

the relationship between community treatment orders and readmission rates is of a different complexity than that between chemotherapy and cancer remission, or between digitalis and cardiac function.

We acknowledge, and celebrate, the contribution of RCTs to evidence-based healthcare. But there remains a need for a plurality of methods. However astute and research-literate the clinician, RCTs select participants in ways that can make generalisation to real-world settings difficult. Realist approaches that help bridge the gap between the ‘what’ and the ‘how’ of clinical outcomes can only be a good thing. And the more complex the intervention – and the more context dependent – the more important this is. For us, RCTs alone are unlikely to be sufficient.

Parity of esteem for psychiatry is undoubtedly worthwhile, but this does not mean we have to imitate other specialities; as so often in the past, we can lead the way instead. *Primus inter pares*.

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doi:10.1192/bjp.2018.217

## Does pharmacotherapy really have as enduring effects as psychotherapy in anxiety disorders? Some doubts

Bandelow *et al* recently presented a meta-analysis testing the assumption that the effects of psychotherapy in anxiety disorders are more enduring than those of pharmacotherapy.<sup>1</sup> From non-significant differences between psychotherapy and pharmacotherapy in pre-follow-up effect sizes the authors concluded that ‘... patients who stopped taking a drug showed the same durable improvement as patients who stopped psychotherapy’.<sup>1</sup>

Besides the severe (and properly discussed) limitation that an unclear percentage of patients may have started new psychological treatment or taken medications in the follow-up period, this meta-analysis raises further serious concerns.

First, the authors did not clearly specify their inclusion criteria. Apparently, they did not require head-to-head comparisons of psychotherapy and pharmacotherapy as an inclusion criterion. Second, as a consequence, Bandelow *et al* compared pre-post and pre-follow-up effect sizes of psychotherapy, medication and placebo obtained from different randomised controlled trials. Thus, the studies being compared may differ with regard to important treatment moderators such as characteristics of patient populations and setting conditions. For these and other reasons analyses of pre-post and pre-follow-up effect sizes should be avoided in meta-analyses.<sup>2</sup>

Third, Bandelow *et al* did not adhere to the logic of equivalence testing that includes the definition of a margin compatible with

equivalence and performing two one-sided tests (TOST).<sup>3</sup> They apparently applied the more usual two-sided superiority test. However, concluding from a non-significant two-sided superiority test that two treatments (i.e. pharmacotherapy and psychotherapy) are equally efficacious (in the long-term) is questionable.<sup>3</sup> The traditional two-sided test and TOST often yield inconsistent results.<sup>4</sup> Fourth, furthermore, Bandelow *et al* seem to have not controlled for researcher allegiance.<sup>5</sup> Thus, a bias in favour of pharmacotherapy cannot be excluded given that the first and last authors disclose multifold collaboration with pharmaceutical companies.

Finally and of note, the authors avoid discussing potential long-term negative effects that any type of psychotropic drug treatment, particularly after long-term use, may have, for example by increasing the risk of experiencing additional psychopathological problems that do not necessarily subside with discontinuation of the drug or of modifying responsiveness to subsequent treatments.<sup>6</sup>

The data presented by Bandelow *et al* suggest that pharmacotherapy may have enduring effects in anxiety disorders as well. However, the authors’ conclusion that in the long-term term psychotherapy and pharmacotherapy are equally efficacious in anxiety disorders is questionable for the reasons given above.

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**Declaration of interest** F.L. and J.H. are trained psychotherapists.

doi:10.1192/bjp.2018.225

## Authors’ reply

We found that gains with psychotherapy were maintained for up to 24 months. We also showed that patients who stopped medication remained stable. This is good news for the affected patients. However, as patients in the placebo groups also did not show deterioration we concluded that enduring effects observed in follow-up studies might be superimposed by spontaneous remission or effects of concurrent treatments.

For detailed inclusion criteria, we had referred to our previous meta-analysis.<sup>1</sup> As there are only a few head-to-head follow-up comparisons of psychotherapy and pharmacotherapy, we decided to calculate pre-post effects. Thus, we were able to include as many as 93 follow-up studies, which also comprised all head-to-head comparisons.

Pre-post effect sizes do not only measure ‘true’ treatment effects, but also natural course and placebo effects. However, when conditions are the same in psychotherapy and pharmacotherapy studies, this comparison is fair. Patients are mainly

interested in a substantial decline in their anxiety scale scores, and this is what we measure with pre–post effects. Follow-up studies for psychotherapy mostly lack a control group, because a waitlist is used as a control during the active treatment period. After termination, the waitlist patients cannot serve as controls anymore because they will now receive the active treatment. Therefore, the pre–post effect size is the only option to compare the results of follow-up studies.

In every meta-analysis, not only in the ones using pre–post effect sizes, populations may be heterogeneous. However, all the included medication studies were comparisons with psychotherapy. Therefore, it is unlikely that our results were biased because of differences in patient populations.

It is also unlikely that allegiance effects in favour of pharmacotherapy have influenced our results, for 4 reasons: (1) In the data set of our previous meta-analysis,<sup>1</sup> on which the present analysis was performed, we found possible allegiance effects in both psychotherapy and pharmacotherapy studies but were unable to find significant differences between the average effect sizes of studies with or without allegiance effects for both treatment modalities. (2) The vast majority of the studies, including those involving medications, were published by behavioural psychotherapists. (3) The patents of all drugs mentioned in the study have expired for long. (4) We published the raw data of our analysis so that anyone who has the feeling that results might be biased can re-calculate the effect sizes. Allegiance effects are also possible in psychotherapy studies.<sup>2</sup> We frankly disclosed our conflicts of interest, but this should also be expected from authors publishing in the field of psychotherapy, in particular when they are strongly promoting certain forms of psychotherapy, such as Dr Leichsenring, who is a fervent advocate for psychoanalysis and has been criticised for possibly biased meta-analyses in the literature.<sup>3</sup> Further, the authors seem

to have overlooked the part in which we mentioned adverse effects of drugs. Enduring side-effects of medications that are used for anxiety disorders are rare, however.<sup>4</sup> Furthermore, medication does not lessen cognitive–behavioural therapy (CBT) gains; we found much higher average effects for CBT plus medication (Cohen's  $d = 2.12$ ) than for CBT alone ( $d = 1.22$ ).<sup>1</sup>

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**Declaration of interest** In the past 12 months and in the near future, B.B has been/will be on the speakers/advisory board for Hexal, Mundipharma, Lilly, Lundbeck, Pfizer and Servier. D.W. has served on the speakers' board of AstraZeneca, Essex Pharma, Lundbeck and Servier.

doi:10.1192/bjp.2018.226