

The other primary outcome to assess efficacy was defined as the rate of participants not receiving the allocated treatment plus the rate of participants who discontinued the allocated treatment. Even when accepting that patients not even starting treatment were included in a measure of treatment efficacy, it seems problematic to ascribe differences in this criterion to the efficacy of transference-focused psychotherapy without excluding accumulative effects of alternative explanations. The higher rate of non-starters among patients randomised to community therapists (the control condition) compared with those randomised to transference-focused psychotherapy (25% *v.* 13%) and the substantially higher rate of patients stopping treatment in the control group within the first month (Fig. 2 of the paper) might reflect a general preference of participants for transference-focused psychotherapy rather than its superior efficacy. Furthermore, the authors have not mentioned that this criterion combining non-starters and ‘drop-outs’ as primary outcome of efficacy was introduced *post hoc* (for *post-hoc* changes in the definition of primary outcome criteria see <http://clinicaltrials.gov/archive/NCT00714311>). Without addressing this issue, the statistical implications of this proceeding are difficult to evaluate.

As for the secondary outcome measures, the picture seems to be mixed. Some of the LOCF analyses indicated lower scores after transference-focused psychotherapy (e.g. number of borderline criteria, level of personality organisation). Other scores (e.g. general psychopathology, depression) were numerically higher after transference-focused psychotherapy and did not improve significantly more under it ( $P=0.92$  and  $P=0.85$  for general psychopathology and depression respectively).

Recapitulating, it seems that the claimed efficacy of transference-focused psychotherapy does not follow from the primary outcome criteria. Accordingly, further research seems necessary to establish the efficacy of this therapy in the treatment of borderline personality disorder.

- 1 Doering S, Hörz S, Rentrop M, Fischer-Kern M, Schuster P, Benecke C, et al. Transference-focused psychotherapy *v.* treatment by community psychotherapists for borderline personality disorder: randomised controlled trial. *Br J Psychiatry* 2010; **196**: 389–95.

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**Author’s reply:** Kleindienst and colleagues argue that our interpretation of the treatment outcome with regard to suicide attempts might lead to misunderstandings. They are right that a  $\chi^2$ -test comparing the absolute number of suicide attempters in both groups, transference-focused psychotherapy and treatment by experienced community psychotherapists, is not significant. However, this test does not seem appropriate in the present context, since the baseline, that is the number of suicide attempters during the year before treatment, was not equal in both groups (18 in the transference-focused psychotherapy group *v.* 12 in the community psychotherapists group). Thus, a statistical approach had to be employed that controls for baseline data. Since no  $\chi^2$ -test exists that controls for baseline values, we defined change scores that allow for baseline control within a Mann–Whitney U-test. This test generated the  $P=0.009$  that, in our opinion, depicts the real changes in suicide attempters in both groups. A between-group effect size of 0.55 for the time  $\times$  group

interaction in suicide attempts was calculated from the  $\chi^2$ -statistics of the change scores ( $\chi^2=7.126$ , d.f.=2,  $P<0.028$ ). Table DS2 of our paper only reports within-group effect sizes; between-group effect sizes were not calculated.

The issue of treatment drop-out is a limitation of this study, which has been thoroughly controlled for and discussed in our paper. After the decision to use treatment drop-out as a primary outcome criterion, we preferred to keep strictly to the intent-to-treat algorithm that demands every randomised patient to be part of the outcome analysis. Nevertheless, to address the understandable criticism raised by Kleindienst and colleagues, we repeated the drop-out analysis after excluding from it patients who did not begin therapy after randomisation. This analysis still revealed a significantly lower number dropping out of the transference-focused psychotherapy group (15 *v.* 23;  $\chi^2=5.750$ , d.f.=1,  $P=0.016$ ).

The changes in the primary outcome criteria had been made following the impression of an ongoing discussion in the literature addressing the adequacy of DSM–IV diagnostic criteria as outcome criteria in treatment studies.<sup>1,2</sup> Since our initial outcome criteria ‘number of DSM–IV borderline criteria’ and ‘GAF score’ revealed an even stronger superiority of transference-focused psychotherapy, we did not report this *post-hoc* change, because a bias in our decision was not suspected.

We thank Kleindienst and colleagues for their criticism and the Editor for giving us the opportunity to clarify important issues regarding our study. We hope that our comments will eliminate doubts concerning the fact that our study documents the efficacy of transference-focused psychotherapy for the treatment of borderline personality disorder.

- 1 Skodol AE, Pagano ME, Bender DS, Shea MT, Gunderson JG, Yen S, et al. Stability of functional impairment in patients with schizotypal, borderline, avoidant, or obsessive–compulsive personality disorder over two years. *Psychol Med* 2005; **35**: 443–51.
- 2 Zanarini MC, Frankenburg FR, Reich DB, Silk KR, Hudson JI, McSweeney LB. The subsyndromal phenomenology of borderline personality disorder: a 10-year follow-up study. *Am J Psychiatry* 2007; **164**: 929–35.

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## Ziprasidone and the relative risk of diabetes

Kessing *et al*<sup>1</sup> describe the risks of diabetes in clinical practice from a large-cohort, observational study of Danish patients requiring antipsychotics. We believe that the relative risks of subsequent incident diabetes that they report for individual antipsychotics are at odds with established literature. The preponderance of evidence has demonstrated that ziprasidone has limited effect on metabolic indices associated with the development of diabetes. We present some of that evidence below.

In the CATIE study of 1493 patients with schizophrenia receiving olanzapine, quetiapine, risperidone, ziprasidone or perphenazine for up to 18 months, ziprasidone was the only drug associated with improvement in glycosylated haemoglobin, total cholesterol and triglycerides. Meyer and colleagues<sup>2</sup> reported that, in the CATIE trial, the prevalence of metabolic syndrome increased for olanzapine (from 34.8% to 43.9%) but decreased for ziprasidone (from 37.7% to 29.9%), and that the comparison between ziprasidone and olanzapine was statistically significant ( $P=0.001$ ).

In the EUFEST study of 498 patients with first-episode schizophrenia assigned to haloperidol, amisulpride, olanzapine,