

traits, which do not readily fit with the others (attention deficit hyperactivity disorder (ADHD) and learning disabilities). A third problem is that schizoaffective disorder was included among the bipolar spectrum disorders in the analyses, a decision that requires further justification.

A fourth problem is that, as described in a previous article,² a diagnosis of bipolar affective disorder not otherwise specified was given to participants who presented with manic symptoms meeting threshold DSM-IV diagnostic criteria but not minimal duration criteria. It is possible that this was the reason for a statistically significant difference in the cumulative incidence of bipolar spectrum disorders between the offspring of well parents and the offspring of parents with a bipolar disorder. Finally, 23% of participants in the group of offspring of a parent with bipolar disorder 1 were recruited within families, making it unclear how many participants had a parent who did not have the disorder.

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Authors' reply: The clinical staging model proposed represents an aggregate view based on results from an ongoing, prospective study of a unique, high-risk cohort. In prior analyses, we found evidence that ADHD and other childhood neurodevelopmental presentations occurred at a higher unadjusted rate in the offspring of parents with lithium-non-responsive illness compared with the offspring of parents with lithium-responsive illness.^{1,2} In this updated analysis, instead of unadjusted lifetime rates we used cumulative incidence, which takes into account censoring and variable age at last assessment and Cox proportional hazard models adjusted for sibling correlation, gender and socioeconomic status. With longer observation, the unadjusted rate of psychotic disorders is now significantly elevated in the offspring of parents with lithium-non-responsive illness compared with the offspring of parents with lithium-responsive illness.

Second, cluster A traits and cognitive deficits are known antecedents to psychotic disorders and therefore we argue that these do in fact 'fit' with ADHD and learning disabilities as early risk syndromes in this high-risk population.³ Third, schizoaffective disorder was included as an end-stage illness in this analysis given the overlap between schizoaffective and psychotic bipolar disorders.⁴ Fourth, all offspring (control and high-risk) were assessed in the same way and all assessments were reviewed masked to family affiliation and diagnoses made by consensus using the same criteria. Therefore, the difference in rates of bipolar disorder not otherwise specified or any other diagnosis cannot be explained by modified diagnostic criteria for high-risk offspring as speculated by Chenard-Poirier & Paris.

Finally, given the high heritability and estimated likelihood that recurrent major depression in these families reflects the bipolar diathesis,⁵ we expanded recruitment to include the offspring of parents who were siblings of the original bipolar proband and who themselves met lifetime criteria for bipolar disorder or recurrent major depression ($n = 20$). Therefore, every high-risk offspring had one parent with a bipolar or bipolar-related recurrent major depressive disorder. We thank Chenard-Poirier & Paris for raising these points and the *Journal* for allowing us to provide this clarification.

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An oversimplification of psychosis, its treatment, and its outcomes?

Jauhar *et al's* meta-analysis¹ of randomised controlled trials in cognitive-behavioural therapy for psychosis (CBTp) is broadly consistent with previous results:² that is, there is an overall significant but modest impact on psychotic symptoms, with blinded studies showing lower effect sizes than those that are not blinded. However, there are a number of problems with this study and especially with its conclusions.

Jauhar *et al* conclude that they find the advocacy by government (including NICE) for CBTp 'puzzling', bearing in mind the low effect sizes found for psychotic symptoms. However, I find it puzzling that the authors comment on NICE recommendations, since a third of the studies included for their overall symptoms analysis (12/34) were not based on therapies recommended by NICE in the first place (based on what we know is effective from the literature so far): they were either group or brief CBT studies. Three further studies were in Chinese, so their relevance to NICE recommendations is hard to tell.

It is a testament to the far-reaching effects of CBTp that the analyses revealed any effects at all, since the authors looked at outcomes that were not always targeted by the therapy. For instance, only a few of the 34 studies included for negative symptoms actually targeted such symptoms specifically. Furthermore, severity of positive symptoms/hallucinations was used as the outcome for studies that did not hypothesise changes in psychotic symptoms since the target was on compliance with command hallucinations,³ emotional dysfunction,⁴ or social functioning.⁵ By contrast, outcomes on depression, anxiety or distress as a result of psychotic symptoms, and trials targeting self-esteem, post-traumatic symptoms, suicidality, or substance misuse, which are all main and legitimate targets in CBTp, were excluded.

The criteria for studies to be included in the final analyses were idiosyncratic. Perhaps the most surprising was the decision to exclude studies that targeted hallucinations specifically from their positive symptoms analyses. A separate 'supplementary' meta-analysis was carried out for those studies, with an effect size of 0.34, which is not reported in the abstract (where only the lower – 0.25 effect on positive symptoms is reported). Clinicians familiar with clinical presentations of patients with psychosis might be surprised at their rationale for excluding trials because patients had a dual diagnosis, or had medication-resistant psychotic symptoms but no further diagnosis specification. None of the follow-up data available was included, meaning that the

Sensky *et al*⁶ (non-significant) end-of-study results contribute to the findings, but the (significant) 9-month and 5-year follow-up results do not.⁷

Meta-analyses can be highly informative, but they are highly prone to bias.⁸ Those with a ‘washing machine’ approach, such as this one (i.e. amalgamating different populations – from acute in-patients to chronic out-patients, from young people with a first episode of psychosis to older adults; different therapies – from 3 sessions of acceptance and commitment therapy to 18 months of weekly cognitive therapy; different modalities – groups or individual; different targets – from compliance with command hallucinations to emotional dysfunction), tell us very little about what works for whom. Unsurprisingly, the heterogeneity statistics were highly significant for all analyses, with I^2 being at 50% or above (i.e. representing ‘substantial heterogeneity’), suggesting that there was too much heterogeneity to obtain meaningful pooled estimates, and that the necessary criteria for rendering a meta-analysis appropriate were not met.⁹

The field of CBTp has now progressed such that it is no longer appropriate to simply lump together psychosis patients assuming that clinical presentations are the same, that therapy is for the same problem, and that the type of CBT is the same. Other recent meta-analyses, which focus on treatment-resistant patients,¹⁰ or on individually tailored, formulation-based CBT for hallucinations and delusions,¹¹ will be more informative to clinicians and researchers about the specific effects of CBTp.

To conclude, the reported analyses reflect an over-simplification of the complexities of psychosis and psychological interventions. The biggest challenges in psychological therapy trial methodology (and in clinical practice) are the quality of/adherence to the therapy delivered and the competence of the therapists, none of which was taken into account in this study. A more meaningful reading of the existing research is that the next steps are to investigate which patients benefit on which outcomes at which stages with which types of therapy, and how to ensure therapist competence (and availability).

Declaration of Interest

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Authors’ reply: One of the founding principles of meta-analysis is to pool data from as many studies as possible.¹ Among other benefits this prevents studies being preselected for consideration on arbitrary grounds. It is difficult to imagine anything more arbitrary than restricting a meta-analysis of CBT for schizophrenia to studies that conform to some notional interpretation of the NICE guideline, as Peters seems to be suggesting, not to mention excluding any that were in Chinese.

Similarly, it would be wrong to exclude studies that used group CBT *a priori*. Here, though, it is entirely legitimate to examine this issue *post hoc*; that is, to ask whether use of group *v.* individual CBT significantly moderates effect size. Carrying out this analysis on our data reveals that the pooled effect sizes for both types of intervention were very similar in the meta-analysis of overall symptoms (effect size in 7 group studies -0.24 *v.* -0.23 in 24 individual studies; $Q=0.006$; $P=0.94$); for positive symptoms, group CBT had a non-significantly smaller effect size than individual CBT (effect size in 8 group studies -0.08 *v.* -0.25 in 23 individual studies; $Q=1.73$; $P=0.19$) (across both analyses, one study employed both group and individual CBT and three were rated as ‘unclear’). This might or might not be considered evidence that group CBT is less effective than individual CBT, but what it does not mean is that inclusion of group studies in our original meta-analyses somehow acted to dilute the pooled estimate – the effect sizes for studies using individual CBT are similar or lower to those we reported for all studies combined (effect sizes were -0.33 for overall symptoms and -0.25 for positive symptoms).

With regard to some of the other points raised by Peters, our diagnostic criteria were broad and similar to those used by NICE, Wykes *et al* and the Cochrane Collaboration. We recognised the possibility that Acceptance and Commitment Therapy might be different from regular CBT and presented an analysis in the article excluding two studies using this^{2,3} and another where CBT took the form predominantly of coping skills enhancement;⁴ this did not materially affect the results. Peters expresses surprise over our decision to exclude studies that specifically targeted hallucinations from the meta-analysis of positive symptoms. As it happens, only three studies of hallucination-directed CBT also reported outcomes for positive symptoms. Adding the data from two of them^{5,6} (data cannot be extracted from one study⁷) to the positive symptoms dataset makes no difference to the pooled effect size (-0.25 ; CI -0.36 – -0.13).

Peters argues that there was too much heterogeneity among the results to obtain meaningful pooled estimates. In fact, the Cochrane Collaboration article she cites⁸ recommends (a) not pooling data using meta-analysis, (b) investigating heterogeneity using subgroup analysis or meta-regression or (c) using a