Psychological and pharmacological interventions for social anxiety disorder in adults: a systematic review and network meta-analysis

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Summary

Background Social anxiety disorder—a chronic and naturally unremitting disease that causes substantial impairment—can be treated with pharmacological, psychological, and self-help interventions. We aimed to compare these interventions and to identify which are most effective for the acute treatment of social anxiety disorder in adults.

Methods We did a systematic review and network meta-analysis of interventions for adults with social anxiety disorder, identified from published and unpublished sources between 1988 and Sept 13, 2013. We analysed interventions by class and individually. Outcomes were validated measures of social anxiety, reported as standardised mean differences (SMDs) compared with a waitlist reference. This study is registered with PROSPERO, number CRD42012003146.

Findings We included 101 trials (13 164 participants) of 41 interventions or control conditions (17 classes) in the analyses. Classes of pharmacological interventions that had greater effects on outcomes compared with waitlist were monoamine oxidase inhibitors (SMD –1·01, 95% credible interval [CrI] –1·56 to –0·45), benzodiazepines (–0·96, –1·56 to –0·36), selective serotonin-reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors (SSRIs and SNRIs; –0·91, –1·23 to –0·60), and anticonvulsants (–0·81, –1·36 to –0·28). Compared with waitlist, efficacious classes of psychological interventions were individual cognitive–behavioural therapy (CBT; 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). Individual CBT compared with psychological placebo (SMD –0·56, 95% CrI –1·00 to –0·11), and SSRIs and SNRIs compared with pill placebo (–0·44, –0·67 to –0·22) were the only classes of interventions that had greater effects on outcomes than appropriate placebo. Individual CBT also had a greater effect than psychodynamic psychotherapy (SMD –0·56, 95% CrI –1·03 to –0·11) and interpersonal psychotherapy, mindfulness, and supportive therapy (–0·82, –1·41 to –0·24).

Interpretation Individual CBT (which other studies have shown to have a lower risk of side-effects than pharmacotherapy) is associated with large effect sizes. Thus, it should be regarded as the best intervention for the initial treatment of social anxiety disorder. For individuals who decline psychological intervention, SSRIs show the most consistent evidence of benefit.

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Introduction

Social anxiety disorder, or social phobia, affects 7% of the population[1] and follows a chronic and debilitating course if untreated.[2] Findings from meta-analyses suggest that the disorder responds well to pharmacological,[3] psychological,[4] and self-help interventions,[5] but most reviews have been limited to pairwise comparisons of subsets of these interventions.

Network meta-analysis has the advantage that all interventions that have been tested in randomised controlled trials (RCTs) can be simultaneously compared and their effects can be estimated relative to each other and to a common reference condition (eg, waitlist). Estimates of the effects of pairs of treatments that have often, rarely, or never been directly compared in a RCT can be calculated. As a consequence, network meta-analysis overcomes some of the limitations of traditional meta-analysis, in which conclusions are largely restricted to comparisons between treatments that have been directly compared in RCTs.

We undertook a network meta-analysis of all psychological and pharmacological interventions that are used in routine clinical practice for the initial treatment of social anxiety disorder and have been tested in RCTs.

Methods

Search strategy and selection criteria

We did a systematic review of interventions for social anxiety disorder according to Preferred Reporting Items

for Systematic reviews and Meta-Analyses (PRISMA) guidelines.[6] We searched the following databases between 1988 and Sept 13, 2013, with no language limits set, for published and unpublished studies on treatment of adults with social anxiety disorder: Australian Education Index, Allied and Complementary Medicine Database, Applied Social Services Index and Abstracts, British Education Index, Cochrane Database of Systematic Reviews, CENTRAL, Cumulative Index to Nursing and Allied Health Literature, Database of Abstracts of Reviews and Effectiveness, Embase, Education Resources in Curriculum, Health Management Information Consortium, Health Technology Assessment, International Bibliography of Social Science, Medline, PreMEDLINE, PsycBOOKS, PsycEXTRA, PsycINFO, Sociological Abstracts, Social Services Abstracts, and Social Sciencies Citation Index (appendix A). We also searched trial registries and reference lists of reviews and included studies. We consulted a group of experts from the National Institute for Health and Care Excellence (NICE) Guideline Development Group to identify relevant studies. We also wrote to authors of included studies to request trial registration details and unpublished outcomes and data; we also asked them to identify other potentially relevant studies.

All citations were screened by one author (KK or EM-W) who excluded citations that were not related to trials or to social anxiety disorder; potentially relevant citations were checked independently by a second author (EM-W or KK). Study characteristics, outcomes, and risk of bias[7] were extracted by one author (KK or EM-W) and checked independently by a second (EM-W or KK).

Randomised clinical trials of interventions for adults aged at least 18 years who fulfilled diagnostic criteria for social anxiety disorder were included. Studies that primarily focused on the treatment of comorbid disorders (eg, substance abuse) were excluded, but participants in the included studies often met criteria for another disorder (eg, depression) and were included. Eligible interventions were oral drugs (fixed or flexible doses), psychological or behavioural interventions (eg, promotion of exercise; panel), and combinations of interventions. Pharmacological interventions did not need to be licensed for social anxiety disorder, but interventions not used routinely in the treatment of social anxiety disorder, according to the consensus of the investigators and the NICE Guideline Development Group for the guideline *Social anxiety disorder: recognition, assessment and treatment*, were excluded (ie, exposure with a cognitive enhancer, surgical interventions, injected drugs, and antipsychotics). Studies of computerised cognitive bias modification were analysed in a separate review (unpublished). We excluded drugs that are no longer marketed (eg, brofaromine) if trials compared them only with placebo because these trials would not provide information about eligible interventions.

We limited the network meta-analysis to interventions that people with social anxiety disorder and clinicians might regard as first-line treatments because network analysis assumes that treatment effects are transferable across studies. Ideally, all trial populations included in the network meta-analysis could have been eligible for all the treatment options investigated. Clinically, people choosing a first-line intervention have a different set of treatment options compared with people choosing second-line interventions; there would be a high risk that the assumption of exchangeability would be violated by the inclusion of clinically heterogeneous populations (eg, people who had not responded to treatments assessed in other studies). We identified eligible interventions by reviewing published and unpublished studies and through consultation with clinicians and experts (including people with social anxiety disorder, pharmacists, psychologists, and psychiatrists). We included interventions rather than

***Panel:* Definition of psychological interventions**

Promotion of exercise
Behavioural change programmes that promote increased physical activity.

Exposure and social skills
Behavioural interventions that involve systematic exposure to social interactions or public speaking, but that do not include explicit cognitive techniques.

Group CBT
Therapist-led, group-based interventions that use both behavioural strategies (eg, exposure) and various cognitive strategies (eg, cognitive restructuring, video feedback, and attention training). Specific CBT manuals were followed for this intervention or the study investigators described the intervention as CBT.

Individual CBT
Individual interventions for which specific CBT manuals were followed or that were described as CBT by study investigators.

Other psychological therapy
Psychological therapies not included elsewhere were grouped to improve estimates of variance for the class model. This class includes the specific effects of interpersonal psychotherapy, mindfulness training, and supportive therapy.

Psychodynamic psychotherapy
Short-term psychodynamic psychotherapy, for which a treatment manual specifically for social anxiety disorder can be followed.

Psychological placebo
A psychological intervention that includes features common to most well-undertaken psychological therapies (ie, non-specific components of treatment) and that was designed as a credible intervention.

Self-help with support
Interventions (usually CBT based) that are delivered by book or computer with limited therapist support (eg, short meetings, email support, or phone calls). For the purpose of clinical trials, participants typically received clinical interviews at the beginning and end of treatment.

Self-help without support
Interventions (usually CBT based) that are delivered exclusively by book or computer. For the purpose of clinical trials, participants were interviewed at the beginning and end of treatment.

CBT=cognitive–behavioural therapy.

excluded them if some experts thought they could be used as a first-line treatment.

Statistical analysis

If a study reported continuous results for participants who completed the study only, as well as continuous results that accounted for missing data (eg, effects calculated using multiple imputation), we extracted the data that accounted for missing data. Studies reported several measures of social anxiety, none of which were common to all trials, so we calculated treatment effects for each study as a standardised mean difference (SMD). To reduce measurement error, we calculated the mean effect (Hedges' *g*) of all eligible scales for studies that reported more than one measure, taking between-scale correlation into account.[8] For trials that reported only the change from baseline, the SD at baseline was used to ensure standardising constants were comparable across trials. Based on published psychometric properties and data from clinically referred participants who completed several measures (appendix A), we assumed that measures were equally responsive and had a mean correlation of 0·65.

See Online for appendix A

Where reported, we also extracted data for recovery from social anxiety disorder (ie, no longer meeting criteria for the diagnosis) assuming that study dropouts had not recovered. We used the relation between continuous outcomes and recovery to estimate the treatment effect for all studies, including those that did not report recovery (appendix A).

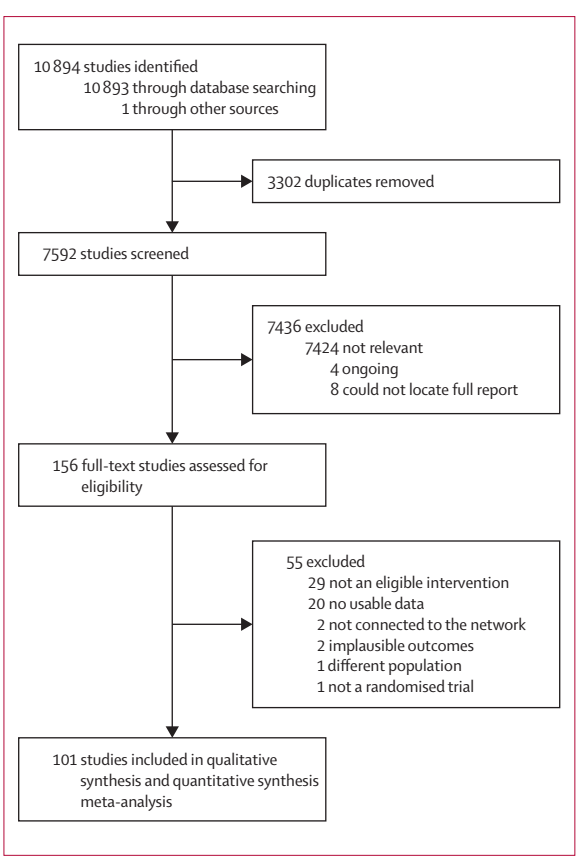

Figure 1: **PRISMA flowchart**
PRISMA=Preferred Reporting Items for Systematic reviews and Meta-Analyses.

We did a Bayesian random-effects network meta-analysis,[9] which accounts for the correlation between trial-specific effects and random effects of trials with more than two arms.[10] We analysed interventions by class (eg, selective serotonin-reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors [SSRIs and SNRIs]) and individually (eg, sertraline). In general, treatments with similar mechanisms of action were grouped in classes in which pooled effects were assumed to be similar. This grouping had the effect of drawing individual treatment effects towards the class mean. We used non-informative priors, except for the prior for within-class variability. Because there were few data to reliably estimate within-class variation, this prior was informative and was restricted with an inverse-gamma prior. This restriction limited variability to a clinically plausible range and had the effect of restricting the effect of outliers within a class; specific interventions with inconsistent results based on limited data would have otherwise had an undue effect on the results. For treatments not belonging to a class, we assumed no class variability and estimated only between-study heterogeneity. Combination interventions were included in a class because analysing of each combination as a distinct class would underestimate true variance (appendix A).

We estimated the effect for each class and for each individual intervention using Markov chain Monte Carlo implemented in WinBUGS version 1.4.3.[11] The first 20 000 iterations were discarded, and 50 000 further iterations were run. Two chains with different initial values were run simultaneously to assess convergence using the Gelman–Rubin diagnostic trace plots. We estimated effects with and without the consistency assumptions for individual treatment effects (ie, without grouping by class) and compared the residual deviance of each to assess consistency.[12] We compared the fit of the standard model to the class model by comparing the residual deviance, and we chose the model with the lowest deviance information criterion.[9] We used treatment effects to estimate change on continuous measures and the absolute rate of recovery for each intervention with 95% credible intervals (CrIs). Main effects are reported compared with waitlist, which was chosen as the reference treatment a priori.

All outcomes and study effects used in the analysis are available online (appendix B).

See Online for appendix B

This study is registered with PROSPERO, number CRD42012003146.

Role of the funding source

NICE commissioned the National Collaborating Centre for Mental Health (NCCMH) to develop guidance for