Paroxetine reduced symptoms and avoidance in generalised social phobia

Stein MB, Liebowitz MR, Lydiard B, et al. ***Paroxetine treatment of generalized social phobia (social anxiety disorder): a randomized controlled trial.*** *JAMA 1998 Aug 26;**280**:708–13.*

Question
In patients with generalised social phobia (social anxiety disorder), how effective is paroxetine compared with placebo?

Design
Randomised, double blind, placebo controlled trial with 12 weeks follow up.

Setting
13 centres in the US and 1 centre in Canada.

Patients
187 patients ⩾18 years of age (mean age 36 y, 57% women) with a *DSM-IV* diagnosis of generalised social phobia. Exclusion criteria included concurrent use of psychoactive medication, narcotic analgesics, warfarin sodium, digitalis glycosides, phenytoin, cimetidine or sulfonylurea derivatives; use of any psychotropic agent or β blockers within the previous 14 weeks; use of depot neuroleptics within the previous 12 weeks; clinically predominant Axis I diagnosis within the previous 6 months; substance abuse or substance dependence; and those considered to be serious suicidal or homicidal risks.

Intervention
After a 1 week, single blind, placebo, run in period, patients were allocated to 11 weeks of paroxetine (n = 94) or placebo (n = 93). The initial dose of paroxetine was 20 mg with increases of 10 mg/day weekly (permitted after the second week of treatment) to a maximum dose of 50 mg/day.

Main outcome measures
Responders (much improved or very much improved) based on the Clinical Global Impression Global Improvement Item and mean change from baseline on the Liebowitz Social Anxiety Scale total score.

Main results
66% of patients in the paroxetine group and 77% in the placebo group completed the 12 week trial. For patients who did not complete the entire study, the last observation was carried forward. 4 patients were lost to follow up before the first efficacy evaluation and were not included in the analysis. 50 patients (55%) in the paroxetine group were responders compared with 22 (24%) in the placebo group {$p < 0.001$}* (table). Mean Liebowitz Social Anxiety Scale total scores were reduced by 39% in the paroxetine group compared with 17% in the placebo group (mean difference favouring paroxetine 22%, 95% CI 9% to 35%). The most frequently occurring adverse effects in the paroxetine group were headache (37%), delayed ejaculation (36%), somnolence (27%), and nausea (26%).

Conclusion
In patients with generalised social phobia, paroxetine reduced symptoms and avoidance compared with placebo.

**p value calculated from data in article.*

Paroxetine v placebo at 12 weeks in patients with generalised social phobia†

Outcome	*Paroxetine*	*Placebo*	*RBI (95% CI)*	*NNT (CI)*
Responder	55%	24%	130% (58% to 249%)	4 (3 to 6)

†Abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.

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Commentary

This study by Stein *et al* is a good example of the current standards of industry sponsored efficacy studies in psychopharmacology. Based on current rules, such studies have high standards in some areas and quite low ones in others. Use of statistical power analysis to give a statistically sound conclusion on the efficacy of paroxetine compared with placebo is an example of high standards. We also know that the quality of clinical data collection, symptom ratings, adverse events, and the management of such data is high with comprehensive monitoring.

To interpret the results clinically, however, other important information is required that is not described in the present study. For example, we need to know how the patients were recruited. Are they patients from general practice, outpatient departments, or from centres that have specialised in controlled trials? There is extensive comorbidity between social phobia and depression, other anxiety disorders, and avoidant personality disorder.[1] In the present study only 9 out of 187 patients had current major depressive disorder and 3 current panic disorder, and it is difficult to judge how similar the participants were to patients in real life clinical practice. When 10% of the patients in a 12 week efficacy study are lost to follow up, questions about clinically valid therapeutic alliances can also be raised.

The methodological limitations of the study are shared with many industry sponsored studies that seem to be mainly targeted at satisfying regulatory agencies rather than proving clinically reliable results. In randomised trials of highly comorbid disorders, such as social phobia, a broad range of such patients should be included, measures of comorbid disorders should be used, and the samples should be large enough to provide reliable answers. In the meantime, this study provides some evidence for the effectiveness of paroxetine in the short term treatment of social phobia, although one can have little confidence that the quantitative results would apply in real life clinical practice.

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1 Merikangas KR, Angst J. *Eur Arch Psychiatry Clin Neurosci* 1995;**244**:297–303.