

Online supplement

Interventions

Interpersonal counselling

Interpersonal counselling is a manualised, briefer version of interpersonal psychotherapy. Interpersonal counselling posits that patients' symptoms occur in a social and interpersonal context, and that interpersonal relations influence symptom onset and treatment response. In the first longer session, the counsellor explores the patient's current interpersonal and social situation (interpersonal diagnosis). In the second session, the counsellor and patient identify specific current stress areas that are contributing to symptoms (interpersonal formulation). The four focal stress areas are grief, interpersonal disputes, role transition and social isolation. Subsequent sessions focus on dealing more positively with the stress area, add homework to accelerate improvement and discuss termination of the interpersonal counselling relationship (session 6).

In the present study, interpersonal counselling was delivered by 18 therapists (resident psychiatrists, clinical psychologists, counsellors) with at least 2 years of clinical experience. They attended a 3-day residential teaching seminar and monthly group supervisions with one of the authors (P.S.) in order to review videotaped cases and to ensure consistency of the intervention.

More detailed information about interpersonal counselling is included in the following publications.

- Weissman MM, Klerman GL (eds). Interpersonal counselling for stress and distress in primary care settings. In *New Applications of Interpersonal Therapy*. American Psychiatric Press, 1993.
- Weissman MM, Markowitz JC, Klerman GL. *Comprehensive Guide to Interpersonal Psychotherapy*. Basic Books, 2000.
- Judd F, Weissman MM, Davis J, Hodgins G, Piterman L. Interpersonal counselling in general practice. *Aust Fam Physician* 2004; 33: 332–7.

Drug treatment

Citalopram was initially administered at a dosage of 10 mg and titrated if needed to 60 mg and sertraline was administered at 25 mg and then titrated up to 200 mg. The pharmacological treatment was followed up by the primary care physician and continued for at least 4–6 months after the patients had responded.

Moderator analyses

A moderator is an attribute that the participant must already have at study entry (such as gender, age, severity of illness), should be clinically plausible and measured with adequate quality. Such an attribute is by definition unrelated to treatment because in a randomised clinical trial (RCT), when randomisation is successful, the two treatment arms are balanced for demographic and clinical characteristics.

To assess potential moderators of treatment response, the optimal study design is a RCT comparing two active treatments. If a study does not include a direct comparison of alternative treatments, it cannot identify moderators of differential treatment response. For example, in the multicentre RCT 'Depression: the search for treatment-relevant phenotypes study', in which patients were randomly assigned to selective serotonin reuptake inhibitors (SSRIs) or interpersonal psychotherapy, need for medical reassurance (coded as low–high) proved to be a moderator of treatment outcome.¹¹ Need for medical reassurance indicates the patient propensity to request frequent diagnostic procedures or medical visits including use of emergency services and are probably related to the risk of treatment discontinuation. Patients with high need for medical reassurance exhibited a faster remission with interpersonal psychotherapy than with SSRI pharmacotherapy, whereas the opposite was found for patients with a low need for medical reassurance. This suggests that, if there are two patients who are identical in all respects except that the first has a high need for medical reassurance and the second a low need for medical reassurance, offering the first an antidepressant as a first-line treatment would result in a poor outcome and offering the second the same treatment would give a substantial benefit.

We selected *a priori* as potential moderators, based on a literature review and clinical relevance: age (<45 years *v.* ≥45 years), gender (male *v.* female), education (≤8 years *v.* >8 years), marital status (unmarried *v.* married), work status (not employed *v.* employed), severity of depression (mild *v.* moderate to severe), level of functional impairment (mild *v.* moderate to severe), duration of depressive episode (<6 months *v.* ≥6 months), previous episodes of depression (no previous episode *v.* one previous episode), comorbid anxiety disorder (no *v.* yes), comorbid physical illness (no *v.* yes), smoking (no *v.* yes), patient's treatment preference (antidepressants *v.* psychological interventions).

As to the analytical model to be used to identify moderators of treatment outcome, the criteria proposed by Kraemer *et al*²⁸ and Pincus *et al*²⁹ prescribe an explicit test of the interaction between moderator and treatment. Our analytical strategy incorporates such a test and is based on logistic regression models. Each potential moderator was explored in a separate model. Each model included as independent variables treatment T (interpersonal counselling *v.* SSRI), site (S), one moderator (M) and their two- and three-way interactions (T × S, T × M, T × S × M). When the main effect of M was significant but the interactions T × M and/or T × M × S were not, the variable was considered a non-specific predictor of outcome. This means that patients with the characteristics M were less likely to respond to any treatment. When the interactions were significant, regardless of a significant main effect, the variable was considered a moderator. Dichotomous variables were coded as −1/2, +1/2 to be centred around the mean, and site was included in the models using 7 dummies coded as 7/8, −1/8.