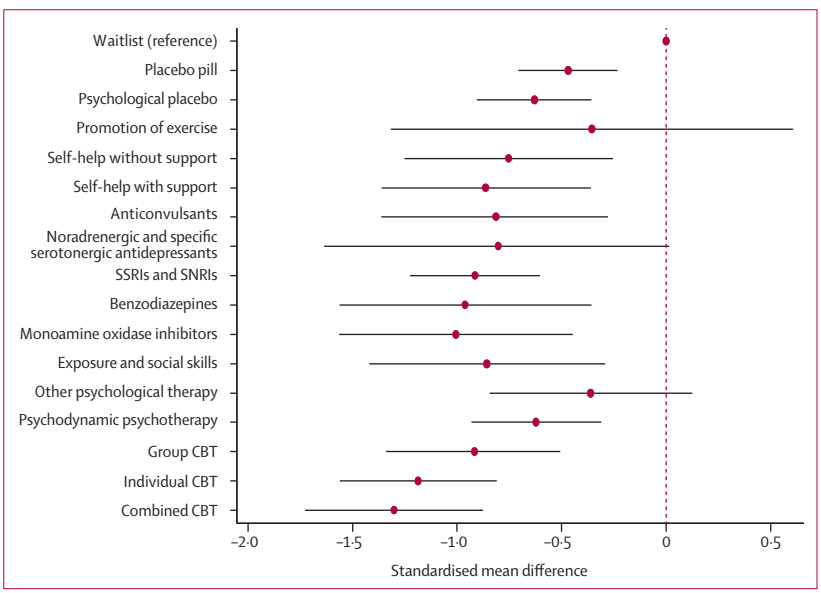

Figure 3: **Effect of each class of intervention compared with waitlist**
Data are standardised mean difference and 95% credible intervals compared with waitlist as a reference. CBT=cognitive–behavioural therapy. SNRI=serotonin–norepinephrine reuptake inhibitor. SSRI=selective serotonin-reuptake inhibitor.