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CORRESPONDENCE

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To the Editor:

Exposure therapy and cognitive behaviour therapy have established efficacy in anxiety disorders. However, a shortage of suitably trained therapists means that the treatments are unavailable to the majority of individuals with anxiety disorders (Barlow & Hofmann, 1996). Computer-assisted therapy is a potential way of alleviating this problem as routine aspects of therapy could be administered by the computer, reducing therapist–patient contact time. Excitingly, Marks *et al*.'s (2004) report of a randomized controlled trial claims that a computer-aided exposure therapy programme (*FearFighter*) is a specific treatment (superior to a computer-aided placebo treatment involving relaxation training) and is as effective as traditional, therapist-assisted exposure therapy. Unfortunately, close reading of the report indicates that the trial is largely uninterpretable.

The problem concerns the way in which drop-outs are dealt with. Drop-outs occur in many trials of psychological treatments. The current convention for managing analyses when there are a substantial number of drop-outs is either to report only an intention-to-treat analysis (with the last available data-point being carried forward in all cases) or to report both intention-to-treat and completers analyses. The Marks *et al*. report deviates from this convention by reporting what is essentially a completers-only analysis.

Completers-only analyses are particularly problematic when drop-out rates are substantial and/or differential. Both issues apply to the Marks *et al*. (2004) report. There was a very large drop-out rate (43%) in the *FearFighter* computerized treatment group, which was significantly greater than the small (6%) drop-out rate in the placebo control group (computerized self-relaxation). In such a circumstance, a completers-only analysis is potentially misleading for two reasons. First, the analysis may be based on comparing groups that are not really selected at random because there are likely to be systematic reasons for drop-out, particularly when it is differential. Second, drop-outs in treatment are very likely to have responded less well. Not including them in an analysis will, therefore, overestimate the size of the treatment effect. If we assume that most of the 46% of *FearFighter*-treated patients who were not included in the analysis either failed to benefit or deteriorated, *FearFighter* may not differ from the placebo control condition.

Although the problems with completers-only analyses are now well known, it seems likely that many readers will not have spotted that Marks *et al*. used what is essentially a completers-only analysis because they state (p. 11) that: 'All analyses were intention-to-treat by analysing subjects in the group to which they were originally randomized (Everitt, 1994).' However, they then provide the qualifier that, 'Where post-baseline data were unavailable, baseline data were not carried forward in the manner often done, as it is unlikely that scores remained frozen at their last observed value (Everitt, 1998).' The qualifier is crucial because no post-baseline data was obtained from 15 (41%) of the *FearFighter* group (see p. 13) and the post-baseline data for two further *FearFighter* patients was lost (see note to Table 2). The proportion of *FearFighter* patients not included in the intention-to-treat analysis would, therefore, appear to be 46% (17 out of 37), essentially the same as the drop-out rate (43%).

For this particular trial, the authors could clarify matters by providing a conventional intention-to-treat analysis carrying forward the last available data-point even in individuals with no post-baseline scores. However, as this involves debatable assumptions, the best way forward for the future is for journals to encourage more rigorous data collection so that trial reports include near complete outcome data for drop-outs as well as completers. Obviously

this places a heavier burden on investigators but the field would greatly benefit, and it is possible. For example, at the same clinic as the Marks *et al*. (2004) study, we have recently completed a randomized controlled trial of psychological treatments in another anxiety disorder with less than 5% drop-outs and with post-baseline data for everyone.

Declaration of Interest

None.

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The Authors reply:

We are glad to be able to correct Professor Clark's widely shared misconception about 'conventional intention-to-treat analysis carrying forward the last available data-point even in individuals with no post-baseline scores'. An authority on this issue, Professor Everitt (1994, p. 13) defines intention-to-treat (ITT) analysis as the analysis together of all randomized patients who were allocated to treatment, whether or not they completed, or even received, that treatment, which ITT is exactly what our paper reports. Doing an ITT analysis is not the same as the method of carrying forward (imputing) the last available observation which Professor Clark advocates robustly. Professor Everitt points out (pp. 97–99) that carrying forward the last available observation makes very unlikely assumptions – common causes of drop-outs in repeated-measures designs include the patient's having: (1) recovered, (2) not improved, (3) unwanted treatment effects, (4) had unpleasant study procedures, (5) concurrent health problems, (6) external reasons unrelated to treatment or clinical progress. Some of these causes may operate singly or in combination. Our report notes 'some drop-outs said they left … because they learned how to improve with self-exposure and it was too bothersome to attend again. It may thus be wrong to assume that no drop-outs improved', which accords with Everitt (1998): 'it is unlikely that scores remained frozen at their last observed value'. Other analyses which are now possible mid-treatment data but we had only pre, post and follow-up data.

Professor Everitt's points and our consultations with other statisticians at the Institute of Psychiatry indicated that carrying forward the last available observations introduces at least as many problems as it solves. We did, in fact, include analysis of our results carrying forward the pre-treatment scores of the drop-outs in an earlier version of our paper – that gave similar results, which is unsurprising given the large effect sizes in our Table 2. Professor Clark claims that not including drop-outs in an analysis will 'overestimate the size of the treatment effect'. Even if we (probably wrongly) counted all drop-outs as failures, pre- to post-treatment effect sizes became, respectively, for the *FearFighter*-guided, Clinician-guided and Relaxation groups: Main Problem: 2·3, 3·1, 0·6; Goals: 3·1, 2·8, 0·3; FQ Global Phobia self: 0·9, 2·1, 0·7; FQ Global Phobia blind assessor: 1·4, 1·3, 0·4; WSA Total blind assessor: 0·8, 0·6, 0·1 – in other words the effect size of at least 0·8 which is usually regarded as clinically meaningful was found on every measure in the *FearFighter* group, almost every measure in the Clinician-guided group, and no measure in the Relaxation group. We removed these results for brevity and clarity except to say 'Even with all drop-outs included the mainly computer-guided exposure group … had 73% less clinician time per patient than did the entirely clinician-guided exposure group.' There was no significant difference on any measure at pre-treatment between drop-outs and completers, or between the number of drop-outs in mainly computer-guided and entirely clinician-guided self-exposure therapy.

It is great that Professor Clark obtained complete post-baseline data and few drop-outs in a trial he conducted at the same site that

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Marks *et al.*'s (2004) patients attended. The same site is hardly the 'same clinic' that he claims, because referrals for and selection criteria used by different research teams and trials over different years can vary considerably, as testified by patients referred to us for help who said his clinic did not accept them. He does not say how many suitable patients did not enter his trial. It is sobering that Professor Clark himself reported the usual problems of refusers and drop-outs in two of his other recent trials: in Stangier *et al.* (2003) 25% (24/95) of randomized patients refused to start (their outcome is not reported) and were replaced and a further 13% (12/95) dropped out before post-treatment or did not reach follow-up, yielding a total of 38% of initially randomized patients who did not reach follow-up. In Clark *et al.* (2003) 19% (14/74 of suitable patients) refused entry, and 10% (6/60 of randomized patients) did not complete the trial, so 27% of suitable patients did not complete treatment. We all support motherhood and apple pie and try to collect complete datasets. Real-world constraints, however, attenuate data collected in most trials despite the best efforts diligent researchers make to collect as full data as possible. Statisticians guide us on how to manage that usual problem.

A *Psychological Medicine* referee said of our results with computer-assisted treatment: 'A reasonable conclusion seems to be that those who remain do as well as those who remain in therapist only treatment. (Computer-assisted treatment could be the first stage in a stepped care approach.)' – we agree.

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A rejoinder from Clark:

The key difficulty with the Marks *et al.* (2004) paper is the asymmetry in the data analysis. As a consequence of differential drop-out and failure to collect end-point scores, the reported analyses use data from scarcely half (54%) of patients randomized to *FearFighter* and almost all (94%) of patients randomized to the placebo treatment. This is a problem irrespective of how one defines 'intention-to-treat'. The field will be grateful to Marks *et al.* for reporting, in their letter, revised effect sizes based on all patients who were randomized (with baseline scores being carried forward when nothing else is available). An indication of whether the difference between *FearFighter* and placebo remained significant on the blind assessor ratings and other measures would have been of further assistance.

Marks *et al.*'s remarks about the Clark *et al.* (2003) and Stangier *et al.* (2003) trials are misleading. In the Clark *et al.* (2003) trial, which was conducted by my team, 60 patients were randomized. The analysis of the main outcome measure uses actual pre-treatment and post-treatment data on all (100%) of the randomized patients, with termination scores being used for the 10% of individuals who finished treatment early. The Stangier *et al.* (2003) trial, which was conducted by an independent German group, did indeed have missing data. Most came from the wait-list condition, which was unusually long (9 months), because it was intended as a control group for both the immediate post-treatment data and the 6-month follow-up data in the cognitive therapy conditions. The differential drop-out in the wait-list showed this was impractical. The main analysis acknowledged this point and just compared the two treatment conditions (individual *versus* group cognitive therapy) with pre-treatment scores being carried forward in the small (9%) and similar number of patients who dropped out of the two treatments.

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To the Editor:
Congratulations to Mike Startup and colleagues (Startup *et al*. 2004) for their excellent study replicating and extending our initial trial applying CBT to promote recovery from acute psychosis (Drury *et al*. 1996*a*, *b*, 2001). Startup and colleagues comment on the contrasting results of our study with the first attempted replication by Lewis *et al*. (2002) in first-episode psychosis ('SOCRATES') which reported a relatively weak effect in accelerating recovery compared to our own. Startup *et al*. consider that in the SOCRATES study CBT was insufficiently sustained to make an impact (5 weeks compared to 12+ weeks in our study) with insufficient follow up. I think this is possible but they omit what I think is the most likely explanation: the high recovery rate in first-episode psychosis under standard care. Loebel *et al*. (1992) report that over 85% of patients recover from the first episode under a standardized drug regime, compared to the much lower rates in those with more established illnesses, such as that observed in the Drury *et al*. (1996*a*, *b*) and Startup *et al*. studies. Even in routine clinical settings (Lewis *et al*. 2002) the overwhelming majority of first episodes recover. In first-episode psychosis, therefore, under routine clinical care, there is little room for an adjunctive therapy like CBT to demonstrate an impact on positive symptoms, thus, a large sample was required to demonstrate a trend in the SOCRATES study. It seems likely that with longer follow-up SOCRATES will demonstrate significant effects, particularly among the subgroup likely to have longer recovery time, e.g. male, early onset, long DUP.

In the Startup *et al*. study by contrast, the patients were 6 years older with nearly five previous admissions and this is the group most prone to readmission and long recovery time where an adjunctive treatment is needed and can demonstrate an effect; in the Startup *et al*. study and in our own, CBT improved the chances of recovery.

These studies suggest that CBT improves the speed and probability of recovery in established, relapsing psychosis and possibly in poorer prognosis, first-episode psychosis.

Declaration of Interest

None.

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The Authors reply:
Max Birchwood is kind with his praise for our trial of CBT to promote recovery from acute psychosis but we do not agree with his alternative explanation why CBT was relatively ineffective in the SOCRATES study (Lewis *et al*. 2002) in promoting recovery from acute psychosis compared with the study by Drury *et al*. (1996*a*, *b*). Whereas we (Startup *et al*. 2004) suggested the explanation might be that the delivery of CBT in the SOCRATES study, which recruited patients suffering either a first or a second psychotic episode, was too intense, or not sufficiently sustained, Birchwood suggests that a more likely explanation is that 'In first episode psychosis … there is little room for an adjunctive therapy like CBT to demonstrate an impact on positive symptoms' because a large percentage of patients recover from a first

episode of psychosis under standard care alone. Data from the North Wales trial (Startup *et al.* 2004) do not support this explanation.

In the North Wales trial, patients who had recently been admitted to hospital suffering an acute psychotic episode were assigned at random to treatment as usual (TAU) or TAU plus CBT, and follow-up assessments of psychotic symptoms and social functioning were conducted at 6 and 12 months after index admission. Using data collected on the number of admissions to psychiatric hospitals, we can further subdivide the two groups into those experiencing their first or second admission (Early psychosis sample, comparable to those in the SOCRATES study, $n=32$ at follow-up) and those with two or more previous admissions (Established psychosis group, $n=37$). We then examine positive psychotic symptoms (global ratings of delusions and hallucinations from the Scale for the Assessment of Positive Symptoms) and global functioning (GAF scores) in ANOVAs with two treatment groups (CBT *v.* TAU) × two admissions groups (early *v.* established psychosis) × three assessments (baseline, 6 months, 12 months). The crucial three-way interactions between treatment group, admissions group and assessment occasion were non-significant for both positive symptoms [$F(2, 51)=0{\cdot}13$, $p=0{\cdot}88$], and global functioning [$F(2, 64)=0{\cdot}28$, $p=0{\cdot}76$]. Since these interactions have limited statistical power, we show in Table 1 the effect sizes for the two groups at the two follow-up assessments. These were calculated as standardized mean differences, with the mean for the TAU group subtracted from the mean for the CBT group, divided by the pooled standard deviation.

It can be seen from Table 1 that differences in effect sizes between the Early and Established psychosis groups are small except in the case of GAF scores at 6-month follow-up where the advantage is in favour of the Early psychosis group. Thus, there is no evidence from these data that people with early psychosis have little to gain from CBT as an adjunctive treatment. Equally, there is no convincing evidence that people with established psychosis fail to benefit.

Table 1. *Effect sizes for the two groups at follow-up*

	6-month assessment		12-month assessment	
Admission group	Positive symptoms	GAF	Positive symptoms	GAF
Early psychosis	−0·52	0·96	−0·78	0·63
Established psychosis	−0·49	0·34	−0·55	0·64

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