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Extended Research Article

Treatment effect modifiers of cognitive behaviour therapy in people with psychosis: an individual participant data meta-analysis of RCTs

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This article

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Abstract

Background: Cognitive–behavioural therapy is a recommended intervention for the treatment of schizophrenia and related psychoses, but there is considerable uncertainty on whether its effectiveness is moderated by patient characteristics and/or intervention characteristics.

Objective(s): To identify treatment effect modifiers of cognitive–behavioural therapy in people with schizophrenia spectrum diagnoses.

Design: An individual participant data meta-analysis of randomised controlled trials comparing cognitive–behavioural therapy to treatment as usual or control active psychosocial control interventions.

Setting: Community and inpatient settings.

Participants: Individuals with schizophrenia spectrum diagnoses.

Interventions: Cognitive–behavioural therapy, as defined by the criteria outlined in the National Institute for Health and Care Excellence guideline on treatment and management of schizophrenia in adults.

Main outcome measures: Overall symptom change as measured by assessments of overall psychotic symptom severity (e.g. the Positive and Negative Syndrome Scales).

Data sources: Corresponding authors of 110 trials identified from the database searches conducted as part of a related aggregate data meta-analysis in February 2018 (later updated in January 2019) were invited to share their trials' individual participant data, and additional trial documentation, when available, pertaining to relevant individual participant data metadata, statistical analyses plans and characteristics of the cognitive–behavioural therapy interventions evaluated in their eligible trials.

Review methods: Reports of retrieved and unretrieved trials were assessed using the Cochrane Risk of Bias tool. Data were cleaned and standardised to allow pooling and analysis. We conducted a series of two-stage individual participant data random-effect meta-analyses across four treatment comparisons: cognitive–behavioural therapy versus treatment as usual; cognitive–behavioural therapy versus other psychosocial interventions/active comparisons (active control psychosocial interventions); cognitive–behavioural therapy integrating additional elements from other therapies ('cognitive–behavioural therapy+') versus treatment as usual; and cognitive–behavioural therapy+ versus active control psychosocial interventions. Treatment by covariate interaction analyses were carried out to examine potential treatment effect modifiers, including participants' demographic characteristics (age, gender, ethnicity), clinical characteristics (illness duration, phase of illness, duration of untreated psychosis, initial severity of psychotic symptoms and affective symptoms), and specific intervention characteristics (treatment duration, number of therapy sessions, level of therapists' training/competence, use of manualised interventions, formulation-based interventions; individual vs. group interventions).

Results: A total of 53 trials were retrieved. Of these, 27 trials (n = 2870) were available for the planned cognitive–behavioural therapy versus treatment as usual primary outcome analyses, 11 trials (n = 961) for the cognitive–behavioural therapy versus active control psychosocial interventions analyses, 14 trials (n = 1985) for cognitive–behavioural therapy+ versus treatment as usual analyses, and 3 trials (n = 28) for the cognitive–behavioural therapy+ versus active control psychosocial interventions analyses. There was no reliable evidence indicating that any of the covariates considered in this evidence synthesis significantly impacted the efficacy of cognitive–behavioural therapy in this client group.

Limitations: Only 54% of the individual participant data requested were provided by data owners, and there is considerable heterogeneity in the features of the cognitive–behavioural therapy interventions included in this evidence synthesis.

Conclusions: The effectiveness of cognitive–behavioural therapy for overall symptom change in this patient group is not significantly affected by the covariates examined in this individual participant data meta-analysis.

Cognitive–behavioural therapy should continue to be offered equally to service users irrespective of their demographic or clinical characteristics.

Future work: Other potential avenues to explore moderators of cognitive–behavioural therapy efficacy are suggested, including the fine-grained analysis of specific intervention components and the added value of interventionist-causal paradigms.

Study registration: This study is registered as PROSPERO CRD42017060068.

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Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/NCFR5074).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

List of abbreviations

AC	active control
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BPRS	Brief Psychiatric Rating Scale
CBT	cognitive–behavioural therapy
CBT+	cognitive–behavioural therapy plus additional elements of other therapies
CBTp	cognitive–behavioural therapy for psychosis
CI	confidence interval
COS	core outcome set
CPRS	Comprehensive Psychopathological Rating Scale
DUP	duration of untreated psychosis
IMPART	Individual Modifiers of Patient Response to Treatment
IPD	individual participant data
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PANSS	Positive and Negative Syndrome Scale
PANSS G2	anxiety item of the PANSS
PPIE	patient and public involvement and engagement
PSYRATS	Psychotic Symptom Rating Scales
RCT	randomised controlled trial
RoB	risk of bias
TAU	treatment as usual, also referred to as standard care

Plain language summary

Psychosis, a mental health condition which can include experiences such as unusual beliefs and hearing voices, can cause great distress and be very difficult to cope with. Treatment guidelines in the United Kingdom and abroad recommend cognitive–behavioural therapy, a type of talking therapy that supports people with psychosis to change the way they think about and react to their experiences. However, while research has shown that cognitive–behavioural therapy can reduce psychosis symptoms for some people, its effectiveness seems to be mixed. For example, some studies show cognitive–behavioural therapy is very useful for psychosis patients, while others find it has little impact compared to other types of mental health support. Some of the differences found in these studies could be explained by the types of participants who took part in them (e.g. their age, gender, ethnicity and how challenging their mental health difficulties are). Another explanation might be the type of cognitive–behavioural therapy they received (e.g. how many therapy sessions they had, or whether they were offered group therapy or individual appointments).

Understanding more about these differences can help to explain who cognitive–behavioural therapy is most helpful for. We therefore invited researchers from across the world to share their results from these studies with us so we could look at them in more detail. We then combined the results together to see (1) if there are groups of patients who are more likely to benefit from cognitive–behavioural therapy, and (2) if there are ways of running cognitive–behavioural therapy sessions which are more effective. However, our findings suggest that the types of participants, and the types of cognitive–behavioural therapy, did not affect how helpful cognitive–behavioural therapy can be. In line with current treatment guidelines, this shows that people with psychosis should continue to be offered cognitive–behavioural therapy no matter what their social or mental health background is.

Scientific summary

Background

Cognitive–behavioural therapy (CBT) is a psychological intervention recommended by the National Institute for Health and Care Excellence (NICE) for the treatment and management of psychosis and schizophrenia. Aggregate data meta-analyses suggest that CBT for psychosis has modest but considerably heterogeneous treatment effects. This inconsistency partly stems from intertrial variation in several key methodological characteristics of the existing randomised controlled trials (RCTs) (e.g. blinding/masking of outcome assessments) but could also reflect the impact of unaccounted-for clinical heterogeneity – that is, specific intervention and patient characteristics that can influence the clinical effectiveness of CBT. For instance, previous trials differed widely in terms of intervention characteristics (e.g. number of sessions, treatment duration, use of manualised interventions), patients' baseline severity of psychotic and other comorbid symptoms, and their demographic characteristics (e.g. age, gender and ethnic origin) and illness duration. The identification of moderators of treatment response and/or subgroups of patients who may particularly benefit from CBT would allow optimisation of treatment delivery, with implications in terms of improved clinical effectiveness, cost savings and maximisation of patients' informed choice of treatment. The impact of these potential treatment effect modifiers, however, remains unaccounted for or at best poorly estimated in meta-analyses of aggregate study-level data due to their reliance on the reporting quality of primary studies and the limited statistical power of 'standard' meta-analytic methods for testing treatment effect moderators. Individual participant data (IPD) meta-analysis, a research synthesis method which summarises the evidence on a particular clinical question by considering individual participant rather than aggregated data from multiple related studies, allows for greater ability to examine the impact of multiple individual-level and study-level factors on the treatment effects considered, and is therefore a method ideally suited for identifying potential treatment effect modifiers of CBT interventions for people with schizophrenia and related psychotic disorders.

Objectives

The CBTp IMPART (cognitive–behavioural therapy for psychosis/Individual Modifiers of Patient Response to Treatment) project was an IPD meta-analysis which aimed to identify potential treatment effect modifiers of CBT in people with diagnoses on the schizophrenia spectrum.

Methods

Randomised controlled trials relevant for this evidence synthesis were identified through the literature searches of a recent aggregate data meta-analysis of this research literature (CRD42013003911). In line with the eligibility criteria of the aggregate data meta-analysis, the present IPD meta-analysis included RCTs comparing CBT to treatment as usual (TAU) and/or other active control psychosocial interventions (AC) in individuals with schizophrenia spectrum diagnoses in any setting (i.e. outpatient community settings as well as inpatient hospital settings). The primary outcome of this IPD meta-analysis was overall symptom change as measured by valid and reliable measures of psychotic symptoms severity – that is, the total score of Positive and Negative Syndrome Scales (PANSSs) or comparable measures that could be converted into PANSS total scores via validated conversion algorithms. In addition to this primary outcome, the original secondary aims of the CBTp IMPART project were to examine treatment effect modifiers of CBTp interventions across a range of outcomes frequently considered in eligible trials, including analyses of minimum clinically important differences and clinically significant deteriorations in PANSS scores as well as change in specific symptom clusters (positive symptoms, negative symptoms and general psychopathology symptoms), specific symptoms often targeted in CBTp interventions (hallucinations severity, delusions severity, hallucination-related subjective distress, delusion-related subjective distress, paranoia severity), affective symptoms (anxiety and depression severity), subjectively defined recovery, quality of life, social and occupational functioning, hospital readmissions and recorded adverse effects.

The data owners [i.e. the corresponding authors/data custodians of RCTs of CBT in patients with schizophrenia carried out in the United Kingdom (UK) and worldwide] of 110 trials identified from literature searches conducted in February 2018 as part of the above-mentioned aggregate data meta-analysis were contacted to request access to their trial data sets, with further contacts informed by a subsequent update of the above searches in January 2019. Data owners were also invited to share, when available, additional documentation that could inform or expedite data checking, cleaning and analysis (e.g. relevant IPD metadata, statistical analysis plans, intervention protocols/manuals and/or descriptions of the CBT interventions evaluated in their eligible trials). IPD data sets received by the project team underwent a range of standard quality and consistency checks of the data, including cross-checking the reanalysed IPD against previously published trial results to highlight inconsistencies or possible errors. Data were cleaned wherever necessary and then standardised to allow pooling and subsequent combined analyses of the data. The primary trial reports of all RCTs for which IPD were sought were assessed for risk of bias (RoB) using the Cochrane Collaboration RoB tool, in order to evaluate potential differences between the characteristics of trials that were included in the CBTp IMPART analyses, and trials for which IPD could not be retrieved.

Due to time and resource constraints, the analyses included in the current report focus only on the planned primary outcome analyses (PANSS total scores) using a two-stage IPD analytic approach; the execution of a one-stage IPD meta-analysis of the primary outcome and all secondary outcome analyses will be undertaken in future and reported elsewhere. Longitudinal mixed-effects models containing treatment effect were fitted to the PANSS total score trajectories within each study, allowing all recorded follow-up PANSS measurements to contribute to the model. Pooled treatment effects and confidence intervals (CIs) for the primary outcome were then estimated using a series of two-stage IPD random-effect meta-analyses across four treatment comparisons: CBT versus TAU, CBT versus other psychosocial interventions/active comparisons, CBT integrating additional active elements from other therapies (CBT+) versus TAU, and CBT+ versus AC. Treatment effect modifiers were examined within each treatment comparison by including treatment–covariate interactions in relevant models which were synthesised using random-effects meta-analysis. The list of covariates considered in CBTp IMPART analyses was informed by patient and public involvement and engagement consultations conducted at the project design stage with individuals with lived experience of psychosis and NHS psychological practitioners. The covariates tested included several participant-level variables considering participants' demographic characteristics (age at trial entry, gender, ethnicity) and participants' clinical characteristics [illness duration, phase of illness (first episode of psychosis vs. multiple episodes), duration of untreated psychosis, initial severity of psychotic symptoms, initial severity of affective symptoms, number of antipsychotic medications at baseline], as well as study-level variables pertaining to specific characteristics of the CBT interventions considered in the included trials (treatment duration, number of therapy sessions, level of therapists' training/competence, use of manualised interventions, formulation-based interventions, individual vs. group interventions).

Results

Data from 53 trials were provided by the contacted data owners, collectively considering a total of 5952 randomised participants (i.e. 48.0% of the 110 trials approached and 54.0% of the total IPD). The retrieved data sets pertained to trials predominantly conducted in the UK, whereas the trials for which IPD could not be included in the CBTp IMPART analyses were from a broader range of countries. The RoB assessment suggested that the included trials had a different overall RoB profile compared to trials that were not retrieved or could not be included in the CBTp IMPART analyses. Specifically, the included trials presented significantly lower risk for selection bias, detection bias, and attrition bias.

A total of 27 trials (n = 2870) were available for the planned CBT versus TAU primary outcome analyses, 11 trials (n = 961) for the CBT versus AC analyses, 14 trials (n = 1985) for the CBT+ versus TAU analyses and 3 trials (n = 235) for the CBT+ versus AC analyses. However, a smaller volume of IPD was available for trials that specifically provided data relevant to the primary outcome analyses and provided data for more than one follow-up point in order to fit the planned longitudinal mixed-model analyses (16 trials with 2089 randomised participants for the CBT vs. TAU comparison; 8 trials with 819 randomised participants for CBT vs. AC; 6 trials with 924 participants for CBT+ vs. TAU; 3 trials with 235 participants for the CBT+ vs. AC).

The main treatment effect analysis for the CBT versus TAU treatment comparison indicated CBT is associated with significant reduction in PANSS scores (mean difference −2.93, 95% CI −4.18 to −1.68) across all follow-ups compared to TAU, with a reasonably consistent direction of treatment effect across the included studies (I^2 = 38%). The main effect analyses for the remaining treatment comparisons did not find evidence of a significant clinical benefit of CBT when compared to AC, or CBT+ interventions when compared to TAU or AC. The treatment by covariate interaction analyses found no reliable evidence indicating that the variables considered in this IPD meta-analysis significantly moderated the effectiveness of CBT in this patient group.

Conclusions

The findings of the CBTp IMPART analyses corroborate the efficacy of CBT interventions compared to TAU evidenced in previous aggregate data meta-analyses of this research literature. While the reduction in PANSS scores observed in the present analyses is modest even when compared to the summary treatment effects of past aggregate data meta-analyses, this is a likely by-product of the analytic approach used in this IPD evidence synthesis, which aimed to utilise all available follow-up data considered in the included trials, as opposed to the more conventional approach involving the estimation of a summary treatment effect at a single follow-up point (e.g. end of treatment or the closest available follow-up following end of treatment). Conversely, our IPD meta-analysis found no evidence of superiority of CBT interventions compared to other active psychosocial interventions. While this finding is consistent with literature suggesting that different empirically validated psychotherapies may be equally effective, our results are incongruent with the findings of another recent IPD meta-analysis that focused specifically on RCTs comparing CBT interventions to other psychological interventions in people with psychosis, which led to findings in support of the superiority of CBT for improving overall psychotic symptom severity. This incongruence may be due to the different analytic approach employed in these IPD meta-analyses, as well as differences in the IPD data sets that were respectively retrieved and included in these two IPD evidence syntheses.

Unlike previous meta-analyses of this research literature, but in line with the approach taken in the aggregate data meta-analysis that informed the CBTp IMPART project, in the present IPD evidence synthesis we differentiated between trials considering CBT interventions fully consistent with the criteria outlined by current NICE guidelines for the treatment and management of schizophrenia and related psychoses, and trials that considered intervention packages that comprised both CBT and additional treatment components derived from other discrete psychological interventions, that is, the 'CBT+ versus TAU' and 'CBT+ versus AC' treatment comparisons. The analyses conducted as part of the CBTp IMPART project suggest that CBT+ interventions are not associated with significant reductions in PANSS scores across subsequent follow-ups relative to comparator treatments (TAU and AC, respectively). However, caution should be exerted when interpreting these findings, in particular relative to the treatment effect of 'purer' CBT intervention protocols outlined in the above-mentioned analyses, as these results may be due to the considerably lower number of trials (and IPD) available for the analyses for the CBT+ versus TAU and CBT+ AC treatment comparisons, as well as the extreme heterogeneity of the 'CBT+' interventions included in this treatment comparison, which may therefore not be linked to a consistent treatment effect.

Pertaining to the main objective of the project – that is, the identification of treatment effect modifiers of CBT interventions – the results of the treatment by covariate interaction analyses suggest that none of the variables examined as part of this IPD meta-analysis represent robust or reliable moderators of the efficacy of CBT interventions in people with diagnoses on the schizophrenia spectrum. In line with these findings, the principal clinical recommendation arising from this evidence synthesis is that CBT should continue to be offered equally to all service users with psychosis irrespective of their demographic characteristics, their clinical characteristics or the severity of their mental health difficulties, in line with current NICE recommendations. While the current IPD evidence synthesis did not identify treatment effect modifiers of CBT interventions in people with schizophrenia spectrum diagnoses, several factors may have limited our ability to identify variables that could maximise or account for heterogeneity in the effectiveness of CBT. First, while the current project represents the largest IPD meta-analysis of this research literature, it was not possible to retrieve a considerable proportion of the IPD that would have been relevant to the analyses planned as part of the CBTp IMPART project, therefore potentially limiting our ability to identify small or moderate treatment effect moderators in certain analyses. Second, while our analytic approach attempted to consider important

variances in the characteristics of the CBT interventions that have been thus far evaluated in available RCTs, the CBT intervention protocols evaluated in this body of clinical trials are highly heterogeneous, for example in terms of their modular structure, components, exact intervention strategies and treatment targets. The work conducted as part of this IPD meta-analysis was not designed to examine whether these more subtle variances in intervention characteristics may be associated with differences in CBT effectiveness. Hence, other potential avenues for examining whether these intervention-related characteristics may be associated with CBT efficacy could be explored as part of future research: for example, approaches that could enable the more fine-grained examination of the efficacy of specific intervention components within CBT intervention protocols, and analyses comparing existing more 'traditional' CBT protocols to newer intervention protocols that have shown evidence of improved efficacy in recent research, such as treatment protocols informed by 'interventionist-causal paradigms' which specifically target, using CBT intervention strategies, psychological mechanisms allegedly involved in the formation and maintenance of specific psychotic symptoms.

Further learning from the CBTp IMPART project is more broadly related to the process of conducting IPD meta-analyses of complex psychological interventions in clients with serious mental health difficulties. The data collection, data management and the cleaning and recoding of IPD proved more challenging than anticipated, and required considerably more time and resources than initially projected. Several initiatives could be implemented to facilitate and expedite future large-scale secondary analysis projects and IPD meta-analyses in this clinical research area, including the development and implementation of core outcome sets suited for the evaluation of psychological interventions in people with schizophrenia and related psychosis to facilitate outcome pooling across trials, the further promotion of use of trial data repositories and data-sharing practices to expedite access to relevant IPD, and the implementation and curation of detailed metadata documentation to facilitate data reuse.

Study registration

This study is registered as PROSPERO CRD42017060068.

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Chapter 1 Introduction

Background

Improving the care of people with schizophrenia and the provision of evidence-based psychological therapies to reduce the personal and societal burden of severe mental illness is a pressing and ongoing NHS priority.[1–4] Schizophrenia, a condition characterised by significant alterations in the person's perceptions, thoughts, behaviours and affect, is a leading cause of disability as well as personal and societal burden. The onset of schizophrenia is typically preceded by a prodromal phase characterised by perceptual alterations, unusual thought content, deterioration in personal functioning and social withdrawal. In a sizeable proportion of individuals, the prodrome develops into an acute phase of the illness characterised by distressing positive symptoms (feelings, perceptions and behaviours that are usually not present in 'healthy' individuals, such as hallucinations and bizarre persecutory delusions) and negative symptoms (thoughts, feelings and behaviours normally present in healthy individuals that are diminished or absent in a person with psychosis, such as flat affect and lack of motivation). Meta-analyses of longitudinal studies indicate that up to one-third of help-seeking prodromal patients transition to full-blown first episode psychosis within 3 years.[5] Prognosis after the first episode is heterogeneous, with a proportion of patients remitting but many going on to experience further episodes. Estimates of long-term recovery vary according to different operational definitions, but recent meta-analytic findings suggest that only 13.5% (8.1–20.0%) achieve full recovery in terms of sustained improvement in symptoms and social functioning.[6]

The point prevalence of schizophrenia spectrum disorders is estimated at 0.7% of the English adult general population.[7] This suggests that, at any one time point, approximately 392,000 individuals might be affected. The combined healthcare and indirect costs (i.e. societal costs incurred as a result of work absence) of schizophrenia in Britain are in excess of £12.5B per annum.[8] Its 'human costs' are even more dramatic, with approximately 25% of patients remaining socially and occupationally impaired many years after diagnosis,[6] and with about 5% committing suicide.[9] Globally, schizophrenia reduces patients' lifespan by 10 years on average, with evidence suggesting that the increased mortality observed in people with schizophrenia – which is due not only to suicide but also to an increased risk for a wide range of physical health problems[10] – has worsened in recent decades despite greater provision of medical care.[11] The severe burden, disability, and societal and health costs caused by schizophrenia highlight the urgent need to improve access to and the clinical effectiveness of evidence-based treatments, a priority recognised by the UK government, the NHS, independent commissions and service users.[12]

Current treatments for psychosis and schizophrenia, as recommended by the National Institute for Health and Care Excellence (NICE) in England[13,14] and corresponding clinical guidelines in other countries,[15–17] include pharmacological and psychological interventions. Despite evidence supporting the efficacy of pharmacological interventions for acute psychotic symptoms, a considerable proportion of patients are refractory to antipsychotic drug treatment.[18] Furthermore, pharmacological interventions are, in a sizeable proportion of patients, associated with a range of distressing and debilitating side effects that can not only compromise further the health and well-being of patients, but also lead to treatment noncompliance or discontinuation in a large number of cases.[19,20] Over the past three decades, the recognition of these issues has fuelled the development and evaluation of psychological interventions that could be routinely offered as efficacious, safe and acceptable treatment options to service users struggling with distressing psychotic symptoms. Cognitive–behavioural therapy (CBT) – a 'talking therapy' developed for the treatment of emotional disorders in the 1960s and 1970s and subsequently adapted to a range of other mental health difficulties, including schizophrenia[21,22] – is a psychological intervention that figures prominently in the NICE guidelines for the management and treatment of psychosis and schizophrenia.[13,14] Despite this, audit data suggest that CBT is not routinely offered to patients with diagnoses on the schizophrenia spectrum.[4] Evidence regarding 'what works for whom' would enable a more targeted allocation of NHS resources by ensuring that CBT is offered to all patients that are most likely to benefit from this treatment.

The efficacy of CBT in patients with schizophrenia spectrum diagnoses has been examined by a considerable number of randomised controlled trials (RCTs) and aggregate data meta-analyses. Convergent evidence across these reviews

indicates that the treatment effect of CBT on the overall severity of psychotic symptoms (the most common outcome of previous aggregate data meta-analyses) was modest, with standardised effect sizes (ESs) ranging between 0.13 and 0.49 in the most recent and comprehensive reviews.[23–28] These meta-analyses also highlighted considerable statistical heterogeneity in the treatment effect of CBT, as indicated by significant Q tests and I^2 values ranging between 40% and 70% in analyses that included a sufficient number of trials to estimate these heterogeneity statistics precisely.

Statistical heterogeneity can stem from both methodological heterogeneity (differences between trials in terms of methodological factors such as use of concealment of allocation and blinding) and clinical heterogeneity (differences in specific interventions or patient characteristics). Using subgroup and metaregression analyses, previous reviews have established that the statistical heterogeneity in CBT treatment effects is explained by intertrial methodological variability; for example, masking/blinding has been shown to moderate the treatment effect of CBT in several independent aggregate data meta-analyses.[25,28] On the other hand, the potential impact of variances in intervention and patient characteristics remains largely unknown. The investigation of these potential treatment modifiers is particularly relevant in the case of patients with diagnoses on the schizophrenia spectrum given the highly heterogeneous symptom profile, course and long-term outcomes of these conditions. Secondary analyses of individual RCTs have suggested that patient characteristics like gender, ethnicity and baseline symptom severity can moderate the outcomes of CBT in people with a diagnosis of schizophrenia.[29–32] However, these investigations are sparse, and their findings may be unreliable due to insufficient sample size (and therefore statistical power) in individual trials. Furthermore, the considerable number of aggregate data meta-analyses in this area has not adequately examined the role of intervention and patient characteristics as possible treatment effect moderators of CBT. This reflects the fact that aggregate data meta-analysis is ill-equipped for the investigation of treatment effect modifiers due to the limited statistical power of aggregate data metaregression methods and reliance on summary statistics and the reporting quality of primary studies.[33–35]

Given the impracticality of examining the treatment effect modifiers of CBT for schizophrenia using further primary research and the limitations of conventional meta-analytic methods, the present evidence synthesis uses individual participant data (IPD) meta-analysis to address this gap in the evidence base. IPD meta-analysis is considered the gold standard approach to evidence synthesis.[36–38] Rather than working on aggregate data extracted from trial reports, IPD meta-analysis evaluates and reanalyses individual-level data from all trials addressing a particular clinical research question. This approach is particularly informative when reviewing complex therapeutic areas with the aim of exploring variation and predictors of variation in treatment outcomes. It is widely recognised that IPD meta-analysis is the only methodology that can be used to explore patient-level treatment effect modifiers in a reliable and statistically robust way; for example, Lambert *et al.*[33] found compelling evidence that aggregate-level metaregression presents dramatically lower statistical power than an equivalent IPD analysis and is usually inadequate to identify clinically small or moderate treatment moderators. IPD meta-analysis is therefore ideally suited to our aims.

While more advanced aggregate data meta-analytic methods, such as network meta-analysis and cumulative meta-analysis, have started to be applied in psychosis research,[39–41] IPD meta-analyses remain sparse in this clinical research area, possibly due to their resource-intensive nature. To date, only two IPD meta-analyses have been conducted to evaluate the efficacy and potential moderators of pharmacological and psychological interventions for schizophrenia and other psychotic disorders. A recent IPD meta-analysis including data from clinical trials of pharmacological interventions considering patients with schizophrenia spectrum disorders has been conducted to evaluate with more precision the percentages of patients who do not respond to antipsychotic medication.[18] Using data from 16 RCTs (with a combined sample of 6221 randomised patients) examining the efficacy of antipsychotic medications on psychotic symptoms severity [assessed using Positive and Negative Syndrome Scale (PANSS) or Brief Psychiatric Rating Scale (BPRS)], this IPD meta-analysis confirmed that substantial numbers of patients present high levels of treatment non-response, and that certain patient characteristics (in particular earlier onset of illness and lower baseline severity of psychotic symptoms) were significantly associated with higher non-response rates. More pertinently to the current project, Turner *et al.*[42] recently reported the findings of an IPD meta-analysis aimed at evaluating the efficacy of cognitive–behavioural therapy for psychosis (CBTp) on measures of positive, negative and general psychotic symptoms' severity (i.e. the PANSSs, the BPRS and the Scale for the Assessment of Negative Symptoms) compared to

other psychological interventions. In this IPD meta-analysis, which included data sets from 14 RCTs (with a combined sample of 898 randomised participants), CBTp was associated with greater reduction in PANSS general symptoms and PANSS total symptoms post treatment, compared to other psychological interventions. However, no significant differences were observed for analyses focusing on positive and negative symptoms of psychosis. Moderation analyses conducted to identify possible sociodemographic moderators (age, gender, marital status, education level, ethnicity, occupation, type of diagnosis and illness duration in years) and clinical moderators (PANSS negative and general psychotic symptoms at baseline, and number of treatment sessions) showed that the treatment effect of CBTp was not significantly influenced by participant and clinical characteristics, suggesting that a broad range of patients with different background and clinical presentations may be able to benefit from psychological intervention.

The present evidence synthesis aimed to employ IPD meta-analysis to advance our understanding of the factors that maximise the clinical effectiveness of CBT in people with schizophrenia spectrum disorders, and in turn to optimise the way CBT is implemented in clinical practice. Rather than focusing exclusively on trials employing active control arms (as in Turner *et al.*[42]), the present IPD meta-analysis also investigated potential treatment effect moderators of CBTp interventions when compared to treatment as usual (TAU), drawing on a larger number of RCTs relative to previously reported IPD meta-analyses in this area. Objectives were prespecified prior to collection of the IPD data sets.

Primary objective

The primary objective of this research synthesis was to identify, using IPD meta-analysis, the treatment effect modifiers of CBT on overall psychotic symptom severity (operationally defined as PANSS scores or equivalent measures of overall psychotic symptom severity) in patients with schizophrenia spectrum diagnoses when compared to (1) standard care (labelled TAU meaning treatment as usual) and (2) other psychosocial treatments (labelled AC meaning active control).

More specifically, the treatment modifiers we aimed to examine as part of the IMPART (Individual Modifiers of Patient Response to Treatment) project were:

1. participants' demographic characteristics:
    a. age at entry in the trial
    b. gender
    c. ethnicity

2. participants' clinical characteristics:
    a. effect of specific diagnostic subgroups
    b. phase of the illness (i.e. first episode psychosis vs. not first episode)
    c. illness duration
    d. duration of untreated psychosis (DUP)
    e. initial severity of psychotic symptoms
    f. initial severity of comorbid affective symptoms (i.e. anxiety and depression)

3. characteristics of the CBT interventions evaluated in eligible RCTs:
    a. treatment duration
    b. number of therapy sessions offered in the trial
    c. measures of therapeutic alliance
    d. minimum study-required level of training and competence
    e. use of manualised interventions
    f. use of formulation-based interventions
    g. individual versus group interventions
    h. whether the intervention was designed to target the outcome under scrutiny
    i. length of study follow-up.

Secondary objectives

In addition to considering changes in overall psychotic symptom severity, given the evidence from aggregate data meta-analyses that the benefits of CBTp may extend beyond amelioration of psychotic symptom severity (e.g. Wykes *et al.*[27]), this evidence synthesis also had the secondary objective to consider a range of secondary outcomes as yet not examined in previous IPD meta-analyses of CBTp trials; these are listed in *Table 1*. However, due to time and resource constraints, the present report only focuses on the primary outcome analyses of the CBTp IMPART project, and results pertaining to the secondary objectives and secondary outcome analyses will be reported elsewhere.

TABLE 1 List of secondary outcomes originally considered in by the CBTp IMPART project

1. Minimum clinically important differences in PANSS scores:
   - Whether a reduction of 11 or more points was achieved between baseline and the end of the treatment period
   - Whether a reduction of 15 or more points was achieved between baseline and the end of the treatment period
2. Clinically significant deterioration in PANSS scores:
   - Whether an increase of 11 or more points was recorded between baseline and the end of the treatment period
   - Whether an increase of 15 or more points was recorded between baseline and the end of the treatment period
3. Change in specific symptom clusters or syndromes (i.e. positive symptoms, negative symptoms and symptoms of general psychopathology, e.g. as measured by the positive, negative and general psychopathology subscales of the PANSS)
4. Change in specific symptoms often targeted by CBTp, namely:
   - Severity of hallucinations [as measured by e.g. the total of the hallucinations subscale of the Psychotic Symptom Rating Scales (PSYRATS)]
   - Severity of delusions (as measured by e.g. the total of the PSYRATS delusions subscale)
   - Subjective distress due to hallucinations (as measured by e.g. the total of the PSYRATS hallucinations items quantifying the amount and intensity of distress associated with hallucinatory experiences)
   - Subjective distress due to delusions (as measured by e.g. the total of the PSYRATS delusions items quantifying the amount and intensity of distress associated with delusional beliefs)
   - Severity of paranoia (as measured by e.g. the suspiciousness item of the PANSS score)
5. Change in severity of affective symptoms, namely:
   - Anxiety [as measured e.g. by scales such as the Beck Anxiety Inventory (BAI)]
   - Depression [as measured e.g. by scales such as the Beck Depression Inventory (BDI)]
6. Subjectively defined recovery (as measured e.g. by scales such as the Questionnaire about the Process of Recovery)
7. Quality of life (as measured e.g. by scales such as the World Health Organization Quality of Life Scale)
8. Social and occupational functioning (as measured e.g. by scales such as Global Assessment of Functioning or the Social and Occupational Functioning Assessment Scale)
9. Early treatment discontinuation
10. Adverse events including:
    - Deaths
    - Attempts at suicide
    - Suicide ideation
    - Serious violent incidents (including self-harm)
11. Hospital readmissions

Chapter 2 Methods

Protocol and registration

This evidence synthesis was undertaken and reported according to current reporting guidelines for IPD meta-analyses.[36] The protocol of this IPD meta-analysis was registered prospectively on PROSPERO (CRD42017060068) and subsequently published in a peer-reviewed journal.[43] In this current report we present methods and results for the primary outcome only. Analyses of secondary outcomes will be reported separately.

Some text in this chapter has been reproduced from our study protocol[43] (https://doi.org/10.1136/bmjopen-2019-035062), published under the Creative Commons Attribution License (CC BY 4.0). This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The text below includes minor additions and formatting changes to the original text.

Identification of trials for inclusion

Potentially eligible trials for this IPD meta-analysis were identified from studies included in an ongoing aggregated data meta-analysis led by a research team that included CBTp IMPART collaborators.[44,45] The exact search strategy employed in this aggregate data meta-analysis is described in more detail in the protocol and future pending publications of this aggregate data meta-analysis, and is reproduced in brief here. Electronic searches were originally conducted in May 2013 and subsequently updated as late as January 2019 on multiple databases (the Cochrane Central Register of Controlled Trials, PubMed, EMBASE and the online clinical trials registers of the US government, European Union, World Health Organization and Current Controlled Trials Ltd) using adaptations of the following generic strategy:

[schizo$ (exp. schizophrenia + psychosis + schizoaffective)] AND [trial (exp. RCT + controlled trial + clinical trial)] AND [cbt (exp. cognitive therapy + behaviour therapy + psychotherapy)].

Eligibility criteria

Study selection criteria for this IPD meta-analysis were consistent with those employed by the parent aggregate data meta-analysis. Trials were included if they met the following criteria.

Study design

Single-blind or open controlled trials utilising random allocation to treatment were included. Studies employing other research designs (case series, crossover studies, cohort analyses) were not eligible.

Target population

Trials were deemed eligible when > 50% of participants had diagnoses on the schizophrenia spectrum (schizophrenia, schizoaffective disorder or early psychosis). Trials where > 50% participants had an established diagnosis of bipolar disorder, intellectual disability, psychosis secondary to a general medical condition or organic pathology, or a primary diagnosis of substance-induced psychosis were excluded. No restriction was placed on participants' age, ethnicity, illness severity and illness duration.

Setting/context

No restriction was placed on the setting/context where participants were managed (e.g. community care, inpatient mental health wards).

Intervention

Consistent with NICE definitions,[13] CBT was defined as a discrete psychological intervention (i.e. in addition to, or separate from, other interventions) where service users:

1. Establish links between, thoughts, beliefs, perceptions and feelings in relation to their current or past symptoms and/or functioning, and
2. Re-evaluate their beliefs, perceptions and reasoning relating to target symptoms
3. and that should involve:
    - Service users monitoring their own thoughts, feelings or behaviours with respect to the symptom or recurrence of symptoms, and/or
    - The promotion of alternative ways of coping with the target symptom, and/or
    - Reduction of distress, and/or
    - Improvement of functioning.

Comparators

Eligible comparators were standard care (the level of care service users would routinely receive had they not been involved in the trial) and other psychosocial interventions (i.e. where standard care is supplemented by additional psychological or social interventions distinct from CBT). These comparators were labelled TAU and active comparator, respectively.

Data collection

Identified RCTs meeting the inclusion criteria are listed in *Appendix 1*. Study selection for the aggregate data meta-analysis was carried out by the original research team who conducted the evidence synthesis. For the purposes of the IMPART project, a single researcher checked the studies included in the aggregate data meta-analysis against the above inclusion criteria ahead of the submission of collaboration requests to data owners to share their anonymised trial data and participate in this IPD meta-analysis. Lack of clarity or discrepancies in selection decisions were discussed with other members of the research team to reach a consensus and, when required, additional information to ascertain eligibility was requested from the RCTs' authors.

Investigator requests

Following the confirmation of eligibility, a member of the IMPART study team e-mailed an invitation for collaboration and request for anonymised IPD to the lead author of each study. Co-authors were also approached in cases where lead authors were no longer working (e.g. they had retired by the time data collection started) or did not reply to our initial collaboration requests. Prospective collaborators were asked to consider, and complete if possible, a data availability form (see *Report Supplementary Material 1*) to evaluate the availability of the following variables relevant to the present IPD meta-analyses.

Individual-level variables

- participant characteristics
    - participant identifier (ID)
    - age (at entry to study)
    - date of randomisation into study
    - gender
    - ethnicity
    - diagnostic subgroup (e.g. schizophrenia, schizophrenia affective disorder, delusion disorder)
    - phase of illness (first episode psychosis vs. multiple episodes)
    - duration of illness
    - date of diagnosis of psychosis (if duration of illness is not available)
    - DUP

- participant's treatment
  - baseline antipsychotic medication(s)
  - baseline antipsychotic medication(s) dosage(s)
  - randomised treatment assignment (e.g. CBT, TAU, AC)
  - number of therapy sessions attended by each individual participant
  - measures of therapeutic alliance (e.g. the California Psychotherapy Alliance Scale (CALPAS) at any follow-up)
  - early treatment discontinuation
  - participant baseline and follow-up data for primary and secondary outcomes considered in the trial.

Study-level variables/information

- types of treatments delivered
- whether therapy was group or individual intervention
- time period during which treatment was delivered
- length of study follow-up
- number of planned therapy sessions
- level of therapists' training and competence
- use of a manualised intervention
- use of a formulation-based intervention
- method of randomisation (generation of random list)
- method of concealment of randomisation
- stratification factors
- blinding methods (if applicable)
- analysis approach (intention to treat/per protocol/other).

The following study documentation was also requested from each included study if available:

- the trial's statistical analysis plan (and any amendments)
- the trial's protocol (and any amendments)
- variable documentation stating coding and labels for variables in data sets
- blank case report form
- references to any published manuscripts relating to the supplied data.

To minimise the work involved for each collaborator, anonymised data were requested on any scale, for any time points recorded in the study (including baseline measurements). The trials' authors were also asked to provide additional information pertaining to the CBT interventions considered in each RCT, to evaluate the extent to which these conformed to the criteria outlined by NICE, and for the purposes of defining several study-level variables related to our moderator analyses focusing on CBT intervention characteristics.

Data transfer and data storage

The transfer of anonymised data from collaborators to the CBTp IMPART study team was conducted using 'datanywhere', a password-protected and connection-encrypted web portal provided by the University of Liverpool (which has since been discontinued). An e-mail was sent to collaborators containing a hyperlink to a specific folder in 'dataanywhere'. A separate e-mail was sent providing a unique password to access the hyperlink. Access to the folder via the hyperlink expired after 10 days, and each collaborator could only upload data files to the specific folder that they had been given access to. All data were stored according to the University of Liverpool's research data management policy (https://www.liverpool.ac.uk/library/research-data-management/) under the principles of Information Security Policy ISO 27001 (available at http://www.liv.ac.uk/csd/security/information-security/).

Data sets were saved in an encrypted folder with access restricted to the CBTp IMPART study statisticians based at the University of Liverpool who had prior permission to access the data. All individuals had received training in data protection and were explicitly forbidden to attempt to reidentify individuals within the data sets or to store any data

anywhere (e.g. computer hard drive, removable drive) other than the secure network drive. All data sets were checked to ensure that personally identifiable information had been removed by collaborators, and to identify low-frequency variables (i.e. variables with a frequency of < 5–10% within the trial) that could have potential for reidentification of patients. Where concerns were raised, we had planned to use guidance from PhUSE De-identification Standards for SDTM 3.2 for further anonymising high risk data (available from: De-identification Standard for SDTM 3.2 Version 1.0.xls), but this was not required.

Risk of bias assessment

The primary trial reports of all RCTs for which IPD were sought were assessed for risk of bias (RoB) using the Cochrane Collaboration RoB tool.[46] Five domains were selected for RoB assessment: two selection bias domains (random sequence generation, and allocation concealment bias), one performance bias domain (blinding of participants and personnel), one detection bias domain (blinding of outcome assessments), and one attrition bias domain (incomplete outcome data at the end-of-treatment follow-up assessment).

Primary outcome

Overall psychotic symptom severity assessed using PANSS scores (or comparable measure of overall psychotic symptom severity e.g. the BPRS) measured during the study period.

Treatment comparisons

In line with the planned analyses of the aggregate data meta-analysis by Hutton *et al.*,[44,45] the CBTp IMPART analyses distinguished between treatment packages fully consistent with the NICE definition of CBT (see *Eligibility criteria*) and treatment packages that incorporated significant elements of other, distinct psychosocial intervention approaches (e.g. mindfulness, motivational interviewing, family intervention) alongside core CBT elements. Unless specified otherwise, patient outcomes were compared between the following treatment groups:

1. CBT versus standard care (TAU)
2. CBT versus other psychosocial intervention (AC)
3. CBT plus elements from other therapies (CBT+) versus standard care (TAU)
4. CBT+ versus other psychosocial intervention (AC).

Prior to conducting analyses, CBTp IMPART study clinicians reviewed and confirmed the classification of CBT and CBT+ studies based on information obtained from the authors of the aggregate data meta-analysis, and classified any additional trials that were retrieved as part of IMPART but omitted in the final aggregate data meta-analysis (e.g. due to lack of sufficient aggregate information in the trial report to enable effect size computation) based on information extracted from the trial reports and/or additional information provided by data owners (see *Investigator requests*). In all cases, the classification of treatment approaches considered in the included studies was conducted without knowledge of the outcomes of patients included in the CBTp IMPART IPD meta-analyses.

For studies that compared more than one active treatment with a comparator (e.g. studies that compared two types of CBT to TAU), we pooled the active treatment arms together.

Treatment effect modifiers

The candidate treatment modifiers were selected a priori as part of the project plan included in the grant application that supported the CBTp IMPART project. The selection of treatment effect modifiers considered in our IPD meta-analyses was informed by: (1) expert knowledge of the variables examined in previous and ongoing RCTs by members of our team and the collaborators who joined the IMPART collaboration; (2) the findings of the studies which examined predictors of outcomes in previous RCTs;[29–32] and (3) patient and public involvement and engagement (PPIE)

consultations with service users with lived experience of psychosis (the Psychosis Research Unit Service User Reference Group, located within Greater Manchester Mental Health NHS Foundation Trust), and clinical psychologists and CBT therapists working with clients with psychosis in NHS secondary care settings in the Greater Manchester Mental Health NHS Foundation Trust.

While we originally planned to consider a broader range of potential treatment effect modifiers (see *Background*), the treatment effect modifiers that were ultimately examined and are considered in the present report were:

1. participant demographic characteristics:
   - age at entry to trial
   - gender
   - ethnicity

2. participant clinical characteristics:
   - phase of illness (first episode psychosis vs. multiple episode psychosis)
   - illness duration
   - DUP
   - initial severity of psychotic symptoms, namely:
     i. baseline total PANSS score
     ii. baseline total PANSS positive subscale
     iii. baseline total PANSS negative subscale

   - initial severity of comorbid affective symptoms, namely:
     i. baseline anxiety measurements (as measured by scales such as the BAI)
     ii. baseline depression measurements (as measured by scales such as the BDI)

   - Number of antipsychotic medications received at baseline

3. Specific intervention characteristics:
   - time period over which treatment was delivered (treatment duration)
   - the number of therapy sessions offered in the study
   - minimum study-required level of therapists' training and competence
   - use of manualised interventions
   - use of formulation-based interventions
   - individual versus group interventions.

Due to time and resource constraints, the present report does not include analyses of the following treatment effect modifiers: effect of specific diagnostic subgroups; dosage equivalence of baseline medication(s); number of therapy sessions attended by the individual; measures of therapeutic alliance; indicator for whether the intervention was designed to target the outcome under scrutiny; length of study follow-up. In some cases, data extraction required more in-depth correspondence with data providers or discussion with clinical experts than was initially expected, lengthening the data preparation process (dosage equivalence of baseline medications; indicator for whether the intervention was designed to target the outcome under scrutiny; length of study follow-up). In other cases (number of therapy sessions attended by the individual; measures of therapeutic alliance), to properly analyse these treatment modifiers, we would have to account for the fact that only those on the active arms of the investigation would record the modifiers; for example, those undergoing standard care (TAU) would not have a value recorded for number of therapy sessions attended, as sessions were never offered. While methods to account for this have been proposed in the literature (e.g. by Dunn *et al.*[47]), the use of these methods was beyond the scope of the current report.

Data standardisation

A range of standard quality and consistency checks of the data were conducted, cross-checking the reanalysed IPD against previously published results to highlight inconsistencies or possible errors. Checks included level of missing data, comparison of supplied time points with reported time points, sequence generation and supplied demographics data, Any queries were raised with collaborators. Data were cleaned wherever necessary and then standardised to allow pooling and subsequent analyses of the data.

Scales

Several of the outcomes and effect modifiers of interest can be measured using alternative scales. To allow the data from multiple studies to be combined in a meaningful way, we adopted the following general approach.

For the primary outcome (and baseline measure), where possible, we converted measures of severity of psychotic symptoms onto a common PANSS scale. Studies that had recorded the primary outcome either using PANSS directly, or on the BPRS scale, contributed to the primary outcome analysis. BPRS scores were converted using the tables provided by Leucht *et al.*[48] linking the BPRS and PANSS total scores. As we were transferring from BPRS to PANSS, and as the table from the mentioned publication supplied multiple PANSS values for each BPRS value (e.g. a BPRS score of 18 could translate to a PANSS score or 30 or 31), we assigned the mean value of the possible PANSS scores [e.g. we translated a BPRS score of 18 to a PANSS score of (30 + 31)/2 = 30.5]. From discussion with clinicians in the field, it was highlighted that assessment scales are tested based on the entire scale, not items or subscales. As such, attempts were not made to transform comparable data onto outcomes that are defined using only subscales or items from full scale measures. We also did not attempt to transfer other scales onto PANSS where we did not have established transfer tables [e.g. we did not transfer from the Comprehensive Psychopathological Rating Scale (CPRS) to PANSS].

When transformation of data onto a single scale was not possible, we planned an analysis of standardised scores[49,50] in conjunction with sensitivity analyses contrasting the use of transformed and standardised variables. However, due to time and resource constraints, in this report we focus on analyses of trials for which a PANSS total score was either provided or could be estimated as above.

Participants' demographic characteristics

Participant-level demographic characteristics were standardised as follows:

- age in years as a continuous variable
- gender as a binary individual-level variable
- ethnicity recoded to Caucasian versus non-Caucasian (since the majority of included trials were undertaken in Western countries and hence most participants included in the present IPD meta-analyses were likely to be European or of European ancestry).

Participants' clinical characteristics

Participant clinical characteristics were standardised as follows:

i. Phase of illness was coded as 'first episode psychosis' versus 'multiple episodes' (i.e. more than one recorded episode of psychosis on entry to the study). If phase of illness was not recorded, we used duration of illness data, where available, and classified phase of illness as 'first episode' if within the first 3 years of their illness, and 'multiple' otherwise.
ii. Illness duration (years) was calculated as date of randomisation minus date of diagnosis if not provided directly. In this and other duration variables, temporal data provided by data owners were transformed onto a common scale using the relationships 1 year = 12 months, 1 year = 52 weeks, and 1 year = 365.25 days.
iii. DUP was calculated as time (years) from first psychotic symptom to time of starting treatment.
iv. Initial severity of psychotic symptoms was measured using baseline PANSS scores, and was considered as three treatment modifiers (which were examined separately), namely:
    - initial severity of psychotic symptoms
    - initial severity of psychotic positive symptoms
    - initial severity of psychotic negative symptoms.

If a study did not record baseline PANSS scores, but provided baseline measures of severity of psychotic symptoms on a scale considered comparable to the PANSS scale, we converted to the PANSS scale. This was only relevant for BPRS, and we used the approach provided by Leucht *et al.*[48] linking the BPRS and PANSS total scores, using the process described above. Transforming between measurement scales for variables recorded by subscales of the PANSS score (e.g. initial severity of psychotic positive symptoms and initial severity of psychotic negative symptoms) was not attempted.

v. Initial severity of comorbid anxiety symptoms was examined using baseline anxiety measurements. It was expected that anxiety would be measured on multiple scales (e.g. BAI or item G2 of the PANSS) in the studies contributing to the IPD meta-analyses. If the majority of studies had employed the same scale, we planned to use the most common scale for the main analysis, with methods sought to convert any other scales used in remaining studies to this scale (e.g. established conversion tables). In the absence of a suitable 'common' scale, we planned to calculate anxiety 'standardised scores' (individual score value divided by the between-patient standard deviation[49]), where there was a clear ordering to the scale and the clinical importance of a jump of *x* units on the scale is the same across the length of the scale;[50] however, standardised score analyses have not been completed for this report due to time and resource constraints, and analyses were conducted for trials providing BAI scores (the most commonly reported scale).
vi. Initial severity of depression was examined using baseline depression measurements. It was expected that depression would be measured on multiple scales (e.g. BDI, Calgary scale, Hamilton scale, or item G6 of the PANSS) in the studies contributing to the meta-analysis. If the majority of studies had employed the same scale, we planned to use the most common scale for the main analysis, with methods sought to convert any other scales used in remaining studies to this scale (e.g. established conversion tables). In the absence of a suitable 'common' scale, we planned to calculate depression 'standardised scores' (individual score value divided by the between-patient standard deviation[49]), where there was a clear ordering to the scale and the clinical importance of a jump of *x* units on the scale is the same across the length of the scale;[50] however, standardised score analyses have not been completed for this report due to time and resource constraints, and analyses were conducted using BDI scores (the most commonly reported scale).
vii. While the original objectives of the project included an analysis of total antipsychotic medication dosage at baseline, this analysis is not included here due to resource and time constraints, and antipsychotic medication at baseline was instead accounted for via the number of antipsychotic medications being received at baseline. This data were coded as a continuous variable in the analysis data set.

Intervention characteristics

The following variables were coded (as study-level treatment effect modifiers; i.e. the same level of each variable applied to the entire trial/each participants within an included trial) based on additional information provided by data owners or, when this was not provided, based on best available information extracted from the published trial reports of the included studies:

i. Time period over which treatment was delivered (treatment duration): the duration of the intervention window during which participants allocated to the CBT/CBT+ intervention could receive the experimental treatment. For this and other duration variables, temporal data provided by data owners or extracted from trial reports were transformed onto a common scale using the relationships 1 year = 12 months, 1 year = 52 weeks, and 1 year = 365.25 days.
ii. The number of therapy sessions offered in the study: this was defined as the maximum permissible number of therapy sessions as reported in intervention manuals, data owners' reports or the published trial report.
iii. Level of therapists' training and competence: this was coded as a dichotomous variable identifying trials that specified the use of therapists suitably trained, competent and/or experienced in the application of CBT (e.g. specification in trial report that CBT-trained therapists or therapists with CBT diplomas were used, as opposed to the sole provision of in-house training in the CBT intervention considered in the study).
iv. Use of manualised interventions: this was a dichotomous variable identifying trials that specified the use of specific manuals or manualised approaches guiding the delivery of the intervention; this was irrespective of whether trials checked intervention adherence and/or the integrity of the reported manualised approach.

v. Use of formulation-based interventions: this was a dichotomous variable identifying trials that clearly specified that the intervention was guided by CBT/psychological formulation.
vi. Individual versus group interventions: this was a dichotomous variable distinguishing between trials which considered group CBT interventions versus trials where CBT was delivered on an individual basis.

Statistical methods for the analysis of primary outcome (Positive and Negative Syndrome Scale)

Unless specified otherwise, all analyses were undertaken including patients in the treatment group they were randomised to using an intention-to-treat analysis. Missing data were not imputed.

A two-stage random-effects meta-analysis framework was adopted to estimate the main effects of treatment and explore treatment effect modifiers. R version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses.

Treatment main effects

For the outcome PANSS, the model denoted (1) was fitted to the data from each study in turn

$$PANSS_{kij} = \beta_{0k} + \beta_{1k} Base\,PANSS_{ki} + \beta_{2k} treat_{ki} + \beta_{3k} time_{kij} + \beta_{0ki}^{(2)} + \beta_{kij} \quad (1)$$

where *k* represents study membership, *i* indexes the individual, and *j* indexes the measurement. In model (1) *BasePANSS* is the baseline PANSS score, *treat* is the treatment and *time* is the time at which measurements are recorded. Fixed-effect coefficients are represented by β terms and random effects are represented by *b* (with the superscript indexing the level at which the random effects act: (2) indicates an individual-level random effect). The error term is represented by ε.

At the individual level, a random intercept $\left(b_{0ki}^{(2)}\right)$ was included. This random-effect structure was selected based on examination of the longitudinal trajectories, and subsequent comparison between models with different random-effects structures. The trajectory plots (see *Report Supplementary Material 2*, *Supplementary Figures 2–5*) indicated variability between individuals in their trajectory intercept, but similarity between individuals in the rest of the shape of the trajectory. This, coupled with the comparison of models with different random-effect structures, led to the selection of random intercept only for the random-effects structure. Random-effect structures were assessed for each of the four separate sets of treatment comparisons.

Separate analyses were conducted for (1) CBT versus TAU, (2) CBT versus other psychosocial intervention (AC), (3) CBT+ versus TAU, and (4) CBT+ versus AC.

The treatment effect coefficient (interpreted as the difference in means) estimated for each study $k\left(\hat{\beta}_{2k}\right)$ was extracted from each study-level model and the function metagen from the R package meta was used to calculate the 'random-effects' pooled treatment effect parameter $\hat{\beta}$ using the below equation:

$$\hat{\beta} = \frac{\sum_{k=1}^{K} w_k \hat{\beta}_{2k}}{\sum_{k=1}^{K} w_k}$$

with $w_k = 1 / \left(v_k + \tau^2\right)$, where v_k denotes $\text{var}\left(\hat{b}_{2k}\right)$, and τ^2 represents the between-study variance estimated using restricted maximum likelihood.

Effect modifiers

For the outcome PANSS and individual-level effect modifiers, the model denoted (2) was fitted to the data from each study in turn to explore the effect of potential modifiers of treatment effect.

$$PANSS = \beta_{0k} + \beta_{1k} BasePANSS_{ki} + \beta_{2k} treat_{ki} + \beta_{3k} time_{kij} + \beta_{4k} X + \beta_{5k}{}^{oX} * treat_{ki} + b_{0ki}^{(2)} + \varepsilon_{kij} \quad (2)$$

With notation as for model (1) and *X* is the potential treatment effect modifier, and *X*treatki* is the interaction between treatment effect modifier and treatment assignment. At the individual level, a random intercept $\left(b_{0ki}^{(2)}\right)$ was included (justification for this random-effect structure given above).

Separate analyses were conducted for (1) CBT versus TAU, (2) CBT versus other psychosocial intervention (AC), (3) CBT+ versus TAU and (4) CBT+ versus AC.

The interaction coefficient estimated by study $k\left(\hat{\beta}_{5k}\right)$ was extracted from each study-level model and the function metagen from the R package meta was used to calculate the 'random-effects' pooled treatment interaction effect parameter $\hat{\beta}1$ using the below equation:

$$\hat{\beta}1 = \frac{\sum_{k=1}^{K} w_k \hat{\beta}_{5k}}{\sum_{k=1}^{K} w_k}$$

with $w_k = 1 / \left(v_k + \tau^2\right)$, where v_k denotes $\text{var}\left(\hat{\beta}_{5k}\right)$, and τ^2 represents the between-study variance estimated using restricted maximum likelihood. In this IPD meta-analysis, between-study heterogeneity was quantified through examination of the I^2.

For study-level effect modifiers, the metareg function in the meta package in R was used.[51] Initially, a two-stage meta-analysis without treatment effect modifiers was performed, as detailed earlier. The results of this two-stage meta-analysis were then adjusted by the treatment effect modifier, using the equation below:

$$\hat{\beta}_k = \beta + \alpha x_k + \varepsilon_k + b_k^{(3)} \quad (3)$$

In the equation above, $\hat{\beta}_k$ represents the study-specific estimate of the treatment effect. The true (unobserved) treatment effect is denoted β. The study-level treatment effect modifier is denoted *xk*, with corresponding coefficient α. The amount by which the study-specific estimate differs from its true value is captured by the sampling error εk. The study-specific random effect $b_k^{(3)}$ captures how the study-specific treatment effect differs from the underlying global true treatment effect.

The coefficient α from the above equation is used to identify whether the study-level treatment effect modifier has a statistically significant effect by examining the confidence interval (CI) of the coefficient. The effect of the study-level treatment effect modifier was explored using a bubble plot.

Chapter 3 Results

Identification of trials for inclusion in the project

The identification of trials suitable for inclusion in the CBTp IMPART project and the submission of investigator requests to access IPD was initiated in July 2018. Identification of trials was guided by the literature searches of an ongoing aggregate data meta-analysis of this research literature. These searches were originally conducted in May 2013 and were updated multiple times prior to the initiation of the IMPART project (in October 2014, January 2017 and February 2018). IPD were sought for 110 trial reports deemed eligible for inclusion in the CBTp IMPART analyses based on the most updated literature searches available at the start of the data collection process for this IPD meta-analysis. Investigators approached for participation in the CBTp IMPART project were able to provide data up until a data collection deadline at the end of March 2020. The full list of trials for which IPD were sought can be found in *Appendix 1*. A flow diagram illustrating the inclusion and exclusion of trials in the CBTp IMPART project is shown in *Figure 1*.

Up to March 2020, the CBTp IMPART team received 53 trial data sets from contacted investigators, collectively providing a total of 5952 randomised participants (i.e. 48.0% of the trials and 54.0% of the total IPD from the 110 trials approached). Further inspection of the retrieved trials revealed that three data sets[52–54] did not include essential data to enable their inclusion in the planned IPD meta-analyses (e.g. missing outcomes of interest or randomisation variables). After their exclusion, 50 RCTs suitable for inclusion in the planned IPD meta-analyses were left (*N* = 5808). The list of trials including at least one outcome of interest for the IMPART analyses is displayed in *Table 2*.

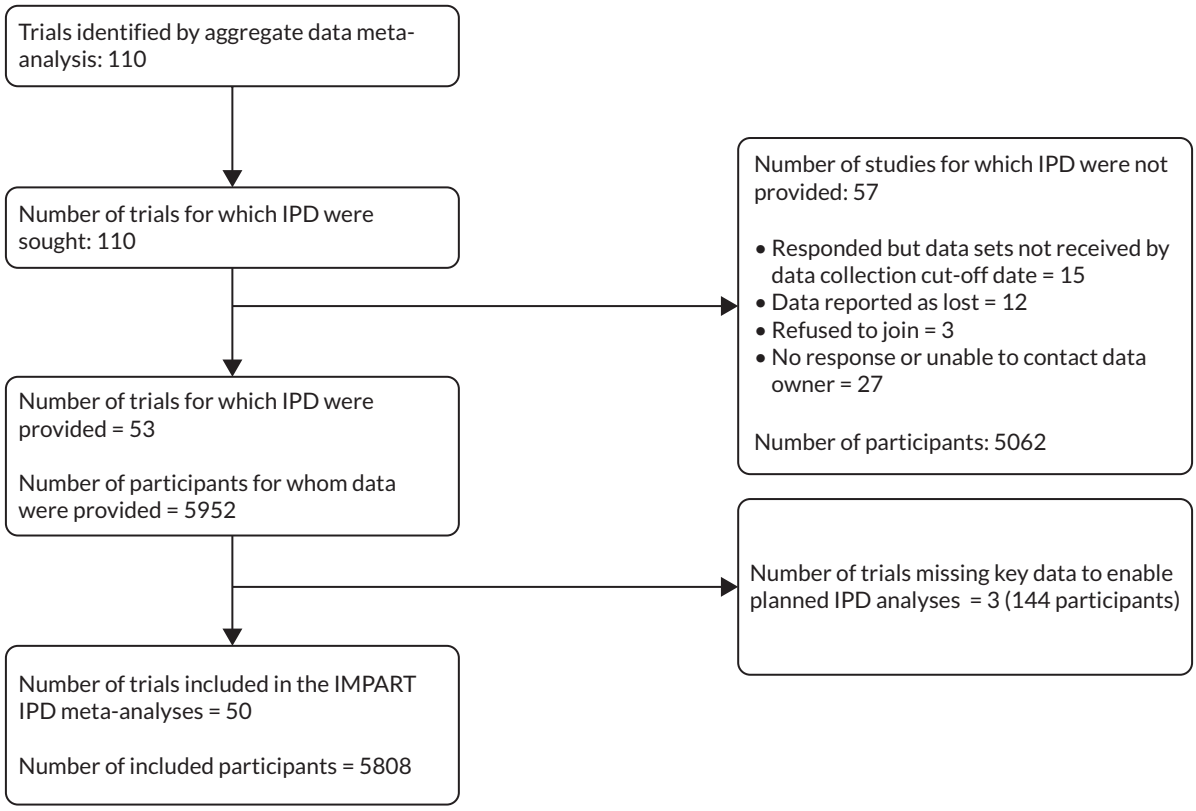

FIGURE 1 Flow diagram summarising the selection of studies for the CBTp IMPART project.

TABLE 2 Randomised controlled trials included in the CBTp IMPART project

Trial reference	Total *N*	*N* CBT arm	*N* TAU arm	*N* AC arm	Type of therapy	Country
Baker *et al.* (2006)[55]	298	147	151	0	CBT+	Australia
Baker *et al.* (2006)[56]	130	65	65	0	CBT+	Australia
Barrowclough *et al.* (2006)[57]	113	57	56	0	CBT	UK
Barrowclough *et al.* (2010)[58]	327	164	163	0	CBT+	UK
Barrowclough *et al.* (2014)[59]	110	75	35	0	CBT+	UK
Bechdolf *et al.* (2010)[60]	88	40	0	48	CBT	Germany
Birchwood *et al.* (2014)[61]	197	98	99	0	CBT	UK
Cather *et al.* (2005)[62]	28	15	0	13	CBT	USA
Chadwick *et al.* (2016)[63]	108	54	54	0	CBT+	UK
Farhall *et al.* (2009)[64]	92	45	47	0	CBT	Australia
Favrod *et al.* (2014)[65]	52	26	26	0	CBT+	Switzerland
Foster *et al.* (2010)[66]	24	12	12	0	CBT	UK
Fowler *et al.* (2009)[67]	77	35	42	0	CBT+	UK
Freeman *et al.* (2014)[68]	30	15	15	0	CBT	UK
Freeman *et al.* (2015)[69]	50	24	26	0	CBT	UK
Freeman *et al.* (2015)[70]	150	73	77	0	CBT	UK
Garety *et al.* (2008)[71]	273	133	140	0	CBT	UK
Granholm *et al.* (2005)[72]	76	37	39	0	CBT+	USA
Granholm *et al.* (2013)[73]	64	31	0	33	CBT+	USA
Granholm *et al.* (2014)[74]	149	73	0	76	CBT+	USA
Gumley *et al.* (2003)[75]	144	72	72	0	CBT	UK
Haddock *et al.* (1999)[76]	20	9	0	11	CBT	UK
Haddock *et al.* (2009)[77]	77	38	0	39	CBT	UK
Jackson *et al.* (2009)[78]	66	36	30	0	CBT	UK
Jolley *et al.* (2003)[79]	21	12	9	0	CBT	UK
Kuipers *et al.* (1997)[80]	54	27	27	0	CBT	UK
Landa *et al.* (2011)[81]	24	12	12	0	CBT	USA
Lecomte *et al.* (2008)[82]	119	46	27	46	CBT	Canada
Li *et al.* (2015)[83]	192	96	0	96	CBT	China
Lincoln *et al.* (2012)[84]	80	40	40	0	CBT	Germany
Madigan *et al.* (2013)[85]	88	59	29	0	CBT	Ireland
Morrison *et al.* (2014)[86]	74	37	37	0	CBT	UK

continued

TABLE 1 Randomised controlled trials included in the CBTp IMPART project (*continued*)

Trial reference	Total *N*	*N* CBT arm	*N* TAU arm	*N* AC arm	Type of therapy	Country
Morrison *et al.* (2016)[87]	29	15	14	0	CBT	UK
Morrison *et al.* (2018)[88]	487	242	245	0	CBT	UK
Naeem *et al.* (2015)[89]	116	59	57	0	CBT	Pakistan
Naeem *et al.* (2016)[90]	33	18	15	0	CBT	Canada
Palma-Sevillano *et al.* (2011)[91]	34	21	13	0	CBT+	Spain
Penadés *et al.* (2006)[92]	40	20	0	20	CBT	Spain
Peters *et al.* (2010)[93]	74	36	38	0	CBT	UK
Rathod *et al.* (2013)[94]	33	15	18	0	CBT	UK
Steel *et al.* (2017)[95]	61	30	31	0	CBT	UK
Steel *et al.* (2020)[96]	100	49	51	0	CBT	UK
Tarrier *et al.* (2004)[97]	308	101	102	105	CBT	UK
Turkington *et al.* (2002)[98]	422	257	165	0	CBT+	UK
Turkington *et al.* (2008)[99]	90	47	0	43	CBT	UK
Valmaggia *et al.* (2005)[100]	58	35	0	23	CBT	Netherlands
van den Berg *et al.* (2015)[101]	102	55	47	0	CBT+	Netherlands
van der Gaag *et al.* (2011)[102]	207	110	97	0	CBT	Netherlands
van der Gaag *et al.* (2012)[103]	77	39	38	0	CBT+	Netherlands
Velligan *et al.* (2015)[104]	142	37	37	33	CBT+	USA

Characteristics of the included trials

Trials were largely from the UK (27 trials) and other European countries (Netherlands = 4; Germany = 2; Spain = 2; Switzerland = 1; Ireland = 1), with fewer trials received from data owners from North America (USA = 6; Canada = 2), Australia (3 trials) and other countries (China = 1; Pakistan = 1). They were published between 1997 and 2020. Sample sizes varied considerably across trials, ranging from 20[76] to 487[88] randomised participants.

Forty RCTs provided data relevant to the comparison of CBT interventions (irrespective of the CBT vs. CBT+ distinction undertaken in our analyses) against TAU, and 12 RCTs provided data relevant to the contrast of CBT interventions against AC psychosocial interventions (with three trials providing data for both TAU and AC analyses). AC interventions evaluated in the received trials included supportive counselling (three trials),[83,97,100] psychoeducation programmes (two trials; Bechdolf *et al.*, 2004 [62,105]), goal-focused supportive contact (two trials[73,74]), befriending (one trial[99]), Cognitive Adaptation Training (one trial[104]), Cognitive Remediation Therapy (one trial[92]), social skills training (one trial[82]) and social activity training (one trial[77]).

As the participants' demographic characteristics (age, gender, ethnicity) and the features of the CBT interventions considered in the included trials were potential treatment effect modifiers in the planned IPD meta-analyses, descriptive analyses of these variables are reported in detail in *Chapter 5*.

Assessment of risk of bias in the included trials

The results of RoB assessment for the 50 trials included in the IMPART analysis are summarised in *Figure 2*. Individual RoB scores for each included trial can be found in *Appendix 3*.

In relation to selection bias, 79% and 72% of the RCTs had a low RoB relating to random sequence generation and allocation concealment bias, respectively. All trials included in IMPART were rated at high risk in relation to performance bias (i.e. blinding of participants and personnel, as a by-product of the intrinsic knowledge of the treatment received by trial participants in clinical trials of psychological therapies). Respectively, 86% and 84% of included RCTs had low risk for detection bias (blinding of outcome assessments) and attrition bias (incomplete outcome data at the end-of-treatment follow-up assessment).

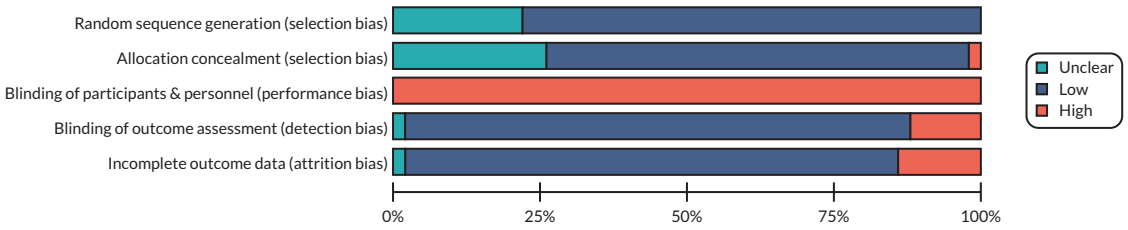

FIGURE 2 Risk of bias assessment results of the 50 trials retrieved for the CBTp IMPART project.

Comparison of included and excluded trials

A list of the trials for which IPD could not be retrieved is provided in *Appendix 2*. While over 50% of the trials included in the present IPD meta-analyses had been conducted in the UK (27 trials), the trials for which IPD were not retrieved or could not be included in the IMPART analyses were from a broader range of countries. These included 15 UK trials, 16 trials from other European countries (Germany = 7; Netherlands = 2; Norway = 2; Italy = 2; France = 1; Poland = 1; Switzerland = 1), 14 trials from North America (USA = 10; Canada = 4), 7 from Australia, 5 from China, and 3 from other countries (Hong Kong, Israel and Turkey). Visual inspection of the publication year of retrieved versus unretrieved trials indicated that earlier RCTs were less likely to provide data and therefore to be included in the present analyses (see *Report Supplementary Material 2*, *Supplementary Figure 1*). The excluded studies had a combined sample size of 5196 randomised participants. The efficacy of CBT against a TAU arm was compared in 38 trials, while 24 trials compared CBT to an AC psychosocial intervention, with 2 trials including both a TAU and an AC arm.

The results of RoB assessment for the 60 trials that could not be included in the present IPD meta-analyses are summarised in *Figure 3*. Individual RoB scores for each trial can be found in *Appendix 4*. The RoB assessment suggested that the included trials had a different overall RoB profile compared to trials that were not retrieved or could not be included in the IMPART analyses. More specifically, the included trials presented significantly lower risk across the selection bias domain (78% vs. 53% low-risk categorisation for random sequence generation, and 72% vs. 43% for allocation concealment), the detection bias domain (86% vs. 63%), and the attrition bias domain (84% vs. 68%). As the assessment was based on the published trial reports, these differences cannot be explained by additional information that was provided by data owners for this IPD meta-analysis. There was no difference on performance bias (100% of trials were rated at high risk across both groups).

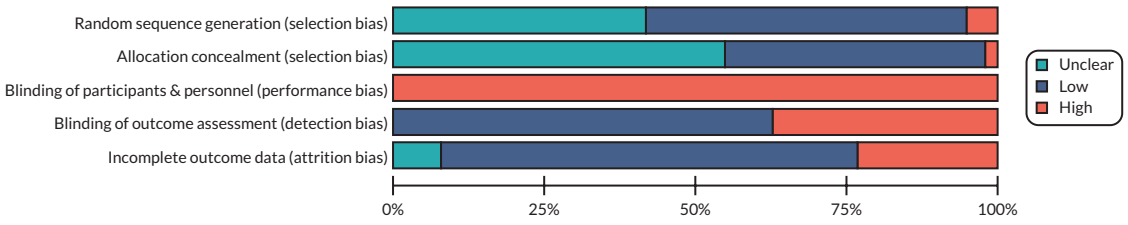

FIGURE 3 Risk of bias assessment of the 60 trials not retrieved for the CBTp IMPART project.

Total sample size across the planned treatment comparisons

In total, six trials[55,56,76,80,82,104] reported the primary outcome on the BPRS scale and were transferred onto the PANSS scale. A total of three studies[94,98,99] used CPRS, but we did not transfer this to PANSS as established methods of conversion between the scales are not available.

A detailed breakdown of available IPD across the four planned treatment comparisons (CBT vs. TAU, CBT vs. AC, CBT+ vs. TAU, and CBT+ vs. AC) is available in *Appendix 5*. Overall, 27 trials with a total of 2870 participants (1461 of whom were assigned to CBT) were available for the planned CBT versus TAU analyses, while 11 trials with a total of 961 participants (484 allocated to CBT) were available for the CBT versus AC analyses. The CBT+ versus TAU analyses considered data from 1985 participants (1059 of whom were allocated to CBT+ interventions) in 14 trials. Only three trials, with a total of 281 participants (139 allocated to CBT+ interventions), were available for the CBT+ versus AC analyses.

Some studies did supply data on the primary outcome but, due to the analysis methods being employed, were unable to contribute to our analysis. Specifically, we included baseline PANSS score as an explanatory variable and performed a longitudinal data analysis to examine the trend in PANSS scores over time. As such, studies were required to supply a baseline PANSS score and plan two or more post-baseline PANSS measurements to contribute to the analysis. Studies by Jolley *et al.*,[79] Steel *et al.* (2016)[95], Lincoln *et al.*,[84] Naeem *et al.*,[90] and Naeem *et al.*[89] did not meet these requirements and so could not contribute to the two-stage analysis we ran (a total of five studies, 311 individuals). Similarly, within a contributing study, any individuals who only supplied a baseline PANSS measurement, or who did not record the treatment effect modifiers under examination, would also be dropped from the analysis (numbers of studies and individuals contributing to analyses are noted in captions/tables as appropriate).

The planned IPD data integrity checks were performed. Where there were any queries about data quality or availability that could not be resolved through discussion with data providers, a study did not contribute to analyses related to the data in question. There were a small number of queries relating to particular treatment effect modifiers, but no significant data integrity issues.

Primary outcome analysis (Positive and Negative Syndrome Scale): cognitive–behavioural therapy versus treatment as usual trials

Main effect of treatment

A total of 16 studies (2089 individuals) contributed to the main treatment effect analysis (*Figure 4*) of CBT versus TAU in the two-stage random-effects model meta-analysis. In the supplied forrest plots, TE refers to treatment effect, and seTE refers to the standard error of the treatment effect. The negative pooled treatment effect of −2.93 (95% CI −4.18 to −1.68) suggests that CBT reduces PANSS score by an average of 2.93 points across all follow-up compared to TAU (statistically significant at the 5% level) with a reasonably consistent direction of treatment effect across the included studies (I^2 = 38%). The funnel plot for the CBT versus TAU treatment comparison (displayed in *Appendix 6*) did not uncover any evidence of substantial asymmetry.

Treatment effect modifiers

Descriptive statistics pertaining to the potential patient- and study-level treatment effect modifiers examined in the CBT versus TAU trials are included in *Appendix 7*.

Patient-level covariates

There is no evidence that the following patient-level characteristics modify the effect of CBT versus TAU (see *Table 1*): age in years, gender, non-Caucasian compared to Caucasian, phase of illness, duration of illness, DUP, baseline PANSS total score, baseline PANSS positive subscale score, baseline PANSS negative subscale score, baseline anxiety as measured by the BAI, baseline depression as measured by the BDI, and baseline number of antipsychotic medications (see *Report Supplementary Material 2*, *Supplementary Figures 6–17*).

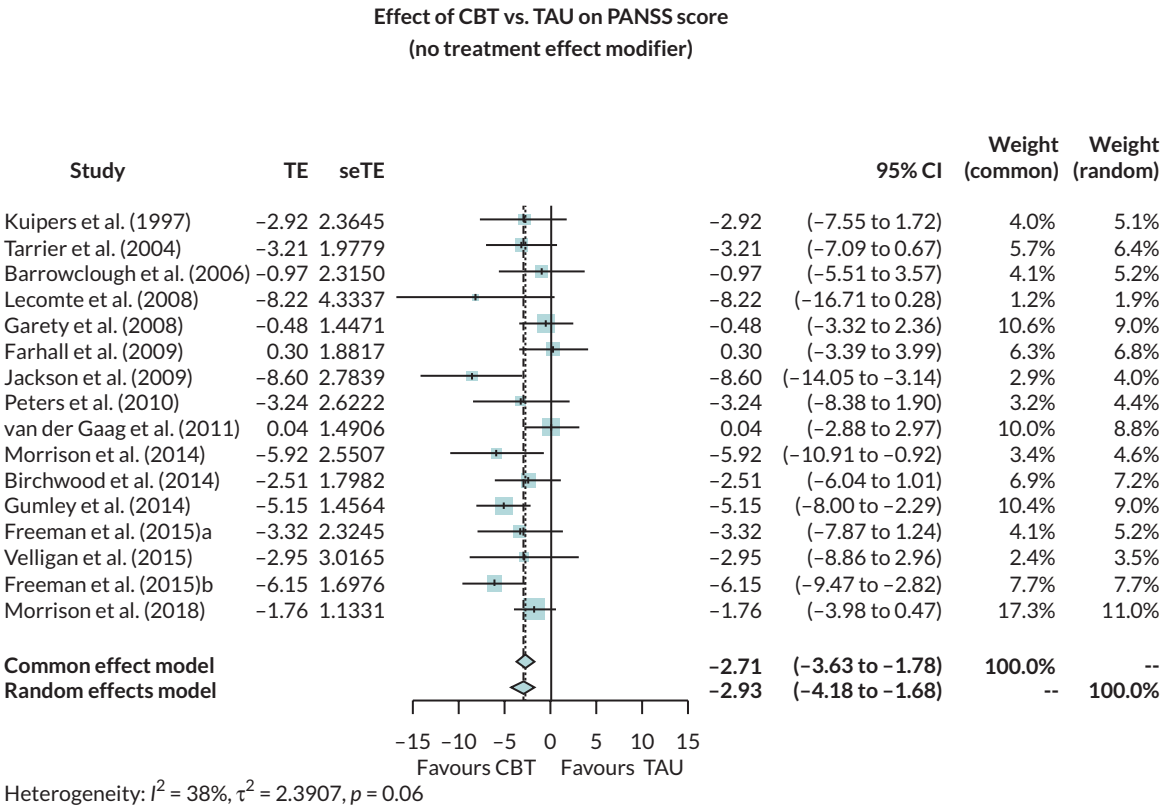

FIGURE 4 Effect of CBT vs. TAU on PANSS score. TE, treatment effect; seTE, standard error of the treatment effect

Study-level effect modifiers

The bubble plots for the study-level effect modifiers for the CBT versus TAU treatment comparison are displayed in the *Report Supplementary Material 2*, *Supplementary Figures 18–22*. There is evidence (statistically significant at the 5% level) of a modifying effect for the study-level treatment duration [effect estimate of 5.14 (95% CI 0.95 to 9.32)] from the metaregression analysis based on 16 studies and 2089 individuals. This means that for every additional year of treatment duration, the difference in mean PANSS score of CBT versus TAU is expected to rise by 5.14 from a baseline value of −5.51 (95% CI −7.95 to −3.07) at duration zero. For example, for a study where the treatment duration is 0.25 years, the difference in mean PANSS for CBT versus TAU is −5.51 + (0.25 × 5.14) = −4.23; for a study where the treatment duration is 0.75, the difference in mean PANSS for CBT versus TAU is −5.51 + (0.75 × 5.14) = −1.66. This analysis seems to suggest that individuals in studies with longer treatment regimens had smaller reductions in PANSS scores over the course of the study. However, this relationship may not necessarily reflect true associations at the patient level due to potential ecological bias, and the assumption of a linear relationship may not be reasonable. Additionally, the range of observed treatment duration for the CBT versus TAU data ranges from 0.08 to 0.75 years; we should not extrapolate outside this range to predict effects of other treatment durations on treatment effect.

There was no evidence that any other examined study-level effects (number of therapy sessions; therapist level; use of formulation-based interventions; individual vs. group interventions) were modifiers of treatment effect (see *Table 3*). Use of manualised interventions could not be explored as all studies in the CBT versus TAU comparison had manualised intervention.

Primary outcome analysis (Positive and Negative Syndrome Scale): cognitive–behavioural therapy versus active control trials

Main effect of treatment

A total of eight studies (819 individuals) contributed to the main treatment effect analysis of CBT versus AC (*Figure 5*). Based on the data available, there was no evidence of a difference in PANSS score as a result of being assigned to CBT

TABLE 3 Summary of treatment effect modifier analyses (CBT vs. TAU, PANSS total score)

	Variable	Number of studies (participants)	Pooled interaction effect[a] (95% CI)	I^2 (%)
Patient-level covariate	Age (years)	16 (2018)	0.01 (−0.09 to 0.10)	12
	Gender (female)	16 (2089)	0.23 (−1.76 to 2.22)	0
	Ethnicity (non-Caucasian)	11 (1505)	−1.44 (−4.77 to 1.88)	0
	Phase of illness	10 (1564)	−0.09 (−3.26 to 3.09)	0
	Duration of illness (years)	11 (1581)	0.00 (−0.16 to 0.15)	0
	DUP (years)	3 (598)	0.07 (−0.47 to 0.62)	0
	PANSS total score	16 (2089)	−0.07 (−0.16 to 0.02)	40
	PANSS positive	12 (1870)	−0.07 (−0.30 to 0.16)	0
	PANSS negative	12 (1870)	−0.19 (−0.44 to 0.06)	21
	Baseline anxiety on BAI	5 (518)	−0.04 (−0.18 to 0.09)	18
	Baseline depression on BDI	5 (460)	0.10 (−0.08 to 0.27)	0
	Baseline number of antipsychotic medications	4 (333)	−0.67 (−3.15 to 1.82)	3
Study-level covariate	Treatment duration (years)	16 (2089)	5.14 (0.95 to 9.32)	13
	Therapy sessions offered	14 (1984)	0.12 (−0.02 to 0.25)	28
	Therapist training	16 (2089)	−2.36 (−5.18 to 0.46)	29
	Manualised interventions	N/A	No estimation possible[b]	–
	Formulation-based intervention		5.40 (−3.69 to 14.48)	40
	Individual vs. group intervention		−0.00 (−4.92 to 4.92)	43

a Two-stage random-effects model.
b All studies in CBT vs. TAU comparison have manualised intervention.

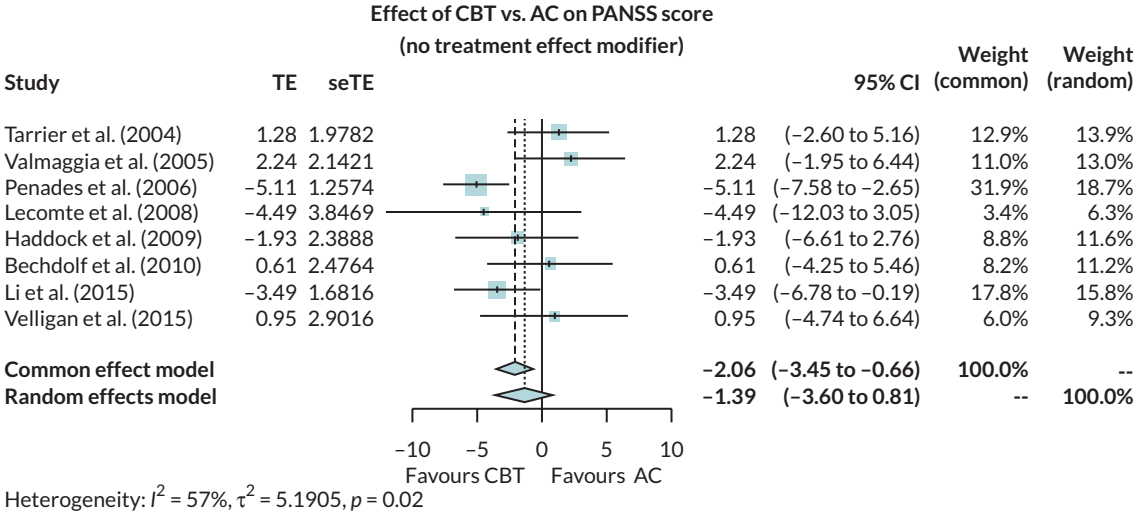

FIGURE 5 Effect of CBT vs. other psychosocial intervention (AC) on PANSS score.

rather than other psychosocial intervention with pooled effect −1.39 (95% CI −3.60 to 0.81) with a moderate degree of heterogeneity across studies (I^2 = 57%). Due to the low numbers of trials considered in this treatment comparison, a funnel plot was not produced.

Treatment effect modifiers

Descriptive statistics pertaining to the potential patient- and study-level treatment effect modifiers examined in the CBT versus AC trials are included in *Appendix 8*.

Patient-level covariates

There is no evidence that the following patient-level characteristics modify the effect of CBT versus other psychosocial (AC) intervention (see *Table 2*): age in years, gender, non-Caucasian compared to Caucasian, phase of illness, duration of illness, DUP, baseline PANSS total score, baseline PANSS total positive subscale score, baseline PANSS total negative subscale score, baseline depression score measured on BDI, baseline number of antipsychotic medications. There was very limited evidence from a single study of 61 participants suggesting baseline anxiety score as a potential modifier of treatment effect of CBT versus AC (−1.41, 95% CI −2.27 to −0.55) (see also *Report Supplementary Material 2*, *Supplementary Figures 23–34*). If we use the BAI values recorded in this study for the first quartile (25th centile, a score of 24), the difference in mean PANSS score for CBT versus AC is −1.39 + (−1.41 × 24) = −35.23. If we repeat this for the third quartile (75th centile, a score of 37), the difference in mean PANSS score for CBT versus AC is −1.39 + (−1.41 × 37) = −53.56. This suggests that those with higher baseline anxiety display a greater treatment effect; however, this is based on data from one small study.

Study-level effect modifiers

The bubble plots for the study-level effect modifiers for the CBT versus AC treatment comparison are displayed in the *Report Supplementary Material 2*, *Supplementary Figures 35–40*. There was no evidence that any of the examined study-level effects (treatment duration; number of therapy sessions; therapist level; manualised intervention; use of formulation-based interventions; individual vs. group interventions) were modifiers of treatment effect for the CBT versus AC comparison (*Table 4*).

Primary outcome analysis (Positive and Negative Syndrome Scale): cognitive–behavioural therapy plus additional elements of other therapies versus treatment as usual trials

Main effect of treatment

A total of six studies (924 individuals) contributed to the main treatment effect analysis of CBT+ versus TAU (*Figure 6*). Based on the data available, there was no evidence of a difference in PANSS score as a result of being assigned to CBT+ rather than TAU, with pooled effect −0.02 (95% CI −1.87 to 1.83) with a low to moderate degree of heterogeneity across studies (I^2 = 29%). Due to the low numbers of trials considered in this treatment comparison, a funnel plot was not produced.

Treatment effect modifiers

Descriptive statistics pertaining to the potential patient- and study-level treatment effect modifiers examined in the CBT versus AC trials are included in *Appendix 9*.

Patient-level covariates

There is no evidence that the following patient-level characteristics modify the effect of CBT+ versus TAU (*Table 5*): age in years, gender, non-Caucasian compared to Caucasian, phase of illness, duration of illness, DUP, baseline PANSS total score, baseline PANSS total positive subscale score, baseline PANSS total negative subscale score, baseline anxiety score, baseline depression score measured on BDI, baseline number of antipsychotic medications (see also *Report Supplementary Material 2*, *Supplementary Figures 41–51*).

Study-level effect modifiers

The bubble plots for the study-level effect modifiers for the CBT+ versus TAU treatment comparison are displayed in the *Report Supplementary Material 2*, *Supplementary Figures 52–55*. There was no evidence that any of the examined

TABLE 4 Summary of treatment effect modifier analyses (CBT vs. AC, PANSS Total score)

	Variable	Number of studies (patients)	Pooled interaction effect[a] (95% CI)	I^2 (%)
Patient-level covariate	Age (years)	8 (727)	−0.07 (−0.22 to 0.08)	0
	Gender (female)	7 (704)	2.22 (−1.48 to 5.91)	0
	Ethnicity (non-Caucasian)	5 (466)	−5.13 (−11.50 to 1.24)	0
	Phase of illness	5 (533)	4.150 (−0.16 to 8.46)	0
	Duration of illness (years)	6 (533)	−0.05 (−0.31 to 0.21)	0
	DUP (years)	1 (183)	−0.06 (−2.46 to 2.35)	–
	PANSS total score	8 (737)	−0.06 (−0.16 to 0.03)	0
	PANSS positive	6 (594)	−0.20 (−0.59 to 0.20)	0
	PANSS negative	6 (594)	−0.12 (−0.42 to 0.19)	0
	Baseline anxiety on BAI	1 (61)	−1.41 (−2.27 to −0.55)	–
	Baseline depression on BDI	2 (130)	−0.43 (−1.20 to 0.34)	69
	Number of antipsychotic medications	2 (133)	4.69 (−1.76 to 11.14)	0
Study-level covariate	Treatment duration (years)	8 (737)	−0.82 (−13.41 to 11.77)	60
	Therapy sessions offered	8 (737)	−0.13 (−0.35 to 0.09)	45
	Therapist training	7 (704)	3.35 (−0.09 to 6.79)	0
	Manualised interventions	7 (704)	−2.87 (−9.45 to 3.72)	59
	Formulation-based intervention	7 (704)	3.23 (−0.17 to 6.64)	0
	Individual vs. group intervention	7 (659)	−3.12 (−12.51 to 6.27)	64

a Two-stage random-effects model.

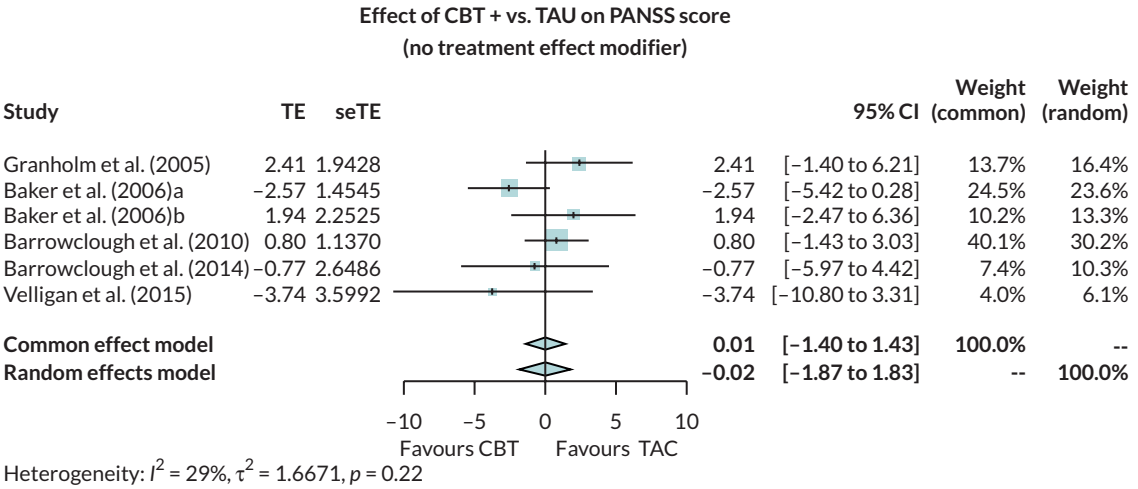

FIGURE 6 Effect of CBT+ vs. TAU on PANSS score.

TABLE 5 Summary of treatment effect modifier analyses (CBT+ vs. TAU, PANSS total score)

	Variable	Number of studies (participants)	Pooled interaction effect[a] (95% CI)	I^2 (%)
Patient-level covariate	Age (years)	6 (920)	0.09 (−0.15 to 0.33)	43
	Gender (female)	6 (924)	1.56 (−1.97 to 5.08)[b]	56
	Ethnicity (non-Caucasian)	3 (234)	−2.65 (−10.06 to 4.76)	0
	Phase of illness	5 (820)	−2.39 (−6.77 to 2.00)	0
	Duration of illness (years)	5 (614)	0.17 (−0.07 to 0.40)	0
	DUP (years)	1 (47)	1.76 (−3.42 to 6.94)	NA
	PANSS total score	6 (924)	−0.01 (−0.10 to 0.08)	0
	PANSS positive	3 (442)	−0.16 (−0.57 to 0.24)	0
	PANSS negative	3 (442)	0.22 (−0.22 to 0.66)	0
	Baseline anxiety on BAI	1 (85)	−0.38 (−0.86 to 0.11)	NA
	Baseline depression on BDI	2 (389)	0.15 (−0.04 to 0.33)	0
	Baseline number of antipsychotic medications	3 (486)	0.44 (−1.97 to 2.85)	0
Study-level covariate (metaregression)	Treatment duration (years)	6 (924)	1.52 (−4.73 to 7.76)	34
	Therapy sessions offered	6 (924)	0.03 (−0.18 to 0.25)	36
	Therapist training	6 (924)	0.61 (−3.66 to 4.88)	39
	Manualised interventions	6 (924)	Not estimable[c]	–
	Formulation-based interventions	6 (924)	0.72 (−3.40 to 4.84)	38
	Individual vs. group intervention	6 (924)	Not estimable[d]	–

a Two-stage random-effects model.
b Due to convergence issues, method for calculating τ^2 was set to maximum likelihood rather than restricted maximum likelihood. This can lead to different estimates for τ^2.
c Metaregression cannot be performed as all studies in this comparison have manualised treatment.
d Metaregression could not be performed as all studies were individual interventions not group interventions.

study-level effects (treatment duration; number of therapy sessions; therapist level; use of formulation-based interventions) were modifiers of treatment effect for the CBT+ versus TAU comparison (see *Table 5*). Use of manualised intervention and effect of individual versus group interventions could not be examined as all studies used manualised intervention and all studies used individual interventions.

Primary outcome analyses (Positive and Negative Syndrome Scale): cognitive–behavioural therapy plus additional elements of other therapies versus other psychosocial intervention active control trials

Main effect of treatment

A total of three studies (235 individuals) contributed to the main treatment effect analysis of CBT+ versus other psychosocial (AC) intervention (*Figure 7*). Based on the data available, there was no evidence of a difference in PANSS score as a result of being assigned to CBT+ rather than other psychosocial (AC) intervention, with pooled effect −1.11 (95% CI −4.56 to 2.34) with a low degree of heterogeneity across studies (I^2 = 0%). Due to the low numbers of trials considered in this treatment comparison, a funnel plot was not produced.

Treatment effect modifiers

Descriptive statistics pertaining to the potential patient- and study-level treatment effect modifiers examined in the CBT versus AC trials are included in *Appendix 10*.

Patient-level covariates

There is no evidence that the following patient-level characteristics modify the effect of CBT+ versus other psychosocial (AC) intervention (see *Table 4*): age in years, gender, non-Caucasian compared to Caucasian, phase of illness, duration of illness, baseline PANSS total score, baseline PANSS total positive subscale score, baseline PANSS total negative subscale score, baseline anxiety score, baseline depression score measured on BDI, baseline number of antipsychotic medications (see also *Report Supplementary Material 2*, *Supplementary Figures 56–66*). None of the studies provided data for the DUP.

Study-level effect modifiers

The bubble plots for the study-level effect modifiers for the CBT+ versus TAU treatment comparison are displayed in the *Report Supplementary Material 2*, *Supplementary Figures 67–68*. There was no evidence that any of the examined study-level effects (treatment duration; number of therapy sessions; therapist level; use of formulation-based interventions) were modifiers of treatment effect for the CBT+ versus TAU comparison (*Table 6*). Use of manualised intervention and effect of individual versus group interventions could not be examined as all studies used manualised intervention and all studies used individual interventions.

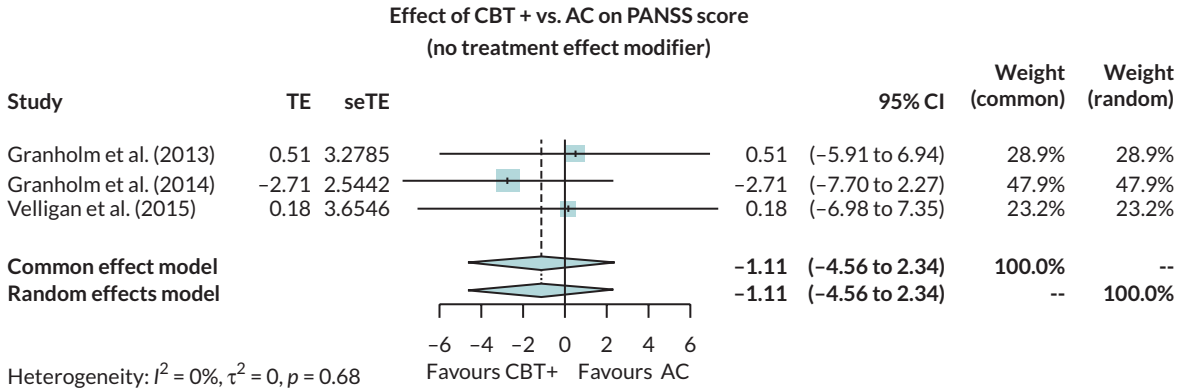

FIGURE 7 Effect of CBT+ vs. other psychosocial (AC) intervention on PANSS score.

TABLE 6 Summary of treatment effect modifier analyses (CBT+ vs. AC, PANSS total score)

	Variable	Number of studies (participants)	Pooled interaction effect[a] (95% CI)	I^2 (%)
Patient-level covariate	Age (years)	3 (231)	0.21 (−0.19 to 0.60)	0
	Gender (female)	3 (235)	−1.32 (−8.58 to 5.95)	0
	Ethnicity (non-Caucasian)	3 (235)	−3.07 (−10.38 to 4.25)	0
	Phase of illness	2 (149)	−4.49 (−23.06 to 14.08)	0
	Duration of illness (years)	3 (200)	0.04 (−0.29 to 0.37)	0
	DUP (years)	No data available	–	–
	PANSS total score	3 (235)	−0.09 (−0.35 to 0.18)	47
	PANSS positive	2 (167)	−0.13 (−0.81 to 0.55)	0
	PANSS negative	2 (167)	−0.01 (−0.53 to 0.51)	0
	Baseline anxiety on BAI	2 (166)	−0.24 (−0.94 to 0.45)	78

TABLE 6 Summary of treatment effect modifier analyses (CBT+ vs. AC, PANSS total score) (*continued*)

	Variable	Number of studies (participants)	Pooled interaction effect[a] (95% CI)	I^2 (%)
	Baseline depression on BDI	2 (167)	−0.06 (−0.43 to 0.31)	0
	Number of antipsychotic medications	2 (167)	−1.71 (−10.17 to 6.74)	50
Study-level covariate	Treatment duration (years)	3 (235)	Not estimable[b]	–
	Therapy sessions offered	3 (235)	0.84 (−3.25,4.93)	0
	Therapist training	3 (235)	Not estimable[c]	–
	Manualised interventions	3 (235)	Not estimable[d]	–
	Formulation-based interventions	3 (235)	1.61 (−4.08 to 7.30)	0
	Individual vs. group intervention	3 (235)	Not estimable[e]	–

a Two-stage random-effects model.
b Metaregression cannot be performed as all studies in this comparison recorded treatment duration of 0.75 years.
c Metaregression cannot be performed as all studies in this comparison recorded qualified therapist as 0 (no).
d Metaregression cannot be performed as all studies in this comparison have manualised treatment.
e Metaregression could not be performed as all studies were individual interventions not group interventions.

Chapter 4 Discussion/interpretation

Cognitive–behavioural therapy is a psychological intervention which, based on the findings of past evidence syntheses, can be beneficial in the treatment of psychosis. Accordingly, CBT features prominently among the interventions recommended by clinical guidelines for the treatment and management of schizophrenia and related psychotic disorders produced by NICE and other equivalent bodies in other countries.[13,15–17] The findings of the CBTp IMPART project corroborate the efficacy of CBT interventions compared to TAU evidenced in previous aggregate data meta-analyses of this research literature, and our results are consistent with previous meta-analytic findings indicating that the overall treatment effect of CBT is small to moderate in magnitude.[23–28] While the reduction in PANSS scores observed in the present analysis is modest even when compared to the summary treatment effects of past aggregate data meta-analyses, the impact of the analytic approach employed in the present IPD evidence synthesis should be considered when appraising the overall treatment effects of CBT. In our evidence synthesis, longitudinal mixed models were used to enable utilisation of all follow-up data points of the included trials provided by investigators who joined the CBTp IMPART Consortium. While this approach has merit in terms of maximising the utilisation of follow-up data, the treatment effect estimates obtained using this approach may not be fully comparable to those obtained via the more conventional approach used by past aggregate data meta-analyses, which typically involves the estimation of a summary treatment effect at a single follow-up point (e.g. end of treatment or the closest available follow-up following the end of treatment). Nonetheless, our findings are consistent with the overall results of other evidence syntheses in this area, including a recent and comprehensive aggregate data network meta-analysis of 53 RCTs of seven psychological interventions, which confirmed that CBT is associated with greater reduction in psychotic symptoms compared to inactive control as well as TAU conditions.[41]

The main treatment effect analyses of our evidence synthesis, however, found no evidence of superiority of CBT interventions compared to other active psychosocial interventions. This finding is consistent with research suggesting that different empirically validated psychotherapies may be equally effective (the so-called ‘Dodo bird debate’ that has been extensively discussed in past literature on the differential efficacy of psychotherapeutic interventions for mental health problems[106]) as well as meta-analytic findings on the application of CBT to the treatment of mental health problems other than psychosis. For example, a recent aggregate data meta-analysis of 409 RCTs found that while CBT is highly effective for the treatment of depression when compared to TAU or waitlist control conditions, its superiority against other psychotherapies for depression is minimal and non-significant after the application of stringent sensitivity analyses.[107] The observed lack of superiority of CBT compared to other active psychological interventions is, however, partially incongruent with the findings of other recent aggregate data and IPD meta-analyses of CBTp. More specifically, the above-mentioned network meta-analysis carried out by Bighelli *et al.*[41] found that CBT reduced symptoms of psychosis above supportive therapy, but it was not possible to compare its efficacy against other specific psychological interventions due to the limited number of comparative trials available. Furthermore, our findings differ from those of an independent IPD meta-analysis conducted by Turner *et al.*,[42] which focused specifically on RCTs comparing CBT interventions to other psychological interventions in people with psychosis. This IPD meta-analysis led to findings in support of the superiority of CBT for improving overall psychotic symptom severity compared to other psychological treatments. This incongruence in findings may be due to the different analytic approaches employed in the present IPD meta-analysis relative to those of Turner *et al.* More specifically, Turner *et al.* carried out a series of one-stage IPD meta-analyses focusing on symptom change at post-treatment follow-up, using score standardisation to combine data from trials that used different instruments to assess outcomes. In contrast, our IPD meta-analysis employed a series of two-stage IPD meta-analyses focusing on trials that provided PANSS total scores (or for which a PANSS total score equivalent could be calculated based on conversion from available BPRS scores) and which provided data for more than one follow-up assessment (e.g. not just a single post-treatment assessment), in line with the longitudinal mixed-model approach utilised in our planned analyses. Other key differences include our decision to analyse separately trials considering CBT interventions fully consistent with the criteria outlined by current NICE guidelines for the treatment and management of schizophrenia and related psychoses,[13] and trials that considered additional treatment components derived from other discrete psychological interventions (i.e. the ‘CBT+ vs. TAU’ and ‘CBT+ vs. AC’ treatment comparisons discussed further below). This distinction was not applied in the analytic approach employed by Turner *et al.*’s IPD meta-analysis, and might therefore partly explain the apparent divergence in our results, in addition to differences in the IPD

data sets that were respectively retrieved and included in these two IPD evidence syntheses. It should be noted that a relatively small number of trials are available contrasting the efficacy of CBT relative to other psychological interventions, compared (for example) to the much larger body of comparative trials considering CBT and other psychotherapies for the treatment of depression. We further note that the available trials that compared different psychological interventions for the treatment of psychosis may not have been sufficiently powered to make any robust non-inferiority or equivalence claim, which would typically require a considerably larger randomised sample relative to a trial designed to test superiority hypotheses.[108] It might therefore be premature to settle the 'Dodo bird debate' in this specific clinical research area until a larger number of well-designed comparative trials are available, including trials with sufficient methodological and statistical rigour to formulate definitive conclusions on the possible superiority, non-inferiority and/or equivalence of CBT compared to other psychological approaches for the treatment of psychosis.

Unlike previous meta-analyses of this research literature, but in line with the approach taken in the ongoing aggregate data meta-analysis that informed the CBTp IMPART project, in the present IPD evidence synthesis we differentiated between RCTs considering CBT interventions fully consistent with the criteria outlined by the current NICE guidelines for the treatment and management of psychosis, and trials that considered interventions that comprised additional components derived from other discrete psychological interventions; that is, the 'CBT+ versus TAU' and 'CBT+ versus AC' treatment comparisons. The main treatment effect analyses conducted as part of the CBTp IMPART project indicated that CBT+ interventions are not associated with significant reductions in PANSS scores across subsequent follow-ups relative to comparator treatments (TAU and AC). However, caution should be exerted when interpreting these findings, particularly in relation to the treatment effect of 'purer' CBT intervention protocols outlined in the findings discussed above. These null results may be in fact due to the considerably lower number of trials (and therefore IPD) available for the analyses for the CBT+ versus TAU and CBT+ AC treatment comparisons. It should be noted that while our distinction between CBT and CBT+ interventions has merits (i.e. explicit consideration that the treatment effects of certain trials may not solely reflect the use of CBT intervention strategies), the precise discrimination of which trials consider 'pure' CBT treatment protocols can be challenging and subject to debate, in light of both the highly heterogeneous intervention protocols considered in the available RCTs and the often integrative nature of CBT as a treatment approach, which over time has increasingly incorporated strategies that were originally developed in the context of other related approaches (e.g. mindfulness skills, imagery rescripting). It is worth considering that the additional interventions subsumed within the CBT+ categorisation were highly heterogeneous, including family intervention, motivational interviewing, psychoeducation, social skills training and mindfulness-based strategies. Therefore, it may be unrealistic to expect a consistent pattern of results across such diverse additional interventions. There is also no clear consensus in the literature whether certain interventions that were regarded as consistent with the CBT definition provided by NICE in our IPD meta-analysis should be considered as psychological interventions for psychosis that are distinct from CBT, and we note that recent independent evidence syntheses have attempted to implement more rigid distinctions than those applied here.[41] These differences in the conceptualisation of CBTp in different evidence syntheses should be taken into account when considering the convergence and potential differences in findings of different meta-analysis of this trial literature.

Pertaining to the principal objective of the project – that is, the identification of treatment effect modifiers of CBT interventions – the results of the treatment by covariate interaction analyses suggest that none of the variables examined as part of the CBTp IMPART project represent robust or reliable moderators of the efficacy of CBT interventions in people with diagnoses on the schizophrenia spectrum. Our analyses of treatment effect modifiers within the CBT versus TAU treatment comparison initially indicated that treatment duration may moderate the efficacy of CBT, with results suggesting that individuals in studies with longer treatment regimens had *smaller* reductions in PANSS scores over the course of the study. However, further inspections of the treatment by covariate interactions within trials that contributed to this analysis revealed that this relationship may not necessarily reflect true associations at the patient level due to potential ecological bias, and the assumption of a linear relationship may not be reasonable. More specifically, the effect may be driven by a small number of trials which employed brief and highly focused treatment protocols targeting specific psychological processes involved in the maintenance of specific symptoms of psychosis.[68–70] While these 'interventionist-causal' trials represent a promising new direction for optimising further the efficacy of psychological treatments for psychosis,[109] their inclusion in this IPD meta-analysis may have led to spurious findings in relation to the overall impact of treatment duration on the efficacy of CBT versus TAU more

generally. Accordingly, treatment duration cannot be regarded as a reliable moderator of the efficacy of CBT based on our findings. Our analyses conducted within the CBT versus AC treatment comparisons also suggested that baseline severity of anxiety symptoms, as assessed by the BAI, moderated the effect of CBT. However, this effect was estimated on a single RCT with relevant outcome and moderator data, and the result therefore cannot be regarded as conclusive evidence in support of this treatment effect moderator.

Overall, the findings of our IPD meta-analysis are consistent with the moderator analyses reported by the independent IPD meta-analysis by Turner *et al.*[42] Both our IPD meta-analysis and the results observed by Turner *et al.* indicate that the efficacy of CBT is largely unaffected by participant-level demographic and symptom severity variables (the list of moderators considered in Turner *et al.*'s IPD meta-analysis included age, gender, education level, marital status, diagnosis, employment status, ethnicity, illness duration and baseline psychotic symptom severity). This suggests that a broad range of service users with different clinical presentations and backgrounds may benefit equally from this recommended psychological intervention for the treatment and management of psychotic symptoms. However, a notable difference in findings pertains to the effect of treatment duration/number of sessions offered as part of the CBT interventions considered in the included trials. While the number of sessions did not impact treatment outcomes in the primary analysis reported by Turner *et al.*, further sensitivity analyses focusing only on trials with low RoB indicated that service users in receipt of a higher number of CBT sessions presented greater reductions in total psychotic symptoms at post-treatment follow-up compared to those who received fewer sessions. While this effect is congruent with the widely accepted assumption that clinical populations characterised by complex and enduring mental health difficulties such as psychosis may benefit from a longer treatment regimen, we did not observe a similar effect in the present IPD meta-analysis (not only on the treatment comparisons between CBT/CBT+ vs. AC trials, but also in trials considering TAU comparators). This difference in findings could once again stem from the different analytic approaches employed in the two IPD evidence syntheses, as discussed previously. However, we also note that our findings are consistent with the results of aggregate data meta-analyses of brief CBT interventions for psychosis, which suggested that treatment duration/number of sessions may not substantially alter treatment outcomes in CBTp interventions.[110]

While the current IPD evidence synthesis did not uncover significant treatment effect modifiers of CBT in people with schizophrenia spectrum diagnoses, several factors may have limited our ability to identify factors that could maximise or account for heterogeneity in the effectiveness of CBT. Despite representing the largest IPD evidence synthesis of interventions focused on the treatment of psychosis symptoms, it was not possible to retrieve a considerable proportion of the IPD that would have been relevant to the analyses planned as part of the project, therefore potentially limiting our ability to identify small or moderate treatment effect moderators in certain analyses. Second, while the analyses we have undertaken attempted to account for a range of participant- and study-level characteristics, the extreme heterogeneity in trial characteristics, treatment protocols and outcome variables that characterises this RCT literature complicates the ability to determine, with high levels of confidence, whether there might be untested factors that could better explain variation in CBT treatment outcomes. For example, our analytic approach attempted to consider important variances in the characteristics of the CBT interventions that have been thus far evaluated in available RCTs, but the CBT intervention protocols evaluated in this body of clinical trials are highly heterogeneous, for example in terms of modular structure, components, exact intervention strategies and treatment targets. The work conducted as part of this IPD meta-analysis was not designed to examine whether these more subtle variances in intervention characteristics may be associated with CBT effectiveness. The considerable variability in study and sample characteristics and the varied approaches taken to their measurement in the original trials also meant that, in several cases, data recoding required considerable simplification of the variables considered in our analyses, for example dichotomisation of complex categorical variables such as ethnicity, resulting in reduced ability to undertake more fine-grained analyses. Furthermore, research examining the views of CBT experts on the potential patient-level factors perceived to be associated with optimal treatment fit and improved outcomes have pointed to the potential importance of variables that are more psychologically sophisticated than the demographic and clinical variables that have been collected as part of RCTs thus far. For example, the findings of a Q-sort study indicated that factors such as 'acceptance and application of the cognitive model', ability to be 'attending to the present', having a 'secure base' and meaningful active collaboration in the therapy process are perceived as key patient characteristics that may lead to improved outcomes.[111] Other variables that are generally assumed to play an important role in improving psychological therapy outcomes (e.g. 'psychological mindedness'[112]), as well

as psychosocial characteristics that have been linked to greater liability to psychosis and symptom persistence in epidemiological research (e.g. economic/deprivation indices, urbanicity, trauma[113,114]), have also not been routinely collected as part of RCTs and were not considered in the analyses conducted as part of the CBTp IMPART project. The relative lack of variability in certain variables in the original trials may also have limited the likelihood of finding moderators of treatment effects. For example, many of the UK trials, which were most commonly included in our analyses, have populations that were predominantly 'White British' in terms of ethnicity, so it may be difficult to identify ethnic groups that are more or less likely to respond to CBT. The classification of other variables at the study level, such as the use of formulation-based CBT interventions, will limit the ability to identify the effects of having an individual case formulation on individual participant outcomes (not everyone in studies classified as formulation-based will necessarily have received one, and such variables would ideally be coded at the individual level and rated for quality or coherence of formulation, as opposed to a study-level variable).

Other factors that could further explain observed variation in the efficacy of CBT in available trials and that could not be accounted for in the present IPD meta-analysis and past evidence synthesis of this research literature, relate to differences within the standard care/TAU offered to patients with psychosis both within and between countries. For example, concomitant treatments that may be offered to service users as part of TAU, as well as other post-randomisation intercurrent events, may modify the observed efficacy of an intervention. An example of this would be the availability of care coordination including management of risk to self and others; in circumstances where this is unavailable, a CBT therapist will often find themself needing to prioritise these functions at the cost of delivering structured CBT, with potential implications for treatment outcomes. Differences may also exist in the characterisation and content of TAU between different phases of psychosis. For example, in the UK, first episode psychosis services are much more likely to include offers of family intervention, vocational interventions and, indeed, CBT for psychosis, in comparison to community mental health teams for people with longer histories of psychosis. While there is greater awareness of the importance of considering post-randomisation intercurrent events and how these may interact with novel experimental treatments in recent approaches that have been proposed for designing and analysing RCTs more efficiently – such as the estimands paradigm from the causal inference literature introduced in the ICH E9 (R1) Addendum on Estimands and Sensitivity Analysis in Clinical Trials[115] – it was not possible to account for such factors in our IPD meta-analysis and the individual trials considered in this evidence synthesis. Another limitation was the exclusive use of the PANSS (or standardised scores derived from similar measures) as the outcome, which is potentially problematic given that some of the included trials focused on other primary outcomes and that CBTp is a collaborative, problem-orientated approach, which aims to work towards idiosyncratic goals that are determined by the participant.[116] Therefore, some of the included trials may have an inherent mismatch between intended treatment target, protocolised intervention approach and the outcome selected for this IPD meta-analysis; however, the exclusion of such trials would have significantly reduced the pool of available participants and trials.

Other limitations include the observed differences in the characteristics of RCTs included in our analyses and RCTs for which we did not receive IPD following data requests. Perhaps unsurprisingly, our attempts to retrieve earlier RCTs were less successful compared to more recently conducted clinical trials, possibly due to the authors/data custodians being no longer contactable or the data having been destroyed. Our descriptive analysis of RoB scores for all trials to which we sought access suggests that the retrieved trials presented lower RoB across several RoB domains, including selection bias, detection bias and attrition bias. As the RoB assessment was based on the published trial reports, these differences cannot be explained by additional information that was provided by data owners for this IPD meta-analysis. While this could be framed as a strength of the current evidence synthesis (due to the lower bias in the included RCTs), we cannot exclude that the inclusion of additional trials with a different RoB profile could have led to different findings, particularly in relation to the main treatment effects of CBT and CBT+ interventions, which would undoubtedly benefit from participant numbers that were as large as possible. We also found that over 50% of the trials included in our IPD meta-analyses had been conducted in the UK, but the trials for which IPD were not retrievable came from a broader range of countries, which might have potential implications for the generalisability of our findings to all national contexts where CBT is currently being evaluated or implemented for the treatment of psychosis. Of note, while the search and study selection strategies we used did not specifically exclude non-English-language studies, we note that none of the data requests that we submitted to non-English-speaking authors led to the retrieval of trial data sets. This included a small number of RCTs conducted in China for which data requests were submitted in Mandarin/Standard Modern Chinese in addition to English. We further note that our data requests were guided by database searches

conducted in early 2018, and consequently our IPD meta-analysis only considers RCTs that had been completed or were approaching completion at the time. It is unlikely that the inclusion of more recent trials would substantially alter the principal conclusion of this IPD meta-analysis. However, our evidence synthesis is not informative on the potential impact of more recent innovations in the delivery of CBT interventions in this patient group, such as digitally supported CBT or 'CBT-informed' digital interventions for psychosis[117] and the use of teletherapy in CBT treatment delivery, which became more widespread following the onset of the COVID-19 pandemic.[118]

Chapter 5 Patient and public involvement

As this was a meta-analysis/secondary data analysis project, PPIE was less prominent in this project relative to the levels expected as part of a primary research study. Nonetheless, the CBTp IMPART project was informed by PPIE activities conducted at the project design stage to inform the planned analyses, and the project team included a PPIE co-applicant. The involvement of relevant stakeholders (NHS service users with psychosis and clinical psychologists/psychological professionals involved in the delivery of CBTp interventions in NHS settings) was particularly relevant to the selection of the outcomes and potential treatment effect modifiers that we planned to examine in this IPD meta-analysis. While the involvement of stakeholders in this IPD meta-analysis is commendable and in line with best research practice, these consultations may have contributed to the selection of an exceedingly large number of secondary aims and outcomes that, in hindsight, proved difficult to deliver within the time frame of the project. A more effective approach to these PPIE consultations could have involved engaging stakeholders in a stricter priority-setting exercise aimed at identifying secondary outcomes all parties agreed should be considered as part of the planned IPD meta-analysis, based on more precise data availability considerations and realistic projections of the time and resources required to deliver each analysis.

Chapter 6 Equality, diversity and inclusion

As a meta-analysis/secondary analysis project, the CBTp IMPART project did not include specific primary research activities aimed at addressing equality, diversity and inclusion issues in research and healthcare delivery contexts. However, the results of some of our analyses – in particular whether participant-level demographic characteristics influence the efficacy of CBT in people with psychosis – are relevant to considerations on the generalisability and transferability of the evidence on the efficacy of CBT to individuals presenting different demographic profiles. As reported above, our treatment by covariate interaction analyses found no evidence that the efficacy of CBT is affected by the gender, age or ethnicity of trial participants. The results of these analyses should, however, be interpreted in the context of the difficulties we experienced in retrieving RCTs conducted in countries other than the UK, which may have indirectly restricted variation in ethnicity within the data we had access to. We also note that our analyses are limited by the different standards used to record ethnicity in both UK trials and trials conducted in other national contexts, and that in order to maximise the use of the data available to us, ethnicity was dichotomised as 'White/Caucasian' versus 'other'. While this simplistic recoding was necessary to ensure comparability across the included IPD data sets, it prevents the more thorough examination of potential differences within more narrowly defined minority ethnic groups, which we recommend for the analysis of future RCTs in this area. Furthermore, the finding that ethnicity was not related to treatment outcomes in this IPD meta-analysis should not be interpreted as evidence that the delivery of CBT would not benefit from cultural adaptations to better fit the needs and preferences of particular minority groups or communities. It has previously been argued that CBT, like most other psychological therapies developed in Western contexts, reflects cultural norms and values that may not generalise to other non-Western cultures. Accordingly, efforts have already gone into adapting the delivery of CBT, including CBTp, to different cultural contexts via acquisition of awareness, knowledge and skills related to a given culture, but without compromising the core theoretical underpinning of CBT.[89,90,119] Ongoing work on the adaptation of CBT to improve acceptability, and potentially its effectiveness, among a wide range of service users from a range of underserved communities remains an important priority for addressing inequalities in mental health treatment uptake.

Chapter 7 Impact and learning

Further learning from the CBTp IMPART project is more broadly related to the process of conducting IPD meta-analyses of complex psychological interventions in clients with serious mental health problems. The data collection, data management and the cleaning and recoding of IPD proved more challenging than anticipated and required considerably more time and resources than initially projected. While IPD meta-analysis is regarded as the gold standard for evidence synthesis, its application to evaluate the effectiveness and treatment effect moderators of psychological therapies is in its infancy. Since the CBTp IMPART project was initiated, a few additional IPD meta-analyses of psychological therapy trials have become available, almost exclusively focusing on the treatment of depression.[120] Applications to trials considering treatments for severe mental health problems are much sparser and currently include, to the best of our knowledge, one IPD meta-analysis of 16 antipsychotic drug RCTs,[18] Turner *et al.*'s meta-analysis of 14 CBT versus other psychological intervention trials,[42] and the present IPD meta-analysis. We note that the number of outcomes and treatment effect moderators we aimed to consider as part of the CBTp IMPART project was considerably more extensive than in other IPD meta-analyses of psychological therapy RCTs published in recent years. Furthermore, compared to other IPD meta-analyses conducted by members of the research team, we found that the recoding and management of RCT data as part of this project proved much more laborious and resource-intensive, especially given the methodological and clinical heterogeneity of the trials and the large number of outcomes and covariates we aimed to consider in our planned analyses. The above, coupled with additional extenuating circumstances (e.g. the impact of the COVID-19 pandemic on both the study team and collaborators/data owners), resulted in extensive delays in the finalisation of all the planned analyses of the project, and the decision to focus the present report only on the analyses of the primary outcome rather than the full set of preplanned secondary and sensitivity analyses we aimed to conduct. Future reviewers aiming to undertake an IPD meta-analysis of psychological interventions for complex mental health problems may find it helpful to consider the challenges faced by the CBTp IMPART project, and implement steps to address them. To maximise their ability to complete IPD evidence syntheses in a timely manner, we recommend reviewers to ensure a more focused review scope (e.g. in terms of both overall number and stricter prioritisation of outcomes and treatment effect modifiers considered) relative to that attempted in our project, and to implement procedures to enable the most efficient allocation of resources (e.g. study selection criteria specifying a minimum sample size requirement for inclusion) and estimate the resources needed to deliver the review in a way that is commensurate with the level of complexity of the data management tasks that are likely to be encountered as part of other IPD meta-analyses of complex mental health interventions.

Furthermore, improvements in the design, data management, curation and data-sharing practices within the field of psychological therapies for psychosis more broadly may prove beneficial to the successful and more time-efficient delivery of future large-scale secondary analysis projects and IPD meta-analyses in this clinical research area. For example, the use of standardised core outcome sets (COSs) is gradually becoming more common across several health research domains, but as yet there is no specific COS for schizophrenia/psychosis. While the implementation of COSs can pose challenges to investigators, and their uptake in RCT research requires further improvement,[121] the development of a COS suited for the evaluation of psychological interventions in people with psychosis could greatly facilitate the delivery of future evidence syntheses[122] as well as outcome pooling across trials to further exploit IPD for secondary analysis purposes. The further promotion of the use of trial data repositories and data-sharing practices could also help to address some of the challenges faced by this and other IPD meta-analyses, such as the lengthy process of requesting and accessing relevant IPD. Crucially, in the light of the difficulty we experienced in retrieving IPD data sets for RCTs that were conducted in countries other than the UK, these initiatives would benefit from support and uptake by regulatory bodies and research funders internationally, rather than being confined to the research governance requirements of particular countries. Initiatives to promote the harmonisation of data storage and curation practices could also expedite the future delivery of similar IPD meta-analyses, for example by mandating publicly funded trials to store and share detailed metadata documentation and statistical analysis plans to facilitate data reuse.

Chapter 8 Implications for decision makers

In line with the above findings, the principal clinical recommendation arising from this evidence synthesis is that CBT should continue to be offered equally to all service users with psychosis irrespective of their demographic characteristics, their clinical characteristics or the severity of their mental health difficulties, as per current NICE recommendations. As our findings suggest that a broad range of service users with different backgrounds and clinical presentations may respond equally to CBT interventions, mental health services and clinicians should be dissuaded from making unwarranted assumptions about who may or may not benefit from CBT, or prioritising access to specific individuals based on their demographic characteristics or clinical profiles (e.g. the severity of psychotic symptoms).

Chapter 9 Research recommendations

The findings of the current IPD meta-analysis and similar independent work suggest simple demographic and clinical characteristics may not substantially alter the effectiveness of CBT in this clinical group. Therefore, we consider it unlikely that further primary or secondary research considering the variables already examined in this evidence synthesis will lead to substantial innovation in our understanding of factors that could maximise treatment response in CBTp interventions and maximise the effectiveness of psychological treatments for a broad range of service users. Other more precise research avenues may, however, lead to breakthroughs in the identification of relevant treatment effect modifiers of CBT and other therapeutic approaches for the treatment of psychosis. First, further examination of the 'active ingredients' and mechanisms of action of psychological interventions should be undertaken via mechanistic evaluations embedded within novel trials, as already recommended by methodological programmes funded by the National Institute for Health and Care Research (NIHR),[47] alongside the evaluation of treatment protocols and specific intervention strategies that may optimise change in evidence-based treatment effect mediators detected in these mechanistic evaluations. Within CBT, relevant mediators/mechanisms of action are likely to include change in schematic beliefs, appraisals of symptoms and linked coping resources and responses. These variables could be more routinely examined in future trials and subsequent secondary research. Other avenues for examining whether intervention-related characteristics may be associated with CBT efficacy could include approaches that could enable the more fine-grained examination of the efficacy of specific intervention components within CBT intervention protocols, for example in large individual trials or multiple trials that utilised the same CBT intervention protocol. Detailed measures of adherence and treatment content at the individual participant level may help to identify particular CBT components or intervention strategies associated with enhanced treatment gains, for example via the application of instrumental variable analysis.[123] It is also possible that the analysis of individual large, methodologically rigorous clinical trials (or multiple trials utilising harmonised treatment and assessment approaches) may overcome some of the potential confounders or limitations of the IPD meta-analytic approach utilised here, by avoiding the requirement to reduce complex variables to dichotomous (and at times 'crude') factors that enable cross-study analyses. Another potentially fruitful approach could be to examine treatment response trajectories in order to determine whether early treatment response is indicative of longer-term outcomes, since this would potentially help identify service users who are likely to respond and allow those less likely to respond to be offered timely access to alternative treatments, in line with the principles of adaptive trial designs. Finally, there is potential value in conducting further analyses comparing existing more 'traditional' CBT protocols to newer, generally more targeted, intervention protocols that have shown evidence of improved efficacy in recent research, for example treatment protocols informed by 'interventionist-causal paradigms' which specifically target, using CBT change strategies, psychological mechanisms allegedly involved in the formation and maintenance of specific psychotic symptoms. The interventionist-causal paradigm has already been applied successfully to the treatment of delusions,[109] with highly promising findings in terms of improved treatment outcomes, and there have been calls for extending its application to other distressing symptoms experienced by many people with psychosis, such as post-traumatic stress and trauma-related psychotic complaints.[124] Further interventionist-causal research to inform the development of more effective and comprehensive interventions for other common symptoms of psychosis, such as auditory verbal hallucinations or 'treatment-refractory' complaints such as negative symptoms, may represent important priorities for future CBT and psychological therapy research.

Chapter 10 Conclusions

The CBTp IMPART project is the largest IPD meta-analysis conducted on the RCT literature for the treatment of psychosis, and involved the reanalysis of clinical trial data provided by study collaborators from 11 different countries. The findings of the project suggest that the efficacy of CBT is not influenced by the demographic, clinical and intervention-related variables examined in our analyses, and that additional research using more precise statistical and methodological approaches is required to identify factors that can maximise the effectiveness of psychological interventions for psychosis and related severe mental problems.

Additional information

CRediT contribution statement

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Graham Dunn: Conceptualisation, Funding acquisition, Resources.

Tim Kendall: Funding acquisition.

Richard Emsley: Resources.

Members of the CBTp IMPART Consortium

The CBTp IMPART Consortium comprises trialists, statisticians and data owners who granted and/or supported access to the trial data sets included in this evidence synthesis. These include:

Professor	Amanda	Baker	University of Newcastle and Hunter New England Mental Health, Australia
Professor	Christine	Barrowclough	University of Manchester, UK (formerly, now retired)
Professor	Andreas	Bechdolf	Vivantes Klinikum Am Urban and Vivantes Klinikum im Friedrichshain, Germany
Professor	Max	Birchwood	University of Warwick, UK
Dr	Corinne	Cather	Harvard University, USA
Professor	Graham	Dunn	University of Manchester, UK (formerly, passed)
Professor	Richard	Emsley	King's College London, UK
Professor	John	Farhall	La Trobe University, Australia
Professor	Jerome	Favrod	University of Applied Sciences and Arts Western Switzerland, Switzerland
Professor	David	Fowler	University of Sussex, UK
Professor	Daniel	Freeman	University of Oxford, UK
Professor	Philippa	Garety	King's College London, UK
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In addition to the above data providers, the Consortium includes authors of the aggregate data meta-analysis that informed the IPD retrieval strategy of the CBTp IMPART project by sharing details of their database searches and quality assessment of included trials, in particular Professor Paul Hutton (Edinburgh Napier University, UK), Dr Peter Taylor (University of Manchester, UK) and Dr Lisa Wood (University College London, UK).

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Data-sharing statement

The members of the CBTp Consortium agreed to make their trial data available for the specific purpose of this IPD meta-analysis, but did not consent to the onward sharing of the trial data sets with other investigators or users. The data sets analysed as part of this study are therefore not suitable for sharing beyond that contained within the manuscript. Further information can be obtained from the corresponding author.

Ethics statement

The IMPART study was granted an exemption from requiring ethical approval from the University of Liverpool Research Integrity and Ethics Committee as the study uses data that are either publicly available or have been provided as anonymised data.

Information governance statement

As a secondary analysis study, the CBTp IMPART project did not handle any personal information.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/NCFR5074.

Primary conflicts of interest: Anthony P. Morrison, Eleanor Longden and Filippo Varese have received research funding from the NIHR, including Health Technology Assessment programme awards, for research projects involving the evaluation of CBT and other psychological interventions for people with psychosis (NIHR300850, PB-PG-0317-20037, 17/31/05, NIHR132269, NIHR130971, NIHR131848, NIHR128623; NIHR301598 NIHR132690). They have also received paid fees for the provision of training on CBT for psychosis and other psychological therapies for psychosis. Anthony P. Morrison and Eleanor Longden have received royalties from academic publishers for books on CBT for psychosis and the value of psychological therapies in people with psychosis more broadly. Over the course of the CBTp IMPART project, several authors have been in receipt of NIHR and UKRI personal awards: Filippo Varese is the recipient of an NIHR Advanced Fellowship focusing on the evaluation of trauma-focused psychological interventions, including but not limited to CBT, in people at ultra-high risk for psychosis; Eleanor Longden has received an NIHR Postdoctoral Fellowship and an NIHR Development and Skills Enhancement Fellowship focusing on novel psychological therapies for people who hear voices, other than CBT; Maria Sudell is the recipient of an MRC Skills Development Fellowship focusing on topics unrelated to this research and has been the Secretary and Chair of the Royal Statistical Society Merseyside Local Group; Catrin Tudur Smith is a member of the NIHR Health Technology Assessment commissioning panel.

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Appendix 1 Full list of trials approached for inclusion in the IMPART project

1. Aghotor *et al.* (2010)[125]
2. Baker *et al.* (2006)[55]
3. Baker *et al.* (2006)[56]
4. Barrowclough *et al.* (2001)[52]
5. Barrowclough *et al.* (2006)[57]
6. Barrowclough *et al.* (2010)[58]
7. Barrowclough *et al.* (2014)[59]
8. Bechdolf *et al.* (2010)[60]
9. Birchwood *et al.* (2014)[61]
10. Bradshaw (2000)[126]
11. Briki *et al.* (2004)[127]
12. Cather *et al.* (2005)[62]
13. Chadwick *et al.* (2009)[128]
14. Chadwick *et al.* (2016)[63]
15. Daniels (1998)[129]
16. Deng *et al.* (2008)[130]
17. Drury *et al.* (1996)[131]
18. Durham *et al.* (2003)[132]
19. Edwards *et al.* (2011)[133]
20. England (2007)[134]
21. Farhall *et al.* (2009)[64]
22. Favrod *et al.* (2014)[65]
23. Foster *et al.* (2010)[66]
24. Fowler *et al.* (2009)[67]
25. Freeman *et al.* (2014)[68]
26. Freeman *et al.* (2015)[69]
27. Freeman *et al.* (2015)[70]
28. Fung *et al.* (2011)[135]
29. Garety *et al.* (2008)[71]
30. Gawęda *et al.* (2015)[136]
31. Gleeson *et al.* (2009)[137]
32. Granholm *et al.* (2002)[138]
33. Granholm *et al.* (2005)[72]
34. Granholm *et al.* (2013)[73]

35. Granholm *et al.* (2014)[74]
36. Grant *et al.* (2012)[139]
37. Grawe *et al.* (2006)[140]
38. Gumley *et al.* (2003)[75]
39. Guo *et al.* (2010)[141]
40. Guo *et al.* (2017)[142]
41. Haddock *et al.* (1999)[76]
42. Haddock *et al.* (2009)[77]
43. Hall *et al.* (2003)[143]
44. Halperin *et al.* (2000)[144]
45. Horan *et al.* (2011)[145]
46. Jackson *et al.* (2008)[146]
47. Jackson *et al.* (2009)[78]
48. Jenner *et al.* (2004)[147]
49. Jolley *et al.* (2003)[79]
50. Kane *et al.* (2016)[148]
51. Kemp *et al.* (2007)[149]
52. Khazaal *et al.* (2007)[150]
53. Klinberg *et al.* (2010)[151]
54. Klinberg *et al.* (2011)[152]
55. Kråkvik *et al.* (2013)[153]
56. Kuipers *et al.* (1997)[80]
57. Landa *et al.* (2011)[81]
58. Leclerc *et al.* (2000)[154]
59. Lecomte *et al.* (1999)[53]
60. Lecomte *et al.* (2008)[82]
61. Levine *et al.* (1998)[155]
62. Li *et al.* (2015)[83]
63. Lincoln *et al.* (2012)[84]
64. Lysaker *et al.* (2005)[156]
65. Madigan *et al.* (2013)[85]
66. McLeod *et al.* (2007)[157]
67. Milton *et al.* (1978)[158]
68. Moritz *et al.* (2011)[159]
69. Moritz *et al.* (2011)[160]
70. Moritz *et al.* (2013)[161]
71. Morrison *et al.* (2014)[86]
72. Morrison *et al.* (2016)[87]

73. Morrison *et al.* (2018)[88]
74. Naeem *et al.* (2015)[89]
75. Naeem *et al.* (2016)[90]
76. O'Connor *et al.* (2007)[162]
77. Palma-Sevillano *et al.* (2011)[91]
78. Penadés *et al.* (2006)[92]
79. Penn *et al.* (2009)[163]
80. Penn *et al.* (2011)[164]
81. Peters *et al.* (2010)[93]
82. Pinninti *et al.* (2010)[165]
83. Pinto *et al.* (1999)[166]
84. Power *et al.* (2003)[167]
85. Rathod *et al.* (2013)[94]
86. Rector *et al.* (2003)[168]
87. Ruggeri *et al.* (2015)[169]
88. Schaub *et al.* (2016)[170]
89. Shawyer *et al.* (2012)[171]
90. Startup *et al.* (2004)[172]
91. Steel *et al.* (2017)[95]
92. Steel *et al.* (2020)[96]
93. Sungur *et al.* (2011)[173]
94. Tarrier *et al.* (1998)[174]
95. Tarrier *et al.* (2004)[97]
96. Tarrier *et al.* (2014)[175]
97. Trower *et al.* (2004)[176]
98. Turkington *et al.* (2000)[177]
99. Turkington *et al.* (2002)[98]
100. Turkington *et al.* (2008)[99]
101. Valmaggia *et al.* (2005)[100]
102. van den Berg *et al.* (2015)[101]
103. van der Gaag *et al.* (2011)[102]
104. van der Gaag *et al.* (2012)[103]
105. van Oosterhout *et al.* (2014)[178]
106. Velligan *et al.* (2015)[104]
107. Waller *et al.* (2015)[54]
108. Wang *et al.* (2003)[179]
109. Wu *et al.* (2008)[180]
110. Wykes *et al.* (2005)[181]

Appendix 2 List and sample size of trials not included in the IMPART project

TABLE 7 List and sample size of trials not included in the IMPART project

Trial	Total N	CBT arm	TAU arm	AC arm	Country
Aghotor *et al.* (2010)[125]	30	16		14	Germany
[a]Barrowclough *et al.* (2001)[52]	32	17	15		UK
Bradshaw (2000)[126]	15	8		7	USA
Briki *et al.* (2004)[127]	50	25		25	France
Chadwick *et al.* (2009)[128]	18	9		9	UK
Daniels (1998)[129]	46	23	23		USA
Deng *et al.* (2008)[130]	128	64	64		China
Drury *et al.* (1996)[131]	40	20	20		UK
Durham *et al.* (2003)[132]	60	22	19	19	UK
Edwards *et al.* (2011)[133]	48	23	25		Australia
England (2007)[134]	65	44	21		UK
Fung *et al.* (2011)[135]	66	34		32	Hong Kong
Gawęda *et al.* (2015)[136]	44	23	21		Poland
Gleeson *et al.* (2009)[137]	81	41	40		Australia
Granholm *et al.* (2002)[138]	15	8	7		USA
Grant *et al.* (2012)[139]	60	31	29		USA
Grawe *et al.* (2006)[140]	50	30	20		Norway
Guo *et al.* (2010)[141]	744	406	338		China
Guo *et al.* (2017)[142]	211	103	108		China
Hall *et al.* (2003)[143]	23	11	12		UK
Halperin *et al.* (2000)[144]	16	7	9		Australia
Horan *et al.* (2011)[145]	68	30		38	USA
Jackson *et al.* (2008)[146]	55	28		27	Australia
Jenner *et al.* (2004)[147]	69	35	34		Netherlands
Kane *et al.* (2016)[148]	205	129	76		USA
Kemp *et al.* (2007)[149]	16	10	6		Australia
Khazaal *et al.* (2007)[150]	46	23		23	Switzerland
Klinberg *et al.* (2010)[151]	330	166		164	Germany
Klinberg *et al.* (2011)[152]	169	90		79	Germany
Kråkvik *et al.* (2013)[153]	45	23	22		Norway

continued

TABLE 7 List and sample size of trials not included in the IMPART project (*continued*)

Trial	Total N	CBT arm	TAU arm	AC arm	Country
Leclerc *et al.* (2000)[154]	150	106	44		Canada
[a]Lecomte *et al.* (1999)[53]	95	51	44		Canada
Levine *et al.* (1998)[155]	12	6		6	Israel
Lysaker *et al.* (2005)[156]	47	23		24	USA
McLeod *et al.* (2007)[157]	20	10	10		UK
Milton *et al.* (1978)[158]	14	7		7	UK
Moritz *et al.* (2011)[159]	48	24		24	Germany
Moritz *et al.* (2011)[160]	36	18	18		Germany
Moritz *et al.* (2013)[161]	135	72		63	Germany
O'Connor *et al.* (2007)[162]	17	11		6	Canada
Penn *et al.* (2009)[163]	62	29		33	USA
Penn *et al.* (2011)[164]	46	23	23		USA
Pinninti *et al.* (2010)[165]	25	14	11		USA
Pinto *et al.* (1999)[166]	37	19		18	Italy
Power *et al.* (2003)[167]	42	21	21		Australia
Rector *et al.* (2003)[168]	42	24	18		Canada
Ruggeri *et al.* (2015)[169]	391	238	153		Italy
Schaub *et al.* (2016)[170]	196	100		96	Germany
Shawyer *et al.* (2012)[171]	37	19		18	Australia
Startup *et al.* (2004)[172]	66	34	32		UK
Sungur *et al.* (2011)[173]	100	50	50		Turkey
Tarrier *et al.* (1998)[174]	79	28	27	24	UK
Tarrier *et al.* (2014)[175]	35	16	19		UK
Trower *et al.* (2004)[176]	32	15	17		UK
Turkington *et al.* (2000)[177]	15	10		5	UK
van Oosterhout *et al.* (2014)[178]	111	51	60		Netherlands
[a]Waller *et al.* (2015)[54]	31	20	11		UK
Wang *et al.* (2003)[179]	260	130	130		China
Wu *et al.* (2008)[180]	100	48		52	China
Wykes *et al.* (2005)[181]	70	37	33		UK

a IPD were received but it was impossible to include the trial in the IMPART analyses due to missing key information.

Appendix 3 Full scores of the risk of bias assessment for the 50 trials included in the CBTp IMPART analyses

	Selection bias		Performance bias	Detection bias	Attrition bias
Trial	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of assessments	Incomplete outcome data
Baker *et al.* (2006)[55]	Low	Low	High	Low	Low
Baker *et al.* (2006)[56]	Low	Unclear	High	Low	Low
Barrowclough *et al.* (2006)[57]	Low	Low	High	Low	Low
Barrowclough *et al.* (2010)[58]	Low	Low	High	Low	Low
Barrowclough *et al.* (2014)[59]	Low	Unclear	High	Low	Low
Bechdolf *et al.* (2010)[60]	Low	Unclear	High	Low	Low
Birchwood *et al.* (2014)[61]	Low	Low	High	Low	Low
Cather *et al.* (2005)[62]	Unclear	Low	High	Low	Low
Chadwick *et al.* (2016)[63]	Low	Low	High	Low	Low
Farhall *et al.* (2009)[64]	Low	Unclear	High	High	Low
Favrod *et al.* (2014)[65]	Unclear	Unclear	High	Low	Low
Foster *et al.* (2010)[66]	Low	Low	High	High	Low
Fowler *et al.* (2009)[67]	Unclear	Unclear	High	Low	Low
Freeman *et al.* (2014)[68]	Low	Low	High	Low	Low
Freeman *et al.* (2015)[69]	Low	Unclear	High	Low	Low
Freeman *et al.* (2015)[70]	Low	Unclear	High	Low	Low
Garety *et al.* (2008)[71]	Low	Low	High	Low	Low
Granholm *et al.* (2005)[72]	Low	High	High	Low	Low
Granholm *et al.* (2013)[73]	Unclear	Low	High	Low	Low
Granholm *et al.* (2014)[74]	Low	Low	High	Low	High
Gumley *et al.* (2003)[75]	Unclear	Unclear	High	High	Low
Haddock *et al.* (1999)[76]	Unclear	Unclear	High	Low	Low
Haddock *et al.* (2009)[77]	Low	Low	High	Low	Low
Jackson *et al.* (2009)[78]	Low	Low	High	Low	High
Jolley *et al.* (2003)[79]	Unclear	Low	High	Low	High
Kuipers *et al.* (1997)[80]	Low	Low	High	High	Low
Landa *et al.* (2011)[81]	Unclear	Unclear	High	Unclear	Unclear
Lecomte *et al.* (2008)[82]	Unclear	Unclear	High	Low	Low
Li *et al.* (2015)[83]	Low	Unclear	High	High	Low
Lincoln *et al.* (2012)[84]	Low	Low	High	Low	Low

	Selection bias		Performance bias	Detection bias	Attrition bias
Trial	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of assessments	Incomplete outcome data
Madigan *et al.* (2013)[85]	Low	Low	High	Low	High
Morrison *et al.* (2014)[86]	Low	Low	High	Low	High
Morrison *et al.* (2016)[87]	Low	Low	High	Low	Low
Morrison *et al.* (2018)[88]	Low	Low	High	Low	Low
Naeem *et al.* (2015)[89]	Low	Low	High	Low	Low
Naeem *et al.* (2016)[90]	Low	Low	High	Low	Low
Palma-Sevillano *et al.* (2011)[91]	Low	Low	High	Low	Low
Penadés *et al.* (2006)[92]	Low	Low	High	Low	Low
Peters *et al.* (2010)[93]	Low	Low	High	High	High
Rathod *et al.* (2013)[94]	Low	Low	High	Low	Low
Steel *et al.* (2017)[95]	Low	Low	High	Low	Low
Steel *et al.* (2020)[96]	Low	Low	High	Low	Low
Tarrier *et al.* (2004)[97]	Low	Low	High	Low	Low
Turkington *et al.* (2002)[98]	Low	Low	High	Low	Low
Turkington *et al.* (2008)[99]	Unclear	Low	High	Low	Low
Valmaggia *et al.* (2005)[100]	Unclear	Low	High	Low	Low
van den Berg *et al.* (2015)[101]	Low	Low	High	Low	Low
van der Gaag *et al.* (2011)[102]	Low	Low	High	Low	Low
van der Gaag *et al.* (2012)[103]	Low	Low	High	Low	Low
Velligan *et al.* (2015)[104]	Low	Low	High	Low	High

Appendix 4 Full scores of the risk of bias assessment for the 60 trials not included in the CBTp IMPART analyses

	Selection bias		Performance bias	Detection bias	Attrition bias
Trial	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of assessments	Incomplete outcome data
Aghotor *et al.* (2010)[125]	Low	Unclear	High	Low	Low
Barrowclough *et al.* (2001)[52]*	Low	Low	High	Low	Low
Bradshaw (2000)[126]	Unclear	Unclear	High	Low	High
Briki *et al.* (2004)[127]	Unclear	Unclear	High	Low	Low
Chadwick *et al.* (2009)[128]	Unclear	Low	High	High	Low
Daniels (1998)[129]	Unclear	Unclear	High	Low	Low
Deng *et al.* (2008)[130]	Unclear	Unclear	High	High	Unclear
Drury *et al.* (1996)[131]	Low	Unclear	Hugh	High	High
Durham *et al.* (2003)[132]	Low	Low	High	Low	Low
Edwards *et al.* (2011)[133]	Unclear	Unclear	High	Low	Unclear
England (2007)[134]	Low	Unclear	High	Low	Low
Fung *et al.* (2011)[135]	Low	Unclear	High	High	Low
Gawęda *et al.* (2015)[136]	High	Unclear	High	High	Low
Gleeson *et al.* (2009)[137]	Low	Low	High	Low	Low
Granholm *et al.* (2002)[138]	Unclear	Unclear	High	High	Low
Grant *et al.* (2012)[139]	Low	Low	High	Low	High
Grawe *et al.* (2006)[140]	Low	Low	High	Low	Low
Guo *et al.* (2010)[141]	Unclear	Unclear	High	High	Low
Guo *et al.* (2017)[142]	Low	Low	High	Low	Low
Hall *et al.* (2003)[143]	Unclear	Unclear	High	High	Low
Halperin *et al.* (2000)[144]	Unclear	Unclear	High	High	Low
Horan *et al.* (2011)[145]	Low	Low	High	Low	Low
Jackson *et al.* (2008)[146]	Unclear	Low	High	Low	Low
Jenner *et al.* (2004)[147]	Low	Low	High	High	Low
Kane *et al.* (2016)[148]	Low	Low	High	Low	High
Kemp *et al.* (2007)[149]	High	Unclear	High	High	Low
Khazaal *et al.* (2007)[150]	Unclear	Unclear	High	High	High
Klinberg *et al.* (2010)[151]	Low	Low	High	Low	High
Klinberg *et al.* (2011)[152]	Low	Low	High	Low	Low
Kråkvik *et al.* (2013)[153]	Low	Low	High	High	High

	Selection bias		Performance bias	Detection bias	Attrition bias
Leclerc *et al.* (2000)[154]	Unclear	Unclear	High	Low	Unclear
Lecomte *et al.* (1999)[53]*	Unclear	Unclear	High	High	Low
Levine *et al.* (1998)[155]	Unclear	Unclear	High	Low	Low
Lysaker *et al.* (2005)[156]	Low	Unclear	High	High	Low
McLeod *et al.* (2007)[157]	Unclear	Unclear	High	Low	Unclear
Milton *et al.* (1978)[158]	Unclear	Unclear	High	Low	Low
Moritz *et al.* (2011)[159]	Low	Low	High	Low	Low
Moritz *et al.* (2011)[160]	Low	Unclear	High	Low	Low
Moritz *et al.* (2013)[161]	Low	Unclear	High	Low	Low
O'Connor *et al.* (2007)[162]	High	Unclear	High	High	High
Penn *et al.* (2009)[163]	Low	Low	High	Low	Low
Penn *et al.* (2011)[164]	Unclear	Unclear	High	Low	Low
Pinninti *et al.* (2010)[165]	Low	Low	High	Low	High
Pinto *et al.* (1999)[166]	Unclear	Unclear	High	High	Low
Power *et al.* (2003)[167]	Unclear	Unclear	High	Low	High
Rector *et al.* (2003)[168]	Unclear	High	High	Low	Low
Ruggeri *et al.* (2015)[169]	Low	Low	High	High	Low
Schaub *et al.* (2016)[170]	Low	Unclear	High	Low	High
Shawyer *et al.* (2012)[171]	Low	Low	High	Low	Low
Startup *et al.* (2004)[172]	Low	Unclear	High	High	High
Sungur *et al.* (2011)[173]	Low	Low	High	Low	Low
Tarrier *et al.* (1998)[174]	Low	Low	High	Low	Low
Tarrier *et al.* (2014)[175]	Low	Low	High	Low	High
Trower *et al.* (2004)[176]	Low	Low	High	Low	Low
Turkington *et al.* (2000)[177]	Unclear	Unclear	High	Low	Low
van Oosterhout *et al.* (2014)[178]	Low	Low	High	Low	High
Waller *et al.* (2015)[54]*	Low	Low	High	Low	Low
Wang *et al.* (2003)[179]	Unclear	Unclear	High	High	Low
Wu *et al.* (2008)[180]	Unclear	Unclear	High	High	Unclear
Wykes *et al.* (2005)[181]	Unclear	Low	High	High	Low

* IPD was received but it was impossible to include trial in the IMPART analyses due to missing key information.

Appendix 5 Sample size breakdown across the planned treatment comparisons

TABLE 8 Number of individuals assigned to each treatment in each included study for the CBT vs. TAU comparison (27 studies)

Citation	CBT	TAU	N
Barrowclough *et al.* (2006)[57]	57	56	113
Birchwood *et al.* (2014)[61]	98	99	197
Farhall *et al.* (2009)[64]	45	47	92
Foster *et al.* (2010)[66]	12	12	24
Freeman *et al.* (2014)[68]	15	15	30
Freeman *et al.* (2015)[69]	24	26	50
Freeman *et al.* (2015)[70]	73	77	150
Garety *et al.* (2008)[71]	133	140	273
Gumley *et al.* (2003)[75]	72	72	144
Jackson *et al.* (2009)[78]	36	30	66
Jolley *et al.* (2003)[79]	12	9	21
Kuipers *et al.* (1997)[80]	27	27	54
Landa *et al.* (2011)[81]	12	12	24
Lecomte *et al.* (2008)[82]	46	27	73
Lincoln *et al.* (2012)[84]	40	40	80
Madigan *et al.* (2013)[85]	59	29	88
Morrison *et al.* (2014)[86]	37	37	74
Morrison *et al.* (2016)[87]	15	14	29
Morrison *et al.* (2018)[88]	242	245	487
Naeem *et al.* (2015)[89]	59	57	116
Naeem *et al.* (2016)[90]	18	15	33
Peters *et al.* (2010)[93]	36	38	74
Rathod *et al.* (2013)[94]	15	18	33
Steel *et al.* (2016)	30	31	61
Tarrier *et al.* (2004)[97]	101	102	203
van der Gaag *et al.* (2011)[102]	110	97	207
Velligan *et al.* (2015)[104]	37	37	74
Total	1461	1409	2870

TABLE 9 Number of individuals assigned to each treatment in each included study for the CBT vs. AC comparison (11 studies)

Citation	CBT	AC	*N*
Bechdolf *et al.* (2010)[60]	40	48	88
Cather *et al.* (2005)[62]	15	13	28
Haddock *et al.* (1999)[76]	9	11	20
Haddock *et al.* (2009)[77]	38	39	77
Lecomte *et al.* (2008)[82]	46	46	92
Li *et al.* (2015)[83]	96	96	192
Penadés *et al.* (2006)	20	20	40
Tarrier *et al.* (2004)[97]	101	105	206
Turkington *et al.* (2008)[99]	47	43	90
Valmaggia *et al.* (2005)[100]	35	23	58
Velligan *et al.* (2015)[104]	37	33	70
Total	484	477	961

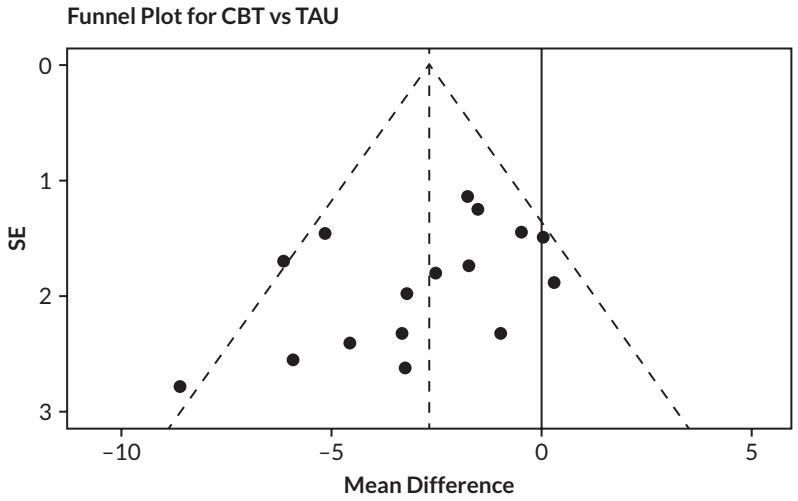
TABLE 10 Number of individuals assigned to each treatment in each included study for the CBT+ vs. TAU comparison (14 studies)

Citation	CBT+	TAU	*N*
Baker *et al.* (2006)[55]	147	151	298
Baker *et al.* (2006)[56]	65	65	130
Barrowclough *et al.* (2010)[58]	164	163	327
Barrowclough *et al.* (2014)[59]	75	35	110
Chadwick *et al.* (2016)[63]	54	54	108
Favrod *et al.* (2014)[65]	26	26	52
Fowler *et al.* (2009)[67]	35	42	77
Granholm *et al.* (2005)[72]	37	39	76
Palma-Sevillano *et al.* (2011)[91]	21	13	34
Steel *et al.* (2020)[96]	49	51	100
Turkington *et al.* (2002)[98]	257	165	422
van den Berg *et al.* (2015)[101]	55	47	102
van der Gaag *et al.* (2012)[103]	39	38	77
Velligan *et al.* (2015)[104]	35	37	72
Total	1059	926	1985

TABLE 11 Number of individuals assigned to each treatment in each included study for the CBT+ vs. AC comparison (three studies)

Citation	CBT+	AC	*N*
Granholm *et al.* (2013)[73]	31	33	64
Granholm *et al.* (2014)[74]	73	76	149
Velligan *et al.* (2015)[104]	35	33	68
Total	139	142	281

Appendix 6 Funnel plot for the cognitive–behavioural therapy versus treatment as usual main treatment effect



Appendix 7 Descriptive statistics of treatment effect modifiers tested for the cognitive–behavioural therapy versus treatment as usual treatment comparison

Participant demographic characteristics

Age at entry to trial

TABLE 12 Baseline data for age at entry to trial in 26 studies (this variable was not available for 1 study)

Age	CBT arm			TAU arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	39.9 (8.3)	39.7 (34.8, 46.1)	0 (0.0)	39.5 (9.3)	39.5 (34.3, 46.7)	0 (0.0)	39.7 (8.8)	39.7 (34.4, 46.2)	0 (0.0)
Birchwood *et al.* (2014)[61]	39.1 (12.3)	38.4 (30.2, 48.8)	0 (0.0)	36.9 (13.4)	37.0 (26.1, 44.9)	0 (0.0)	38.0 (12.9)	37.6 (28.0, 45.8)	0 (0.0)
Farhall *et al.* (2009)[64]	32.1 (9.6)	30.0 (24.0, 38.0)	0 (0.0)	33.6 (10.8)	32.0 (24.5, 41.5)	0 (0.0)	32.8 (10.2)	31.0 (24.0, 38.0)	0 (0.0)
Foster *et al.* (2010)[66]	40.0 (10.0)	42.0 (32.2, 47.2)	0 (0.0)	39.1 (9.2)	39.5 (35.8, 44.5)	0 (0.0)	39.5 (9.4)	40.0 (34.8, 47.2)	0 (0.0)
Freeman *et al.* (2014)[68]	41.9 (11.5)	44.0 (38.0, 50.5)	0 (0.0)	41.5 (13.1)	45.0 (29.5, 49.5)	0 (0.0)	41.7 (12.1)	44.5 (32.5, 50.5)	0 (0.0)
Freeman *et al.* (2015)[69]	39.6 (11.6)	41.0 (33.8, 44.5)	0 (0.0)	42.2 (13.5)	44.0 (31.5, 53.8)	0 (0.0)	40.9 (12.6)	42.0 (33.0, 50.8)	0 (0.0)
Freeman *et al.* (2015)[70]	40.9 (10.5)	41.0 (32.0, 49.0)	0 (0.0)	42.1 (12.2)	41.0 (33.0, 52.0)	0 (0.0)	41.5 (11.4)	41.0 (32.2, 49.0)	0 (0.0)
Garety *et al.* (2008)[71]	39.0 (10.7)	38.0 (32.0, 45.0)	0 (0.0)	36.8 (10.9)	36.0 (28.0, 44.5)	0 (0.0)	37.8 (10.8)	38.0 (30.0, 45.0)	0 (0.0)
Gumley *et al.* (2003)[75]	35.8 (9.6)	34.0 (28.0, 42.2)	0 (0.0)	36.7 (10.1)	35.0 (30.0, 44.5)	0 (0.0)	36.2 (9.8)	34.5 (29.0, 44.0)	0 (0.0)
Jackson *et al.* (2009)[78]	24.1 (4.7)	22.5 (21.0, 27.0)	0 (0.0)	22.3 (4.4)	21.0 (19.0, 25.5)	0 (0.0)	23.3 (4.6)	22.0 (20.0, 26.8)	0 (0.0)
Kuipers *et al.* (1997)[80]	38.8 (11.9)	37.0 (30.5, 45.5)	0 (0.0)	41.6 (12.2)	39.0 (32.0, 48.0)	0 (0.0)	40.2 (12.0)	39.0 (31.0, 47.0)	0 (0.0)
Landa *et al.* (2011)[81]	47.1 (15.0)	52.5 (39.2, 57.8)	0 (0.0)	44.8 (11.7)	48.5 (36.2, 52.5)	0 (0.0)	46.0 (13.2)	48.5 (36.2, 57.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	24.0 (4.6)	22.0 (20.5, 27.0)	3 (6.5)	23.7 (4.5)	23.5 (20.0, 26.0)	1 (3.7)	23.9 (4.5)	22.0 (20.0, 27.0)	4 (5.5)
Lincoln *et al.* (2012)[84]	33.1 (10.4)	34.0 (24.0, 39.0)	0 (0.0)	33.1 (10.9)	30.0 (25.0, 40.0)	0 (0.0)	33.1 (10.6)	31.0 (24.8, 40.0)	0 (0.0)
Madigan *et al.* (2013)[85]	27.6 (8.4)	27.0 (20.0, 32.5)	0 (0.0)	28.2 (7.8)	27.0 (22.0, 33.0)	0 (0.0)	27.8 (8.1)	27.0 (21.0, 33.0)	0 (0.0)
Morrison *et al.* (2014)[86]	32.9 (13.1)	27.0 (23.0, 41.0)	0 (0.0)	30.5 (11.1)	27.0 (21.0, 37.2)	1 (2.7)	31.7 (12.1)	27.0 (22.0, 41.0)	1 (1.4)
Morrison *et al.* (2016)[87]	39.0 (14.5)	42.0 (26.0, 50.0)	0 (0.0)	29.4 (10.0)	27.0 (23.0, 34.2)	0 (0.0)	34.3 (13.3)	29.0 (23.0, 45.0)	0 (0.0)
Morrison *et al.* (2018)[88]	42.2 (10.7)	42.0 (34.0, 49.0)	0 (0.0)	42.8 (10.4)	43.0 (34.0, 50.0)	0 (0.0)	42.5 (10.6)	42.0 (34.0, 50.0)	0 (0.0)
Naeem *et al.* (2015)[89]	31.7 (8.4)	30.0 (25.5, 36.0)	0 (0.0)	31.1 (7.5)	30.0 (26.0, 35.0)	0 (0.0)	31.4 (7.9)	30.0 (25.8, 36.0)	0 (0.0)
Naeem *et al.* (2016)[90]	42.0 (11.5)	44.0 (33.0, 47.0)	0 (0.0)	38.6 (12.0)	32.0 (28.0, 49.0)	0 (0.0)	40.5 (11.7)	44.0 (30.0, 49.0)	0 (0.0)
Peters *et al.* (2010)[93]	34.0 (9.8)	31.0 (27.0, 38.2)	0 (0.0)	39.6 (10.2)	38.0 (32.0, 47.8)	0 (0.0)	36.9 (10.3)	33.5 (29.0, 43.8)	0 (0.0)
Rathod *et al.* (2013)[94]	32.2 (12.4)	34.0 (19.5, 42.5)	0 (0.0)	35.0 (10.7)	34.5 (26.5, 42.2)	0 (0.0)	33.7 (11.4)	34.0 (21.0, 43.0)	0 (0.0)
Steel *et al.* (2016)	43.8 (10.1)	46.0 (38.5, 49.5)	0 (0.0)	40.7 (10.2)	42.0 (35.0, 46.0)	0 (0.0)	42.3 (10.2)	43.0 (37.0, 47.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	31.4 (11.6)	29.1 (22.2, 38.0)	1 (1.0)	28.8 (9.7)	27.0 (22.4, 31.1)	1 (1.0)	30.1 (10.7)	27.5 (22.3, 34.0)	2 (1.0)
van der Gaag *et al.* (2011)[102]	36.7 (11.3)	36.5 (27.0, 44.8)	0 (0.0)	37.5 (10.6)	36.0 (29.0, 45.0)	0 (0.0)	37.0 (10.9)	36.0 (28.0, 45.0)	0 (0.0)
Velligan *et al.* (2015)[104]	40.0 (11.6)	41.0 (30.5, 48.5)	2 (5.4)	41.1 (9.9)	43.5 (32.8, 50.0)	1 (2.7)	40.6 (10.7)	43.0 (31.0, 49.0)	3 (4.1)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Gender

TABLE 13 Baseline data for gender in 25 studies (this variable was not available for 2 studies)

Gender	CBT arm		TAU arm		Both arms	
Citation	*N* Male (%)	*N* missing (%)	*N* Male (%)	*N* missing (%)	*N* Male (%)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	41 (71.9)	0 (0.0)	41 (73.2)	0 (0.0)	82 (72.6)	0 (0.0)
Birchwood *et al.* (2014)[61]	61 (62.2)	0 (0.0)	52 (52.5)	0 (0.0)	113 (57.4)	0 (0.0)
Farhall *et al.* (2009)[64]	26 (57.8)	0 (0.0)	28 (59.6)	0 (0.0)	54 (58.7)	0 (0.0)
Freeman *et al.* (2014)[68]	11 (73.3)	0 (0.0)	9 (60.0)	0 (0.0)	20 (66.7)	0 (0.0)
Freeman *et al.* (2015)[69]	16 (66.7)	0 (0.0)	18 (69.2)	0 (0.0)	34 (68.0)	0 (0.0)
Freeman *et al.* (2015)[70]	42 (57.5)	0 (0.0)	44 (57.1)	0 (0.0)	86 (57.3)	0 (0.0)
Garety *et al.* (2008)[71]	96 (72.2)	0 (0.0)	96 (68.6)	0 (0.0)	192 (70.3)	0 (0.0)
Gumley *et al.* (2003)[75]	54 (75.0)	0 (0.0)	51 (70.8)	0 (0.0)	105 (72.9)	0 (0.0)
Jackson *et al.* (2009)[78]	31 (86.1)	0 (0.0)	18 (60.0)	0 (0.0)	49 (74.2)	0 (0.0)
Kuipers *et al.* (1997)[80]	14 (51.9)	0 (0.0)	19 (70.4)	0 (0.0)	33 (61.1)	0 (0.0)
Landa *et al.* (2011)[81]	6 (50.0)	0 (0.0)	8 (66.7)	0 (0.0)	14 (58.3)	0 (0.0)
Lecomte *et al.* (2008)[82]	30 (65.2)	0 (0.0)	23 (85.2)	0 (0.0)	53 (72.6)	0 (0.0)
Lincoln *et al.* (2012)[84]	22 (55.0)	0 (0.0)	23 (57.5)	0 (0.0)	45 (56.2)	0 (0.0)
Madigan *et al.* (2013)[85]	46 (78.0)	0 (0.0)	23 (79.3)	0 (0.0)	69 (78.4)	0 (0.0)
Morrison *et al.* (2014)[86]	17 (45.9)	0 (0.0)	22 (59.5)	0 (0.0)	39 (52.7)	0 (0.0)
Morrison *et al.* (2016)[87]	12 (80.0)	0 (0.0)	11 (78.6)	0 (0.0)	23 (79.3)	0 (0.0)
Morrison *et al.* (2018)[88]	176 (72.7)	0 (0.0)	173 (70.6)	0 (0.0)	349 (71.7)	0 (0.0)
Naeem *et al.* (2015)[89]	39 (66.1)	0 (0.0)	31 (54.4)	0 (0.0)	70 (60.3)	0 (0.0)
Naeem *et al.* (2016)[90]	8 (44.4)	0 (0.0)	9 (60.0)	0 (0.0)	17 (51.5)	0 (0.0)
Peters *et al.* (2010)[93]	26 (72.2)	0 (0.0)	20 (52.6)	0 (0.0)	46 (62.2)	0 (0.0)
Rathod *et al.* (2013)[94]	9 (60.0)	0 (0.0)	11 (61.1)	0 (0.0)	20 (60.6)	0 (0.0)
Steel *et al.* (2016)	18 (60.0)	0 (0.0)	20 (64.5)	0 (0.0)	38 (62.3)	0 (0.0)
Tarrier *et al.* (2004)[97]	72 (71.3)	0 (0.0)	69 (67.6)	0 (0.0)	141 (69.5)	0 (0.0)
van der Gaag *et al.* (2011)[102]	76 (69.1)	0 (0.0)	71 (73.2)	0 (0.0)	147 (71.0)	0 (0.0)
Velligan *et al.* (2015)[104]	17 (45.9)	0 (0.0)	20 (54.1)	0 (0.0)	37 (50.0)	0 (0.0)
Overall	966 (66.1)	24 (1.6)	910 (64.6)	21 (1.5)	1876 (65.4)	45 (1.6)

Ethnicity

TABLE 14 Baseline data for ethnicity (defined as proportion of Caucasian participants) in 17 studies (this variable was not available for 10 studies)

Ethnicity	CBT arm		TAU arm		Both arms	
Citation	*N* Caucasian (%)	*N* missing (%)	*N* Caucasian (%)	*N* missing (%)	*N* Caucasian (%)	*N* missing (%)
Birchwood *et al.* (2014)[61]	67 (68.4)	0 (0.0)	61 (61.6)	1 (1.0)	128 (65.0)	1 (0.5)
Freeman *et al.* (2014)[68]	15 (100.0)	0 (0.0)	13 (86.7)	0 (0.0)	28 (93.3)	0 (0.0)
Freeman *et al.* (2015)[70]	68 (93.2)	0 (0.0)	68 (88.3)	0 (0.0)	136 (90.7)	0 (0.0)
Freeman *et al.* (2015)[69]	22 (91.7)	0 (0.0)	25 (96.2)	0 (0.0)	47 (94.0)	0 (0.0)
Garety *et al.* (2008)[71]	88 (66.2)	0 (0.0)	105 (75.0)	0 (0.0)	193 (70.7)	0 (0.0)
Jackson *et al.* (2009)[78]	27 (75.0)	0 (0.0)	21 (70.0)	0 (0.0)	48 (72.7)	0 (0.0)
Kuipers *et al.* (1997)[80]	22 (81.5)	0 (0.0)	20 (74.1)	0 (0.0)	42 (77.8)	0 (0.0)
Landa *et al.* (2011)[81]	7 (58.3)	0 (0.0)	6 (50.0)	0 (0.0)	13 (54.2)	0 (0.0)
Lecomte *et al.* (2008)[82]	31 (67.4)	2 (4.3)	14 (51.9)	1 (3.7)	45 (61.6)	3 (4.1)
Morrison *et al.* (2016)[87]	14 (93.3)	0 (0.0)	13 (92.9)	0 (0.0)	27 (93.1)	0 (0.0)
Morrison *et al.* (2018)[88]	222 (91.7)	0 (0.0)	222 (90.6)	1 (0.4)	444 (91.2)	1 (0.2)
Naeem *et al.* (2016)[90]	14 (77.8)	0 (0.0)	15 (100.0)	0 (0.0)	29 (87.9)	0 (0.0)
Peters *et al.* (2010)[93]	19 (52.8)	5 (13.9)	19 (50.0)	12 (31.6)	38 (51.4)	17 (23.0)
Rathod *et al.* (2013)[94]	0 (0)	0 (0.0)	0 (0)	0 (0)	0 (0)	0 (0)
Steel *et al.* (2016)	21 (70.0)	0 (0.0)	23 (74.2)	0 (0.0)	44 (72.1)	0 (0.0)
Tarrier *et al.* (2004)[97]	91 (90.1)	0 (0.0)	86 (84.3)	3 (2.9)	177 (87.2)	3 (1.5)
Velligan *et al.* (2015)[104]	8 (21.6)	0 (0.0)	10 (27.0)	0 (0.0)	18 (24.3)	0 (0.0)
Overall	736 (50.4)	510 (34.9)	721 (51.2)	474 (33.6)	1457 (50.8)	984 (34.3)

Participant clinical characteristics

Positive and Negative Syndrome Scale: total scores at baseline

TABLE 15 Baseline values of primary outcome PANSS for 22 studies (this outcome was not recorded in 5 studies)

PANSS		CBT arm			TAU arm			Both arms		
	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	PANSS	61.6 (11.3)	60.0 (53.0, 69.0)	0 (0.0)	66.0 (13.9)	67.0 (56.8, 74.0)	0 (0.0%)	63.8 (12.8)	64.0 (54.0, 72.0)	0 (0.0)
Birchwood *et al.* (2014)[61]	PANSS	70.7 (17.1)	69.0 (58.0, 82.0)	1 (1.0)	72.7 (16.0)	70.0 (62.0, 79.8)	1 (1.0%)	71.7 (16.6)	70.0 (60.0, 81.0)	2 (1.0)
Farhall *et al.* (2009)[64]	PANSS	59.9 (11.9)	62.0 (49.0, 67.0)	0 (0.0)	58.7 (12.1)	58.0 (50.0, 63.0)	0 (0.0%)	59.3 (12.0)	59.0 (49.8, 66.0)	0 (0.0)
Freeman *et al.* (2015)[69]	PANSS	83.6 (16.2)	83.5 (72.8, 96.2)	0 (0.0)	79.7 (14.1)	78.5 (71.0, 89.0)	0 (0.0%)	81.6 (15.1)	82.0 (71.2, 94.5)	0 (0.0)
Freeman *et al.* (2015)[70]	PANSS	82.0 (13.6)	82.0 (74.0, 89.0)	0 (0.0)	79.0 (13.5)	78.5 (68.8, 89.2)	1 (1.3%)	80.4 (13.6)	81.0 (71.0, 89.0)	1 (0.7)
Garety *et al.* (2008)[71]	PANSS	63.2 (13.7)	63.0 (53.0, 71.0)	0 (0.0)	65.8 (15.8)	63.0 (55.0, 76.0)	0 (0.0%)	64.6 (14.8)	63.0 (54.0, 73.0)	0 (0.0)
Gumley *et al.* (2003)[75]	PANSS	55.3 (11.3)	56.0 (46.5, 63.0)	2 (2.8)	52.4 (12.0)	50.0 (44.0, 60.0)	5 (6.9%)	53.9 (11.7)	54.0 (45.0, 61.0)	7 (4.9)
Jackson *et al.* (2009)[78]	PANSS	59.4 (11.9)	59.5 (50.8, 65.2)	0 (0.0)	57.0 (12.7)	56.5 (48.2, 60.8)	0 (0.0%)	58.3 (12.3)	58.0 (49.2, 63.0)	0 (0.0)
Jolley *et al.* (2003)[79]	PANSS	56.0 (10.8)	54.0 (49.2, 59.8)	0 (0.0)	60.1 (19.5)	52.0 (51.0, 67.0)	0 (0.0%)	57.8 (14.9)	52.0 (50.0, 62.0)	0 (0.0)
Kuipers *et al.* (1997)[80]	BPRS	26.4 (6.5)	27.0 (21.0, 31.0)	0 (0.0)	24.5 (7.1)	22.0 (18.5, 31.0)	1 (3.7%)	25.5 (6.8)	24.0 (21.0, 31.0)	1 (1.9)
Lecomte *et al.* (2008)[82]	BPRS	42.6 (12.4)	42.5 (31.8, 51.2)	2 (4.3)	41.0 (9.6)	40.0 (34.0, 47.0)	3 (11.1%)	42.0 (11.4)	41.0 (32.8, 49.2)	5 (6.8)
Lincoln *et al.* (2012)[84]	PANSS	65.4 (14.1)	63.0 (55.8, 75.0)	0 (0.0)	60.8 (13.6)	60.5 (50.5, 71.0)	0 (0.0%)	63.1 (13.9)	61.0 (53.0, 71.2)	0 (0.0)
Morrison *et al.* (2014)[86]	PANSS	70.2 (13.8)	70.0 (60.0, 76.0)	0 (0.0)	73.3 (13.4)	71.0 (62.0, 80.0)	0 (0.0%)	71.8 (13.6)	70.0 (61.0, 78.8)	0 (0.0)
Morrison *et al.* (2018)[88]	PANSS	82.8 (13.7)	83.0 (74.0, 91.0)	0 (0.0)	83.3 (14.0)	81.0 (72.0, 93.0)	0 (0.0%)	83.0 (13.8)	83.0 (73.0, 92.0)	0 (0.0)
Naeem *et al.* (2015)[89]	PANSS	63.3 (14.2)	63.0 (53.0, 70.5)	0 (0.0)	60.5 (11.8)	58.0 (52.0, 69.0)	0 (0.0%)	61.9 (13.1)	59.0 (52.0, 70.2)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS	78.9 (14.6)	80.0 (71.8, 88.8)	0 (0.0)	82.1 (19.7)	84.0 (75.5, 100.0)	0 (0.0%)	80.4 (16.9)	81.0 (74.0, 90.0)	0 (0.0)
Peters *et al.* (2010)[93]	PANSS	59.6 (12.3)	59.0 (50.2, 65.2)	0 (0.0)	60.7 (11.9)	60.0 (52.0, 70.0)	0 (0.0%)	60.2 (12.0)	59.0 (51.2, 69.0)	0 (0.0)
Rathod *et al.* (2013)[94]	CPRS	32.7 (21.5)	37.0 (11.0, 49.5)	0 (0.0)	24.5 (16.6)	22.0 (13.2, 31.5)	0 (0.0%)	28.2 (19.1)	29.0 (13.0, 39.0)	0 (0.0)
Steel *et al.* (2016)	PANSS	73.8 (19.1)	72.0 (61.2, 83.8)	0 (0.0)	71.0 (17.3)	71.0 (58.5, 78.0)	0 (0.0%)	72.4 (18.1)	72.0 (59.0, 80.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	87.8 (17.7)	89.0 (75.0, 99.0)	0 (0.0)	87.0 (16.8)	87.0 (77.0, 97.0)	0 (0.0%)	87.4 (17.2)	87.0 (76.5, 99.0)	0 (0.0)
van der Gaag *et al.* (2011)[102]	PANSS	67.8 (13.2)	67.0 (58.0, 76.0)	0 (0.0)	70.2 (12.8)	70.0 (59.0, 80.0)	0 (0.0%)	68.9 (13.0)	69.0 (58.0, 78.5)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS	63.5 (12.6)	62.0 (54.0, 71.0)	0 (0.0)	63.1 (12.6)	64.0 (55.0, 72.0)	0 (0.0%)	63.3 (12.5)	62.0 (54.0, 71.8)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: positive symptoms scores at baseline

TABLE 16 Baseline values of PANSS positive symptoms for 17 studies (this outcome was not recorded in 10 studies)

PANSS positive symptoms		CBT arm			TAU arm			Both arms		
	Original Scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	PANSS	17.2 (4.2)	16.0 (14.0, 20.0)	0 (0.0)	17.7 (3.7)	17.0 (15.0, 20.0)	0 (0.0)	17.4 (3.9)	17.0 (14.0, 20.0)	0 (0.0)
Birchwood *et al.* (2014)[61]	PANSS	19.1 (4.9)	19.0 (16.0, 21.8)	0 (0.0)	19.6 (4.8)	19.0 (16.0, 22.5)	0 (0.0)	19.4 (4.9)	19.0 (16.0, 22.0)	0 (0.0)
Farhall *et al.* (2009)[64]	PANSS	14.7 (5.9)	13.0 (9.0, 19.0)	0 (0.0)	14.6 (5.6)	13.0 (10.5, 17.5)	0 (0.0)	14.6 (5.7)	13.0 (10.0, 19.0)	0 (0.0)
Freeman *et al.* (2015)[70]	PANSS	21.9 (4.1)	22.0 (19.0, 25.0)	0 (0.0)	21.4 (3.6)	22.0 (18.8, 24.0)	1 (1.3)	21.7 (3.8)	22.0 (19.0, 24.0)	1 (0.7)
Garety *et al.* (2008)[71]	PANSS	17.8 (5.5)	18.0 (13.0, 22.0)	0 (0.0)	18.5 (5.3)	18.5 (15.0, 22.0)	0 (0.0)	18.2 (5.4)	18.0 (14.0, 22.0)	0 (0.0)
Gumley *et al.* (2003)[75]	PANSS	10.9 (3.2)	10.0 (8.0, 13.0)	2 (2.8)	10.5 (2.7)	11.0 (8.5, 12.0)	5 (6.9)	10.7 (2.9)	10.0 (8.0, 12.0)	7 (4.9)
Jackson *et al.* (2009)[78]	PANSS	13.9 (5.3)	12.5 (11.0, 16.2)	0 (0.0)	12.5 (4.3)	12.0 (9.0, 14.8)	0 (0.0)	13.3 (4.9)	12.0 (10.0, 16.0)	0 (0.0)
Jolley *et al.* (2003)[79]	PANSS	14.6 (1.9)	15.0 (13.8, 16.0)	0 (0.0)	15.7 (5.5)	17.0 (11.0, 17.0)	0 (0.0)	15.0 (3.8)	16.0 (13.0, 17.0)	0 (0.0)
Lincoln *et al.* (2012)[84]	PANSS	15.2 (4.4)	14.5 (12.8, 17.0)	0 (0.0)	14.7 (4.6)	14.5 (11.0, 17.2)	0 (0.0)	14.9 (4.5)	14.5 (12.0, 17.0)	0 (0.0)
Morrison *et al.* (2014)[86]	PANSS	20.3 (5.2)	19.0 (16.0, 25.0)	0 (0.0)	21.6 (4.5)	21.0 (19.0, 24.0)	0 (0.0)	21.0 (4.9)	21.0 (17.2, 24.8)	0 (0.0)
Morrison *et al.* (2018)[88]	PANSS	24.7 (5.9)	25.0 (20.0, 29.0)	0 (0.0)	25.2 (5.7)	25.0 (21.0, 29.0)	0 (0.0)	24.9 (5.8)	25.0 (21.0, 29.0)	0 (0.0)
Naeem *et al.* (2015)[89]	PANSS	17.3 (6.2)	18.0 (13.5, 21.0)	0 (0.0)	16.3 (5.0)	16.0 (13.0, 19.0)	0 (0.0)	16.8 (5.6)	17.0 (13.0, 21.0)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS	20.4 (7.4)	22.0 (14.2, 25.0)	0 (0.0)	21.2 (4.3)	23.0 (19.0, 24.0)	0 (0.0)	20.8 (6.1)	23.0 (17.0, 25.0)	0 (0.0)
Peters *et al.* (2010)[93]	PANSS	17.1 (4.7)	16.5 (14.0, 19.2)	0 (0.0)	17.8 (4.8)	16.0 (14.2, 20.8)	0 (0.0)	17.4 (4.8)	16.0 (14.0, 20.0)	0 (0.0)
Steel *et al.* (2016)	PANSS	19.1 (6.0)	18.0 (16.0, 21.8)	0 (0.0)	18.3 (5.3)	18.0 (14.0, 22.0)	0 (0.0)	18.7 (5.6)	18.0 (15.0, 22.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	23.7 (4.8)	23.0 (20.0, 27.0)	0 (0.0)	23.3 (4.7)	23.0 (20.2, 26.8)	0 (0.0)	23.5 (4.8)	23.0 (20.0, 27.0)	0 (0.0)
van der Gaag *et al.* (2011)[102]	PANSS	17.1 (4.0)	17.0 (14.0, 19.0)	0 (0.0)	17.9 (3.8)	18.0 (15.0, 21.0)	0 (0.0)	17.5 (3.9)	18.0 (14.5, 20.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: negative symptoms scores at baseline

TABLE 17 Baseline values of PANSS negative symptoms for 17 studies (this outcome was not recorded in 10 studies)

PANSS negative symptoms		CBT arm			TAU arm			Both arms		
	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	PANSS	13.2 (3.6)	13.0 (11.0, 16.0)	0 (0.0)	15.1 (4.8)	15.0 (11.8, 18.0)	0 (0.0)	14.1 (4.3)	13.0 (11.0, 17.0)	0 (0.0)
Birchwood *et al.* (2014)[61]	PANSS	15.9 (6.3)	15.0 (11.0, 20.0)	1 (1.0)	16.2 (6.3)	15.0 (11.0, 21.0)	1 (1.0)	16.0 (6.3)	15.0 (11.0, 21.0)	2 (1.0)
Farhall *et al.* (2009)[64]	PANSS	15.4 (6.3)	14.0 (11.0, 19.0)	0 (0.0)	14.2 (5.4)	12.0 (10.0, 18.0)	0 (0.0)	14.8 (5.9)	13.0 (10.0, 18.2)	0 (0.0)
Freeman *et al.* (2015)[70]	PANSS	16.4 (4.4)	16.0 (13.0, 20.0)	0 (0.0)	14.6 (4.6)	14.0 (11.0, 17.0)	1 (1.3)	15.5 (4.6)	15.0 (12.0, 19.0)	1 (0.7)
Garety *et al.* (2008)[71]	PANSS	12.6 (5.3)	12.0 (8.0, 14.0)	0 (0.0)	13.1 (6.3)	11.0 (8.8, 16.0)	0 (0.0)	12.9 (5.8)	12.0 (8.0, 15.0)	0 (0.0)
Gumley *et al.* (2003)[75]	PANSS	12.8 (4.4)	12.0 (9.0, 15.0)	2 (2.8)	12.6 (5.3)	12.0 (8.0, 15.5)	5 (6.9)	12.7 (4.9)	12.0 (9.0, 15.0)	7 (4.9)
Jackson *et al.* (2009)[78]	PANSS	14.2 (4.2)	13.5 (11.0, 16.2)	0 (0.0)	15.0 (5.3)	14.0 (11.0, 18.8)	0 (0.0)	14.5 (4.7)	14.0 (11.0, 17.8)	0 (0.0)
Jolley *et al.* (2003)[79]	PANSS	9.4 (3.9)	8.5 (7.0, 9.2)	0 (0.0)	12.2 (9.3)	9.0 (7.0, 11.0)	0 (0.0)	10.6 (6.7)	9.0 (7.0, 11.0)	0 (0.0)
Lincoln *et al.* (2012)[84]	PANSS	14.9 (4.6)	14.0 (11.0, 18.0)	0 (0.0)	13.4 (4.6)	13.0 (10.0, 15.2)	0 (0.0)	14.2 (4.6)	13.0 (10.0, 17.0)	0 (0.0)
Morrison *et al.* (2014)[86]	PANSS	13.5 (3.2)	13.0 (12.0, 15.0)	0 (0.0)	15.5 (5.3)	15.0 (12.0, 18.0)	0 (0.0)	14.5 (4.4)	13.5 (12.0, 16.0)	0 (0.0)
Morrison *et al.* (2018)[88]	PANSS	19.3 (6.1)	18.5 (15.0, 23.0)	0 (0.0)	19.4 (6.4)	19.0 (15.0, 24.0)	0 (0.0)	19.4 (6.2)	19.0 (15.0, 23.0)	0 (0.0)
Naeem *et al.* (2015)[89]	PANSS	14.7 (3.8)	15.0 (13.0, 17.0)	0 (0.0)	14.4 (3.4)	14.0 (12.0, 17.0)	0 (0.0)	14.6 (3.6)	14.5 (12.0, 17.0)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS	18.8 (5.9)	20.0 (13.2, 23.8)	0 (0.0)	19.5 (5.8)	19.0 (15.0, 24.0)	0 (0.0)	19.1 (5.8)	19.0 (14.0, 24.0)	0 (0.0)
Peters *et al.* (2010)[93]	PANSS	11.1 (4.2)	10.0 (8.8, 12.2)	0 (0.0)	12.1 (5.4)	10.0 (8.0, 15.0)	0 (0.0)	11.6 (4.8)	10.0 (8.0, 13.8)	0 (0.0)
Steel *et al.* (2016)	PANSS	16.3 (6.1)	15.0 (12.0, 19.0)	0 (0.0)	15.3 (5.4)	15.0 (12.0, 17.5)	0 (0.0)	15.8 (5.7)	15.0 (12.0, 19.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	19.0 (6.2)	18.0 (14.0, 23.0)	0 (0.0)	18.7 (6.0)	18.0 (15.0, 22.0)	0 (0.0)	18.9 (6.1)	18.0 (14.0, 23.0)	0 (0.0)
van der Gaag *et al.* (2011)[102]	PANSS	14.9 (4.5)	15.0 (11.0, 17.0)	0 (0.0)	15.2 (4.5)	15.0 (12.0, 18.0)	0 (0.0)	15.0 (4.5)	15.0 (11.0, 18.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: general psychopathology scores at baseline

TABLE 18 Baseline values of PANSS general psychopathology scores for 15 studies (this outcome was not recorded in 12 studies)

PANSS general psychopathology		CBT arm			TAU arm			Both arms		
	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	PANSS	31.2 (6.8)	30.0 (27.0, 37.0)	0 (0.0)	33.4 (8.2)	33.5 (27.8, 39.2)	0 (0.0)	32.3 (7.6)	32.0 (27.0, 38.0)	0 (0.0)
Birchwood *et al.* (2014)[61]	PANSS	35.8 (8.8)	36.0 (29.0, 42.0)	1 (1.0)	37.0 (8.4)	36.0 (31.2, 42.0)	1 (1.0)	36.4 (8.6)	36.0 (30.0, 42.0)	2 (1.0)
Farhall *et al.* (2009)[64]	PANSS	29.9 (4.9)	30.0 (26.0, 33.0)	0 (0.0)	29.9 (5.7)	29.0 (26.0, 34.0)	0 (0.0)	29.9 (5.3)	29.0 (26.0, 34.0)	0 (0.0)
Freeman *et al.* (2015)[70]	PANSS	43.6 (8.1)	44.0 (39.0, 48.0)	0 (0.0)	43.1 (8.0)	43.0 (37.0, 50.0)	1 (1.3)	43.3 (8.0)	43.0 (38.0, 50.0)	1 (0.7)
Garety *et al.* (2008)[71]	PANSS	32.9 (7.3)	33.0 (27.0, 37.0)	0 (0.0)	34.2 (8.2)	33.0 (28.8, 39.0)	0 (0.0)	33.5 (7.8)	33.0 (28.0, 38.0)	0 (0.0)
Gumley *et al.* (2003)[75]	PANSS	31.7 (7.5)	31.0 (26.2, 37.0)	2 (2.8)	29.3 (6.6)	29.0 (25.0, 33.0)	5 (6.9)	30.5 (7.1)	30.0 (26.0, 35.0)	7 (4.9)
Jackson *et al.* (2009)[78]	PANSS	31.2 (7.4)	30.0 (27.0, 34.5)	0 (0.0)	29.5 (7.2)	28.0 (24.5, 32.8)	0 (0.0)	30.5 (7.3)	29.5 (26.2, 33.8)	0 (0.0)
Jolley *et al.* (2003)[79]	PANSS	32.0 (6.8)	31.0 (26.5, 36.2)	0 (0.0)	32.2 (7.2)	30.0 (28.0, 35.0)	0 (0.0)	32.1 (6.8)	30.0 (27.0, 36.0)	0 (0.0)
Lincoln *et al.* (2012)[84]	PANSS	35.4 (7.6)	35.0 (30.8, 40.2)	0 (0.0)	32.7 (7.2)	32.5 (28.5, 35.2)	0 (0.0)	34.0 (7.5)	33.0 (29.0, 38.2)	0 (0.0)
Morrison *et al.* (2014)[86]	PANSS	36.4 (7.9)	36.0 (31.0, 41.0)	0 (0.0)	36.1 (7.1)	34.0 (32.0, 43.0)	0 (0.0)	36.3 (7.5)	35.0 (31.0, 42.5)	0 (0.0)
Naeem *et al.* (2015)[89]	PANSS	31.3 (8.1)	30.0 (25.0, 35.0)	0 (0.0)	29.7 (6.9)	30.0 (25.0, 34.0)	0 (0.0)	30.5 (7.6)	30.0 (25.0, 35.0)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS	39.7 (7.0)	40.0 (35.5, 45.0)	0 (0.0)	41.5 (14.0)	41.0 (34.0, 53.0)	0 (0.0)	40.5 (10.6)	41.0 (35.0, 47.0)	0 (0.0)
Peters *et al.* (2010)[93]	PANSS	31.4 (7.7)	31.0 (24.8, 36.2)	0 (0.0)	30.8 (6.2)	30.5 (26.2, 34.5)	0 (0.0)	31.1 (7.0)	31.0 (26.0, 35.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	45.1 (9.7)	44.0 (38.0, 52.0)	0 (0.0)	45.0 (9.3)	44.5 (38.2, 51.0)	0 (0.0)	45.0 (9.5)	44.0 (38.0, 51.0)	0 (0.0)
van der Gaag *et al.* (2011)[102]	PANSS	35.7 (7.8)	35.0 (30.0, 41.0)	0 (0.0)	37.1 (7.1)	37.0 (32.0, 42.0)	0 (0.0)	36.4 (7.5)	36.0 (31.0, 42.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Anxiety scores at baseline

TABLE 19 Baseline anxiety scores for 13 studies (this outcome was not recorded in 14 studies)

Anxiety		CBT arm			TAU arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Farhall *et al.* (2009)[64]	HADS	9.2 (4.3)	9.0 (7.0, 13.0)	0 (0.0)	8.3 (4.7)	8.0 (4.0, 11.5)	0 (0.0)	8.7 (4.5)	9.0 (5.8, 12.0)	0 (0.0)
Freeman *et al.* (2015)[70]	BAI	24.8 (13.6)	21.0 (14.8, 33.8)	1 (1.4)	26.1 (13.7)	23.0 (17.0, 35.0)	1 (1.3)	25.5 (13.6)	23.0 (16.0, 35.0)	2 (1.3)
Garety *et al.* (2008)[71]	BAI	19.1 (13.2)	17.0 (8.0, 26.8)	11 (8.3)	19.1 (14.3)	15.0 (8.5, 30.0)	12 (8.6)	19.1 (13.8)	16.5 (8.0, 28.8)	23 (8.4)
Jackson *et al.* (2009)[78]	PANSS G2	3.2 (1.6)	3.5 (1.0, 5.0)	0 (0.0)	3.1 (1.4)	3.0 (2.2, 4.0)	0 (0.0)	3.2 (1.5)	3.0 (1.2, 4.8)	0 (0.0)
Kuipers *et al.* (1997)[80]	BAI	17.7 (11.0)	17.0 (9.0, 23.0)	2 (7.4)	17.3 (14.8)	8.5 (7.0, 27.8)	1 (3.7)	17.5 (12.9)	15.0 (7.0, 25.0)	3 (5.6)
Lecomte *et al.* (2008)[82]	BAI	32.1 (10.4)	28.0 (24.0, 37.0)	7 (15.2)	33.8 (9.6)	32.0 (27.0, 38.0)	6 (22.2)	32.7 (10.1)	30.0 (24.8, 37.0)	13 (17.8)
Naeem *et al.* (2015)[89]	PANSS G2	3.4 (1.6)	4.0 (2.0, 5.0)	0 (0.0)	2.8 (1.3)	3.0 (1.0, 4.0)	0 (0.0)	3.1 (1.5)	3.0 (1.0, 4.0)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS G2	3.8 (1.2)	4.0 (3.0, 4.8)	0 (0.0)	4.1 (1.8)	4.0 (4.0, 5.0)	0 (0.0)	3.9 (1.5)	4.0 (3.0, 5.0)	0 (0.0)
Peters *et al.* (2010)[93]	BAI	19.1 (9.0)	19.5 (12.0, 23.0)	0 (0.0)	20.0 (13.7)	19.5 (8.5, 27.8)	0 (0.0)	19.5 (11.6)	19.5 (11.0, 26.8)	0 (0.0)
Rathod *et al.* (2013)[94]	BARS	7.6 (5.1)	8.0 (3.5, 11.0)	0 (0.0)	5.7 (5.3)	5.0 (1.2, 8.0)	0 (0.0)	6.5 (5.2)	7.0 (2.0, 10.0)	0 (0.0)
Steel *et al.* (2016)	BAI	26.9 (12.6)	28.0 (19.0, 32.0)	5 (16.7)	21.3 (10.2)	21.0 (12.0, 27.0)	6 (19.4)	24.1 (11.7)	22.5 (14.2, 30.8)	11 (18.0)
Tarrier *et al.* (2004)[97]	PANSS G2	3.7 (1.4)	4.0 (3.0, 5.0)	0 (0.0)	3.4 (1.3)	3.5 (3.0, 4.0)	0 (0.0)	3.5 (1.4)	4.0 (3.0, 5.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS anxiety item	4.5 (1.6)	5.0 (3.0, 6.0)	0 (0.0)	4.1 (1.7)	4.0 (3.0, 5.0)	0 (0.0)	4.3 (1.6)	4.5 (3.0, 5.8)	0 (0.0)

BARS, Brief Anxiety Rating Scale; HADS, Hospital Anxiety and Depression Scale. LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Depression scores at baseline

TABLE 20 Baseline depression scores for 20 studies (this outcome was not recorded in 7 studies)

Depression score		CBT arm			TAU arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Birchwood *et al.* (2014)[61]	CDSS	12.4 (6.3)	13.0 (7.2, 17.0)	0 (0.0)	11.7 (5.7)	11.0 (7.0, 15.0)	0 (0.0)	12.1 (6.0)	12.0 (7.0, 17.0)	0 (0.0)
Farhall *et al.* (2009)[64]	HADS	8.0 (4.8)	8.0 (4.0, 11.0)	0 (0.0)	7.7 (4.3)	7.0 (5.0, 10.8)	1 (2.1)	7.9 (4.5)	7.0 (4.0, 11.0)	1 (1.1)
Freeman *et al.* (2014)[68]	BDI	32.1 (11.8)	32.0 (26.5, 38.0)	0 (0.0)	35.1 (8.4)	34.0 (30.0, 40.0)	0 (0.0)	33.6 (10.2)	34.0 (28.0, 39.5)	0 (0.0)
Garety *et al.* (2008)[71]	BDI	22.2 (12.2)	21.0 (13.2, 31.0)	3 (2.3)	20.9 (13.5)	18.5 (10.0, 30.2)	4 (2.9)	21.5 (12.9)	20.0 (11.2, 31.0)	7 (2.6)
Jackson *et al.* (2009)[78]	CDSS	5.3 (4.2)	4.0 (2.0, 7.2)	0 (0.0)	5.7 (4.3)	5.0 (2.0, 8.8)	0 (0.0)	5.5 (4.2)	5.0 (2.0, 8.0)	0 (0.0)
Jolley *et al.* (2003)[79]	CDSS	5.8 (4.2)	5.0 (2.0, 8.2)	0 (0.0)	4.6 (2.8)	5.0 (3.0, 6.0)	0 (0.0)	5.3 (3.6)	5.0 (2.0, 7.0)	0 (0.0)
Kuipers *et al.* (1997)[80]	BDI	23.6 (10.1)	22.0 (18.5, 27.5)	0 (0.0)	20.0 (10.1)	19.0 (13.0, 26.0)	1 (3.7)	21.8 (10.2)	22.0 (14.0, 26.0)	1 (1.9)
Lecomte *et al.* (2008)[82]	BDI	14.6 (11.6)	12.0 (6.0, 21.0)	1 (2.2)	17.7 (10.5)	17.0 (9.0, 24.0)	2 (7.4)	15.7 (11.2)	13.5 (7.2, 23.8)	3 (4.1)
Lincoln *et al.* (2012)[84]	BDI	17.6 (8.2)	18.0 (11.0, 24.0)	0 (0.0)	16.2 (9.3)	15.0 (9.0, 23.2)	0 (0.0)	16.9 (8.8)	17.0 (10.0, 24.0)	0 (0.0)
Madigan *et al.* (2013)[85]	CDSS	5.1 (5.7)	3.0 (1.0, 7.0)	0 (0.0)	5.0 (6.4)	2.0 (0.0, 7.2)	1 (3.4)	5.1 (5.9)	2.0 (0.5, 7.0)	1 (1.1)
Morrison *et al.* (2014)[86]	BDI	10.5 (5.2)	11.0 (6.0, 15.0)	0 (0.0)	9.4 (4.0)	9.5 (6.0, 12.8)	3 (8.1)	10.0 (4.7)	10.0 (6.0, 13.5)	3 (4.1)
Morrison *et al.* (2016)[87]	BDI	10.5 (4.2)	10.5 (8.2, 13.0)	1 (6.7)	9.6 (6.6)	9.5 (3.2, 16.5)	0 (0.0)	10.0 (5.4)	10.0 (6.5, 14.2)	1 (3.4)
Morrison *et al.* (2018)[88]	CDSS	7.1 (4.8)	6.0 (3.0, 11.0)	9 (3.7)	7.4 (4.7)	7.0 (4.0, 10.8)	7 (2.9)	7.2 (4.7)	6.0 (4.0, 11.0)	16 (3.3)
Naeem *et al.* (2015)[89]	PANSS G6	3.3 (1.7)	3.0 (1.5, 5.0)	0 (0.0)	3.1 (1.5)	4.0 (1.0, 4.0)	0 (0.0)	3.2 (1.6)	3.0 (1.0, 5.0)	0 (0.0)
Naeem *et al.* (2016)[90]	PANSS G6	2.8 (2.1)	2.0 (1.0, 4.0)	0 (0.0)	3.1 (1.8)	3.0 (1.5, 4.0)	0 (0.0)	3.0 (1.9)	3.0 (1.0, 4.0)	0 (0.0)
Peters *et al.* (2010)[93]	BDI	18.8 (10.0)	18.0 (10.8, 26.8)	0 (0.0)	21.3 (13.1)	19.0 (10.0, 31.8)	0 (0.0)	20.1 (11.7)	18.0 (10.0, 29.8)	0 (0.0)
Rathod *et al.* (2013)[94]	MADRS	9.3 (6.9)	9.0 (2.5, 14.0)	0 (0.0)	6.3 (5.0)	5.5 (3.2, 8.0)	0 (0.0)	7.7 (6.0)	6.0 (3.0, 10.0)	0 (0.0)
Steel *et al.* (2016)	BDI	30.3 (10.5)	30.0 (21.0, 39.0)	5 (16.7)	23.0 (10.2)	21.0 (19.0, 25.0)	6 (19.4)	26.7 (10.9)	24.5 (19.2, 33.0)	11 (18.0)
Tarrier *et al.* (2004)[97]	PANSS G6	3.4 (1.5)	4.0 (2.0, 4.0)	0 (0.0)	3.4 (1.5)	3.0 (2.0, 4.0)	0 (0.0)	3.4 (1.5)	4.0 (2.0, 4.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS depression item	3.4 (1.7)	4.0 (2.0, 5.0)	0 (0.0)	3.5 (1.6)	4.0 (2.0, 5.0)	0 (0.0)	3.4 (1.6)	4.0 (2.0, 5.0)	0 (0.0)

CDSS, Calgary Depression Scale for Schizophrenia; HADS, Hospital Anxiety and Depression Scale; LQ, lower quartile; PANSS G6, depression item of the PANSS; SD, standard deviation; UQ, upper quartile.

Specific diagnostic subgroup

TABLE 21 Specific diagnostic subgroup data in 17 studies (this variable was not available for 10 studies)

Diagnostic Subgroup		CBT arm					TAU arm						Both arms				
Citation	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)
Birchwood *et al.* (2014)[61]	63 (64.3)	16 (16.3)	18 (18.4)	1 (1.0)	0 (0.0)	0 (0.0)	52 (52.5)	16 (16.2)	29 (29.3)	2 (2.0)	0 (0.0)	0 (0.0)	115 (58.4)	32 (16.2)	47 (23.9)	3 (1.5)	0 (0.0)	0 (0.0)
Farhall *et al.* (2009)[64]	24 (53.3)	1 (2.2)	10 (22.2)	10 (22.2)	0 (0.0)	0 (0.0)	27 (57.4)	6 (12.8)	11 (23.4)	3 (6.4)	0 (0.0)	0 (0.0)	51 (55.4)	7 (7.6)	21 (22.8)	13 (14.1)	0 (0.0)	0 (0.0)
Freeman *et al.* (2014)[68]	12 (80.0)	2 (13.3)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	10 (66.7)	4 (26.7)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	22 (73.3)	6 (20.0)	2 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)
Freeman *et al.* (2015)[69]	16 (66.7)	5 (20.8)	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	17 (65.4)	5 (19.2)	4 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	33 (66.0)	10 (20.0)	7 (14.0)	0 (0.0)	0 (0.0)	0 (0.0)
Freeman *et al.* (2015)[70]	58 (79.5)	5 (6.8)	10 (13.7)	0 (0.0)	0 (0.0)	0 (0.0)	53 (68.8)	6 (7.8)	18 (23.4)	0 (0.0)	0 (0.0)	0 (0.0)	111 (74.0)	11 (7.3)	28 (18.7)	0 (0.0)	0 (0.0)	0 (0.0)
Garety *et al.* (2008)[71]	114 (85.7)	11 (8.3)	4 (3.0)	0 (0.0)	0 (0.0)	4 (3.0)	118 (84.3)	20 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.4)	232 (85.0)	31 (11.4)	4 (1.5)	0 (0.0)	0 (0.0)	6 (2.2)
Gumley *et al.* (2014)	59 (81.9)	12 (16.7)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	59 (81.9)	10 (13.9)	3 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	118 (81.9)	22 (15.3)	4 (2.8)	0 (0.0)	0 (0.0)	0 (0.0)
Kuipers *et al.* (1997)[80]	23 (85.2)	3 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.7)	23 (85.2)	1 (3.7)	2 (7.4)	0 (0.0)	0 (0.0)	1 (3.7)	46 (85.2)	4 (7.4)	2 (3.7)	0 (0.0)	0 (0.0)	2 (3.7)
Landa *et al.* (2011)[81]	7 (58.3)	5 (41.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (50.0)	6 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (54.2)	11 (45.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	18 (39.1)	5 (10.9)	0 (0.0)	8 (17.4)	2 (4.3)	13 (28.3)	10 (37.0)	3 (11.1)	0 (0.0)	5 (18.5)	2 (7.4)	7 (25.9)	28 (38.4)	8 (11.0)	0 (0.0)	13 (17.8)	4 (5.5)	20 (27.4)
Lincoln *et al.* (2012)[84]	27 (67.5)	6 (15.0)	7 (17.5)	0 (0.0)	0 (0.0)	0 (0.0)	29 (72.5)	7 (17.5)	4 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	56 (70.0)	13 (16.2)	11 (13.8)	0 (0.0)	0 (0.0)	0 (0.0)
Madigan *et al.* (2013)[85]	25 (42.4)	1 (1.7)	15 (25.4)	14 (23.7)	4 (6.8)	0 (0.0)	13 (44.8)	0 (0.0)	9 (31.0)	5 (17.2)	2 (6.9)	0 (0.0)	38 (43.2)	1 (1.1)	24 (27.3)	19 (21.6)	6 (6.8)	0 (0.0)
Morrison *et al.* (2016)[87]	6 (40.0)	1 (6.7)	8 (53.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (14.3)	0 (0.0)	11 (78.6)	1 (7.1)	0 (0.0)	0 (0.0)	8 (27.6)	1 (3.4)	19 (65.5)	1 (3.4)	0 (0.0)	0 (0.0)
Naeem *et al.* (2015)[89]	57 (96.6)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	56 (98.2)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	113 (97.4)	3 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Steel *et al.* (2016)	20 (66.7)	10 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	25 (80.6)	6 (19.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	45 (73.8)	16 (26.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

continued

TABLE 21 Specific diagnostic subgroup data in 17 studies (this variable was not available for 10 studies) (*continued*)

Diagnostic Subgroup	CBT arm						TAU arm						Both arms				
Citation	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)
Tarrier *et al.* (2004)[97]	34 (33.7)	17 (16.8)	50 (49.5)	0 (0.0)	0 (0.0)	0 (0.0)	42 (41.2)	14 (13.7)	46 (45.1)	0 (0.0)	0 (0.0)	0 (0.0)	76 (37.4)	31 (15.3)	96 (47.3)	0 (0.0)	0 (0.0)	0 (0.0)
van der Gaag *et al.* (2011)[102]	94 (85.5)	16 (14.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	78 (80.4)	19 (19.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	172 (83.1)	35 (16.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Overall	657 (45.0)	118 (8.1)	127 (8.7)	33 (2.3)	6 (0.4)	520 (35.6)	620 (44.0)	124 (8.8)	138 (9.8)	16 (1.1)	4 (0.3)	507 (36.0)	1277 (44.5)	242 (8.4)	265 (9.2)	49 (1.7)	10 (0.3)	1027 (35.8)

Phase of illness (first episode vs. not first episode)

TABLE 22 First episode vs. not first episode data in 19 studies (this variable was not available for 8 studies)

Phase of illness	CBT arm		TAU arm		Both arms	
Citation	First episode (%)	*N* missing (%)	First episode (%)	*N* missing (%)	First episode (%)	*N* missing (%)
Barrowclough *et al.* (2006)[57]	4 (7.0)	2 (3.5)	5 (8.9)	0 (0.0)	9 (8.0)	2 (1.8)
Birchwood *et al.* (2014)[61]	8 (8.2)	10 (10.2)	15 (15.2)	9 (9.1)	23 (11.7)	19 (9.6)
Garety *et al.* (2008)[71]	26 (19.5)	2 (1.5)	36 (25.7)	5 (3.6)	62 (22.7)	7 (2.6)
Gumley *et al.* (2003)[75]	11 (15.3)	4 (5.6)	17 (23.6)	7 (9.7)	28 (19.4)	11 (7.6)
Jackson *et al.* (2009)[78]	35 (97.2)	1 (2.8)	28 (93.3)	1 (3.3)	63 (95.5)	2 (3.0)
Kuipers *et al.* (1997)[80]	3 (11.1)	2 (7.4)	3 (11.1)	1 (3.7)	6 (11.1)	3 (5.6)
Landa *et al.* (2011)[81]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	46 (100.0)	0 (0.0)	27 (100.0)	0 (0.0)	73 (100.0)	0 (0.0)
Lincoln *et al.* (2012)[84]	1 (2.5)	0 (0.0)	5 (12.5)	0 (0.0)	6 (7.5)	0 (0.0)
Madigan *et al.* (2013)[85]	59 (100.0)	0 (0.0)	29 (100.0)	0 (0.0)	88 (100.0)	0 (0.0)
Morrison *et al.* (2016)[87]	4 (26.7)	0 (0.0)	3 (21.4)	0 (0.0)	7 (24.1)	0 (0.0)
Morrison *et al.* (2018)[88]	12 (5.0)	15 (6.2)	6 (2.4)	14 (5.7)	18 (3.7)	29 (6.0)
Naeem *et al.* (2015)[89]	25 (42.4)	0 (0.0)	15 (26.3)	0 (0.0)	40 (34.5)	0 (0.0)

TABLE 22 First episode vs. not first episode data in 19 studies (this variable was not available for 8 studies) (*continued*)

Phase of illness	CBT arm		TAU arm		Both arms	
Citation	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**
Naeem *et al.* (2016)[90]	14 (77.8)	0 (0.0)	15 (100.0)	0 (0.0)	29 (87.9)	0 (0.0)
Peters *et al.* (2010)[93]	10 (27.8)	1 (2.8)	11 (28.9)	1 (2.6)	21 (28.4)	2 (2.7)
Steel *et al.* (2016)	0 (0.0)	1 (3.3)	0 (0.0)	1 (3.2)	0 (0.0)	2 (3.3)
Tarrier *et al.* (2004)[97]	85 (84.2)	0 (0.0)	85 (83.3)	0 (0.0)	170 (83.7)	0 (0.0)
van der Gaag *et al.* (2011)[102]	25 (22.7)	0 (0.0)	19 (19.6)	0 (0.0)	44 (21.3)	0 (0.0)
Velligan *et al.* (2015)[104]	6 (16.2)	13 (35.1)	3 (8.1)	15 (40.5)	9 (12.2)	28 (37.8)

Illness duration

TABLE 23 Illness duration data in 16 studies (this variable was not available for 11 studies)

Illness duration	CBT arm			TAU arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Barrowclough *et al.* (2006)[57]	12.8 (7.9)	10.7 (6.5, 18.8)	2 (3.5)	14.5 (8.1)	13.1 (8.2, 20.5)	0 (0.0)	13.7 (8.0)	12.6 (7.1, 19.1)	2 (1.8)
Birchwood *et al.* (2014)[61]	17.6 (12.6)	15.6 (7.6, 27.1)	10 (10.2)	13.8 (10.8)	10.7 (5.8, 18.9)	9 (9.1)	15.7 (11.9)	11.6 (6.5, 24.3)	19 (9.6)
Garety *et al.* (2008)[71]	10.9 (8.4)	9.0 (4.0, 17.0)	2 (1.5)	10.1 (8.6)	7.0 (3.0, 14.5)	5 (3.6)	10.5 (8.5)	8.0 (4.0, 15.8)	7 (2.6)
Gumley *et al.* (2003)[75]	9.4 (6.7)	7.6 (4.4, 13.4)	4 (5.6)	9.5 (7.0)	9.1 (2.8, 15.0)	7 (9.7)	9.5 (6.9)	8.8 (3.8, 14.0)	11 (7.6)
Jackson *et al.* (2009)[78]	0.3 (0.5)	0.2 (0.1, 0.4)	1 (2.8)	0.5 (1.1)	0.2 (0.1, 0.3)	1 (3.3)	0.4 (0.8)	0.2 (0.1, 0.4)	2 (3.0)
Kuipers *et al.* (1997)[80]	12.1 (7.4)	10.0 (7.0, 19.0)	2 (7.4)	13.3 (8.4)	11.0 (7.5, 18.8)	1 (3.7)	12.7 (7.9)	11.0 (7.0, 19.0)	3 (5.6)
Landa *et al.* (2011)[81]	23.9 (11.1)	26.0 (18.5, 31.5)	0 (0.0)	22.0 (13.9)	19.5 (9.0, 35.2)	0 (0.0)	23.0 (12.3)	24.0 (9.0, 35.2)	0 (0.0)
Lincoln *et al.* (2012)[84]	11.3 (10.0)	8.0 (3.8, 18.0)	0 (0.0)	9.7 (6.8)	8.0 (5.0, 13.2)	0 (0.0)	10.5 (8.6)	8.0 (4.0, 14.2)	0 (0.0)
Madigan *et al.* (2013)[85]	1.1 (2.3)	0.0 (0.0, 1.0)	4 (6.8)	0.9 (1.7)	0.0 (0.0, 1.0)	5 (17.2)	1.1 (2.1)	0.0 (0.0, 1.0)	9 (10.2)
Morrison *et al.* (2018)[88]	18.7 (10.5)	18.0 (11.5, 25.0)	15 (6.2)	19.8 (10.3)	20.0 (12.0, 25.0)	14 (5.7)	19.2 (10.4)	19.0 (12.0, 25.0)	29 (6.0)
Naeem *et al.* (2015)[89]	4.8 (3.2)	4.0 (2.0, 7.0)	0 (0.0)	5.8 (3.8)	6.0 (3.0, 7.0)	0 (0.0)	5.3 (3.5)	5.0 (2.5, 7.0)	0 (0.0)
Peters *et al.* (2010)[93]	6.8 (5.7)	6.0 (2.5, 9.5)	1 (2.8)	9.0 (8.4)	7.0 (3.0, 12.0)	1 (2.6)	7.9 (7.2)	6.0 (3.0, 10.2)	2 (2.7)
Steel *et al.* (2016)	19.4 (10.5)	19.0 (11.0, 28.0)	1 (3.3)	17.1 (11.8)	14.5 (8.0, 22.8)	1 (3.2)	18.3 (11.2)	15.0 (9.0, 27.0)	2 (3.3)
Tarrier *et al.* (2004)[97]	0.8 (1.6)	0.2 (0.1, 0.7)	16 (15.8)	0.6 (0.9)	0.2 (0.1, 0.6)	18 (17.6)	0.7 (1.3)	0.2 (0.1, 0.6)	34 (16.7)
van der Gaag *et al.* (2011)[102]	10.3 (7.7)	9.0 (4.2, 14.8)	0 (0.0)	11.0 (8.4)	10.0 (4.0, 17.0)	0 (0.0)	10.6 (8.0)	10.0 (4.0, 16.0)	0 (0.0)
Velligan *et al.* (2015)[104]	16.2 (11.7)	18.0 (5.2, 22.2)	13 (35.1)	13.0 (7.0)	13.5 (6.8, 18.0)	15 (40.5)	14.7 (9.7)	15.0 (6.0, 20.0)	28 (37.8)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Duration of untreated psychosis

TABLE 24 Duration of untreated psychosis data in 5 studies (this variable was not available for 22 studies)

DUP	CBT arm			TAU arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Jackson *et al.* (2009)[78]	0.3 (0.5)	0.2 (0.1, 0.4)	1 (2.8)	0.5 (1.1)	0.1 (0.1, 0.3)	1 (3.3)	0.4 (0.8)	0.2 (0.1, 0.4)	2 (3.0)
Madigan *et al.* (2013)[85]	1.2 (2.3)	0.3 (0.1, 1.0)	4 (6.8)	1.0 (1.7)	0.3 (0.1, 1.1)	5 (17.2)	1.2 (2.1)	0.3 (0.1, 1.0)	9 (10.2)
Morrison *et al.* (2018)[88]	2.6 (4.7)	0.7 (0.1, 2.0)	47 (19.4)	3.1 (4.5)	1.5 (0.2, 4.0)	42 (17.1)	2.9 (4.6)	1.0 (0.2, 3.0)	89 (18.3)
Steel *et al.* (2016)	3.5 (9.4)	0.0 (0.0, 0.0)	2 (6.7)	2.3 (4.6)	0.0 (0.0, 2.2)	1 (3.2)	2.9 (7.3)	0.0 (0.0, 0.0)	3 (4.9)
Tarrier *et al.* (2004)[97]	0.8 (1.6)	0.2 (0.1, 0.9)	0 (0.0)	0.6 (0.8)	0.2 (0.1, 0.5)	1 (1.0)	0.7 (1.3)	0.2 (0.1, 0.7)	1 (0.5)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Number of antipsychotic medications at baseline

TABLE 25 Number of antipsychotic medications data in 5 studies (this variable was not available for 22 studies)

Number of antipsychotic medications	CBT arm			TAU arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Birchwood *et al.* (2014)[61]	2.7 (1.4)	3.0 (2.0, 4.0)	3 (3.1)	2.3 (1.2)	2.0 (1.0, 3.0)	1 (1.0)	2.5 (1.3)	2.0 (1.0, 3.0)	4 (2.0)
Jackson *et al.* (2009)[78]	1.3 (0.6)	1.0 (1.0, 2.0)	0 (0.0)	1.2 (0.9)	1.0 (1.0, 2.0)	0 (0.0)	1.3 (0.7)	1.0 (1.0, 2.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	2.5 (1.0)	2.0 (2.0, 3.0)	8 (17.4)	2.4 (1.3)	2.0 (1.0, 3.0)	7 (25.9)	2.5 (1.1)	2.0 (2.0, 3.0)	15 (20.5)
Peters *et al.* (2010)[93]	0.9 (0.2)	1.0 (1.0, 1.0)	0 (0.0)	0.9 (0.2)	1.0 (1.0, 1.0)	0 (0.0)	0.9 (0.2)	1.0 (1.0, 1.0)	0 (0.0)
Rathod *et al.* (2013)[94]	0.9 (0.5)	1.0 (1.0, 1.0)	0 (0.0)	0.9 (0.4)	1.0 (1.0, 1.0)	0 (0.0)	0.9 (0.4)	1.0 (1.0, 1.0)	0 (0.0)
Overall	2.0 (1.3)	2.0 (1.0, 3.0)	1241 (84.9)	1.8 (1.2)	1.0 (1.0, 2.0)	1205 (85.5)	1.9 (1.2)	1.0 (1.0, 3.0)	2446 (85.2)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Specific intervention characteristics

TABLE 26 Data pertaining to treatment duration (study-level variable available for 27 studies), number of sessions offered in the trial (study-level variable available for 25 studies), and number of sessions attended (individual-level variable available for 14 studies that provided relevant IPD)

Citation	Treatment duration (years)	Number of sessions offered	CBT sessions attended			CBT-qualified therapists	Manualised intervention	Formulation-based intervention	Individual or group	Intended target/ trial primary outcome[a]
			Mean (SD)	Median (LQ, UQ)	*N* missing (%)					
Barrowclough *et al.* (2006)[57]	0.50	18	10.4 (6.5)	13.0 (2.0, 16.0)	0 (0.0)	1	1	1	1	Overall psychotic symptom severity
Birchwood *et al.* (2014)[61]	0.75	25	–	–	–	1	1	1	0	(Not an outcome of interest in IMPART)
Farhall *et al.* (2009)[64]	0.75	24	17.1 (7.5)	19.0 (14.0, 24.0)	0 (0.0)	0	1	1	0	Overall psychotic symptom severity
Foster *et al.* (2010)[66]	0.08	4	3.7 (1.2)	4.0 (4.0, 4.0)	0 (0.0)	NA	1	1	0	Paranoia
Freeman *et al.* (2014)[68]	0.15	6	–	–	–	0	1	NA	0	Paranoia
Freeman *et al.* (2015)[69]	0.23	8	7.3 (1.9)	7.5 (6.0, 8.0)	0 (0.0)	1	1	1	0	Hallucination severity and delusions severity
Freeman *et al.* (2015)[70]	0.15	6	–	–	–	1	1	1	0	Delusions severity
Garety *et al.* (2008)[71]	0.75	20	14.2 (7.9)	17.0 (7.0, 20.0)	0 (0.0)	1	1	1	0	Readmission to hospital
Gumley *et al.* (2003)[75] [b]	0.25	5	4.6 (1.2)	5.0 (5.0, 5.0)	1 (1.4)	1	1	1	0	Readmission to hospital
Jackson *et al.* (2009)[78]	0.50	26	11.0 (5.0)	13.0 (9.0, 15.0)	27 (75.0)	1	1	1	0	NA
Jolley *et al.* (2003)[79]	0.50	18	7.3 (6.6)	6.5 (0.0, 12.0)	0 (0.0)	0	0	1	0	Overall psychotic symptom severity
Kuipers *et al.* (1997)[80]	0.75	No specified fixed number	–	–	–	1	1	1	0	Overall psychotic symptom severity
Landa *et al.* (2011)[81] [c]	0.29	30	26.0 (4.3)	27.5 (23.8, 29.2)	0 (0.0)	NA	1	NA	0	Paranoia
Lecomte *et al.* (2008)[82]	0.25	24	12.3 (8.6)	14.0 (4.0, 20.8)	12 (26.1)	0	1	0	1	Overall psychotic symptom severity
Lincoln *et al.* (2012)[84]	0.73	No specified fixed number	–	–	–	NA	1	1	0	Overall psychotic symptom severity
Madigan *et al.* (2013)[85]	0.25	12	–	–	–	1	0	0	0	NA

continued

TABLE 26 Data pertaining to treatment duration (study-level variable available for 27 studies), number of sessions offered in the trial (study-level variable available for 25 studies), and number of sessions attended (individual-level variable available for 14 studies that provided relevant IPD) (*continued*)

Citation	Treatment duration (years)	Number of sessions offered	CBT sessions attended			CBT-qualified therapists	Manualised intervention	Formulation-based intervention	Individual or group	Intended target/ trial primary outcome[a]
			Mean (SD)	Median (LQ, UQ)	*N* missing (%)					
Morrison *et al.* (2014)[86]	0.75	26	–	–	–	1	1	1	0	Overall psychotic symptom severity
Morrison *et al.* (2016)[87]	0.33	12	–	–	–	0	0	1	0	NA
Morrison *et al.* (2018)[88]	0.75	26	20.4 (10.1)	23.0 (13.0, 28.0)	0 (0.0)	1	1	1	0	Overall psychotic symptom severity
Naeem *et al.* (2015)[89]	0.33	7	–	–	–	0	1	1	0	Overall psychotic symptom severity
Naeem *et al.* (2016)[90]	0.31	16	–	–	–	0	1	0	0	Overall psychotic symptom severity
Peters *et al.* (2010)[93]	0.50	No specified fixed number	11.9 (6.8)	14.0 (8.2, 16.0)	0 (0.0)	1	1	1	0	Overall psychotic symptom severity
Rathod *et al.* (2013)[94]	0.38	16	–	–	–	1	1	1	0	Overall psychotic symptom severity
Steel *et al.* (2016)	0.50	16	–	–	–	0	1	0	0	NA
Tarrier *et al.* (2004)[97]	0.1	20	15.2 (5.5)	17.0 (12.0, 19.0)	7 (6.9)	1	1	1	0	Overall psychotic symptom severity, readmission to hospital
van der Gaag *et al.* (2011)[102]	0.50	26	13.1 (8.2)	13.0 (7.0, 18.8)	0 (0.0)	0	1	1	0	Social and occupational functioning
Velligan *et al.* (2015)[104]	0.75	38	–	–	–	0	1	1	0	Overall psychotic symptom severity, social and occupational functioning

a Coded according to the originally planned primary and secondary outcome analyses of the IMPART project.
b For Gumley at al. (2003), data refer to 'engagement phase' CBT sessions offered to all participants in the CBT arm.
c Landa *et al.* (2011) was classified as a trial involving individual therapy as participants received equal numbers of group and individual therapy sessions.
LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Appendix 8 Descriptive statistics of treatment effect modifiers tested for the cognitive–behavioural therapy versus active control treatment comparison

Participant demographic characteristics

Age at entry to trial

TABLE 27 Baseline data for age at entry to trial in 11 studies

Age	CBT arm			AC arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Bechdolf *et al.* (2010)[60]	32.2 (9.9)	31.0 (24.8, 37.5)	0 (0.0)	31.4 (10.6)	29.0 (23.8, 35.5)	0 (0.0)	31.8 (10.3)	30.0 (24.0, 37.0)	0 (0.0)
Cather *et al.* (2005)[62]	38.1 (11.6)	39.0 (31.0, 45.0)	0 (0.0)	43.1 (12.2)	45.0 (35.0, 52.0)	0 (0.0)	40.4 (12.0)	42.0 (32.5, 47.2)	0 (0.0)
Haddock *et al.* (1999)[76]	28.1 (7.2)	29.0 (24.0, 33.0)	0 (0.0)	30.0 (7.9)	30.0 (25.0, 34.5)	0 (0.0)	29.1 (7.5)	30.0 (24.0, 33.8)	0 (0.0)
Haddock *et al.* (2009)[77]	35.7 (12.5)	34.5 (26.3, 44.4)	0 (0.0)	33.9 (9.7)	34.0 (25.0, 40.7)	0 (0.0)	34.8 (11.1)	34.0 (25.9, 42.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	24.0 (4.6)	22.0 (20.5, 27.0)	3 (6.5)	24.0 (6.2)	22.0 (20.0, 26.0)	1 (2.2)	24.0 (5.4)	22.0 (20.0, 26.0)	4 (4.3)
Li *et al.* (2015)[83]	29.2 (8.4)	27.0 (23.0, 34.2)	0 (0.0)	33.6 (9.6)	32.0 (26.0, 39.2)	0 (0.0)	31.4 (9.3)	30.0 (24.8, 37.0)	0 (0.0)
Penadés *et al.* (2006)	35.9 (8.3)	33.0 (29.0, 41.5)	0 (0.0)	34.4 (8.5)	31.5 (28.5, 40.0)	0 (0.0)	35.1 (8.3)	33.0 (29.0, 41.5)	0 (0.0)
Tarrier *et al.* (2004)[97]	31.4 (11.6)	29.1 (22.2, 38.0)	1 (1.0)	29.3 (9.7)	27.1 (22.1, 32.5)	4 (3.8)	30.3 (10.7)	27.8 (22.1, 34.4)	5 (2.4)
Turkington *et al.* (2008)[99]	49.4 (8.7)	50.0 (44.0, 54.0)	38 (80.9)	48.1 (15.0)	47.0 (38.0, 63.0)	34 (79.1)	48.8 (12.0)	50.0 (44.0, 54.8)	72 (80.0)
Valmaggia *et al.* (2005)[100]	35.4 (10.6)	33.0 (27.0, 41.5)	0 (0.0)	35.5 (11.4)	37.0 (28.5, 38.0)	0 (0.0)	35.4 (10.8)	34.5 (27.2, 40.0)	0 (0.0)
Velligan *et al.* (2015)[104]	40.0 (11.6)	41.0 (30.5, 48.5)	2 (5.4)	43.5 (10.7)	44.5 (37.8, 52.0)	1 (3.0)	41.7 (11.2)	44.0 (31.5, 50.5)	3 (4.3)
Overall	32.4 (11.0)	30.0 (23.3, 39.0)	44 (9.1)	32.7 (11.0)	30.3 (24.0, 39.0)	40 (8.4)	32.5 (11.0)	30.0 (24.0, 39.0)	84 (8.7)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Gender

TABLE 28 Baseline data for gender in eight studies (this variable was not available for three studies)

Gender	CBT arm		AC arm		Both arms	
Citation	*N* male (%)	*N* missing (%)	*N* male (%)	*N* missing (%)	*N* male (%)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	18 (45.0)	0 (0.0)	22 (45.8)	0 (0.0)	40 (45.5)	0 (0.0)
Cather *et al.* (2005)[62]	9 (60.0)	0 (0.0)	7 (53.8)	0 (0.0)	16 (57.1)	0 (0.0)
Haddock *et al.* (2009)[77]	34 (89.5)	0 (0.0)	32 (82.1)	0 (0.0)	66 (85.7)	0 (0.0)
Lecomte *et al.* (2008)[82]	30 (65.2)	0 (0.0)	34 (73.9)	0 (0.0)	64 (69.6)	0 (0.0)
Li *et al.* (2015)[83]	33 (34.4)	0 (0.0)	40 (41.7)	0 (0.0)	73 (38.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	72 (71.3)	0 (0.0)	74 (70.5)	0 (0.0)	146 (70.9)	0 (0.0)
Turkington *et al.* (2008)[99]	32 (68.1)	0 (0.0)	21 (48.8)	0 (0.0)	53 (58.9)	0 (0.0)
Velligan *et al.* (2015)[104]	17 (45.9)	0 (0.0)	18 (54.5)	0 (0.0)	35 (50.0)	0 (0.0)
Overall	245 (50.6)	29 (6.0)	248 (52.0)	31 (6.5)	493 (51.3)	60 (6.2)

Ethnicity

Participant clinical characteristics

TABLE 29 Baseline data for ethnicity (defined as proportion of Caucasian participants) in eight studies (this variable was not available for three studies)

Ethnicity	CBT arm		AC arm		Both arms	
Citation	*N* Caucasian (%)	*N* missing (%)	*N* Caucasian (%)	*N* missing (%)	*N* Caucasian (%)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	35 (87.5)	0 (0.0)	43 (89.6)	0 (0.0)	78 (88.6)	0 (0.0)
Cather *et al.* (2005)[62]	9 (60.0)	0 (0.0)	10 (76.9)	0 (0.0)	19 (67.9)	0 (0.0)
Haddock *et al.* (2009)[77]	29 (76.3)	3 (7.9)	32 (82.1)	2 (5.1)	61 (79.2)	5 (6.5)
Lecomte *et al.* (2008)[82]	31 (67.4)	2 (4.3)	31 (67.4)	1 (2.2)	62 (67.4)	3 (3.3)
Li *et al.* (2015)[83]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	91 (90.1)	0 (0.0)	84 (80.0)	4 (3.8)	175 (85.0)	4 (1.9)
Turkington *et al.* (2008)[99]	32 (68.1)	0 (0.0)	21 (48.8)	0 (0.0)	53 (58.9)	0 (0.0)
Velligan *et al.* (2015)[104]	8 (21.6)	0 (0.0)	8 (24.2)	0 (0.0)	16 (22.9)	0 (0.0)

Positive and Negative Syndrome Scale: total score at baseline

TABLE 30 Baseline PANSS scores for 11 studies

PANSS score		CBT arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	PANSS	65.7 (17.5)	64.0 (54.5, 79.0)	1 (2.5)	64.6 (18.2)	61.0 (51.5, 78.0)	1 (2.1)	65.1 (17.8)	62.0 (52.0, 79.0)	2 (2.3)
Cather *et al.* (2005)[62]	PANSS	71.5 (19.6)	72.0 (59.0, 75.5)	0 (0.0)	71.8 (16.5)	69.0 (55.0, 83.0)	0 (0.0)	71.7 (17.9)	70.5 (57.2, 77.2)	0 (0.0)
Haddock *et al.* (1999)[76]	BPRS	53.0 (7.0)	54.0 (46.5, 57.0)	1 (11.1)	53.2 (8.2)	51.0 (51.0, 56.0)	0 (0.0)	53.1 (7.5)	52.0 (49.0, 57.0)	1 (5.0)
Haddock *et al.* (2009)[77]	PANSS	63.0 (12.5)	63.0 (55.2, 71.2)	0 (0.0)	64.6 (13.2)	65.0 (56.5, 71.0)	0 (0.0)	63.8 (12.8)	64.0 (56.0, 71.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	BPRS	42.6 (12.4)	42.5 (31.8, 51.2)	2 (4.3)	41.1 (13.3)	40.0 (31.0, 49.0)	0 (0.0)	41.9 (12.8)	41.0 (31.0, 49.8)	2 (2.2)
Li *et al.* (2015)[83]	PANSS	73.1 (13.1)	70.5 (62.0, 78.2)	0 (0.0)	71.9 (11.0)	70.0 (63.0, 77.2)	0 (0.0)	72.5 (12.1)	70.0 (63.0, 78.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS	67.6 (11.6)	70.0 (61.2, 76.0)	0 (0.0)	66.6 (13.7)	68.5 (59.8, 73.5)	0 (0.0)	67.0 (12.5)	70.0 (60.5, 75.2)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	87.8 (17.7)	89.0 (75.0, 99.0)	0 (0.0)	89.5 (17.0)	86.0 (78.0, 98.0)	0 (0.0)	88.7 (17.3)	86.0 (77.0, 98.8)	0 (0.0)
Turkington *et al.* (2008)[99]	CPRS	36.3 (13.9)	33.5 (27.0, 42.8)	0 (0.0)	36.4 (14.5)	34.0 (25.2, 44.0)	0 (0.0)	36.3 (14.1)	33.8 (25.6, 43.5)	0 (0.0)
Valmaggia *et al.* (2005)[100]	PANSS	67.9 (18.3)	63.8 (55.0, 72.0)	0 (0.0)	73.8 (12.2)	75.0 (65.2, 83.5)	0 (0.0)	69.7 (16.4)	65.0 (57.0, 81.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS	63.5 (12.6)	62.0 (54.0, 71.0)	0 (0.0)	62.1 (12.9)	61.0 (54.0, 70.0)	0 (0.0)	62.9 (12.7)	61.5 (54.0, 71.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: positive symptoms scores at baseline

TABLE 31 Baseline PANSS positive symptoms scores for seven studies (this outcome was not recorded in four studies)

PANSS positive symptoms		CBT arm			AC arm			Both		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	PANSS	14.2 (5.2)	13.0 (10.0, 18.0)	1 (2.5)	15.1 (5.4)	14.0 (11.0, 18.0)	1 (2.1)	14.7 (5.3)	14.0 (10.2, 18.0)	2 (2.3)
Cather *et al.* (2005)[62]	PANSS	20.0 (4.9)	20.0 (17.0, 22.5)	0 (0.0)	19.5 (4.4)	19.0 (17.0, 22.0)	0 (0.0)	19.8 (4.6)	19.5 (17.0, 22.2)	0 (0.0)
Haddock *et al.* (2009)[77]	PANSS	18.5 (5.0)	18.0 (14.2, 22.0)	0 (0.0)	18.4 (4.4)	18.0 (15.0, 21.0)	0 (0.0)	18.4 (4.7)	18.0 (15.0, 21.0)	0 (0.0)
Li *et al.* (2015)[83]	PANSS	18.6 (5.7)	18.0 (14.8, 23.0)	0 (0.0)	17.8 (5.6)	17.0 (14.0, 22.0)	0 (0.0)	18.2 (5.7)	18.0 (14.0, 22.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS	11.3 (2.5)	12.0 (10.8, 12.0)	0 (0.0)	11.1 (2.8)	11.5 (9.0, 12.5)	0 (0.0)	11.2 (2.6)	12.0 (9.0, 12.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	23.7 (4.8)	23.0 (20.0, 27.0)	0 (0.0)	23.3 (4.4)	23.0 (20.0, 27.0)	0 (0.0)	23.5 (4.6)	23.0 (20.0, 27.0)	0 (0.0)
Valmaggia *et al.* (2005)[100]	PANSS	17.9 (4.6)	19.0 (14.0, 20.2)	0 (0.0)	22.2 (4.8)	22.0 (19.2, 25.0)	0 (0.0)	19.2 (4.9)	20.0 (17.0, 22.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: negative symptoms scores at baseline

TABLE 32 Baseline PANSS negative symptoms scores for seven studies (this outcome was not recorded in four studies)

PANSS negative symptoms		CBT arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	PANSS	17.6 (7.1)	16.0 (12.0, 23.5)	1 (2.5)	17.7 (7.4)	16.0 (12.0, 22.0)	0 (0.0)	17.7 (7.2)	16.0 (12.0, 22.5)	0 (0.0)
Cather *et al.* (2005)[62]	PANSS	14.7 (6.3)	13.0 (11.0, 16.0)	0 (0.0)	16.0 (4.6)	14.0 (13.0, 19.0)	0 (0.0)	15.3 (5.5)	14.0 (12.0, 17.2)	0 (0.0)
Haddock *et al.* (2009)[77]	PANSS	12.8 (4.3)	11.5 (9.0, 16.8)	0 (0.0)	13.3 (4.5)	13.0 (10.0, 15.0)	0 (0.0)	13.0 (4.4)	13.0 (9.0, 16.0)	0 (0.0)
Li *et al.* (2015)[83]	PANSS	17.5 (5.3)	17.0 (13.8, 22.0)	0 (0.0)	17.8 (5.0)	18.0 (15.0, 21.0)	0 (0.0)	17.7 (5.1)	18.0 (14.0, 21.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS	21.0 (6.6)	20.0 (16.8, 24.5)	0 (0.0)	20.0 (8.4)	18.0 (13.8, 23.5)	0 (0.0)	20.5 (7.5)	18.0 (14.0, 24.2)	90 (100.0)
Tarrier *et al.* (2004)[97]	PANSS	19.0 (6.2)	18.0 (14.0, 23.0)	0 (0.0)	20.2 (6.6)	19.0 (16.0, 24.0)	0 (0.0)	19.6 (6.4)	19.0 (15.0, 23.8)	70 (100.0)
Valmaggia *et al.* (2005)[100]	PANSS	37.6 (15.0)	41.0 (27.0, 50.0)	0 (0.0)	39.8 (14.3)	44.0 (37.8, 46.0)	0 (0.0)	38.2 (14.2)	44.0 (27.0, 50.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: general psychopathology scores at baseline

TABLE 33 Baseline PANSS general psychopathology scores for seven studies (this outcome was not recorded in four studies)

PANSS general psychopathology		CBT arm			AC arm			Both arms		
Citation	Original Scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	PANSS	33.8 (9.8)	31.0 (27.5, 39.0)	1 (2.5)	32.1 (8.8)	30.0 (26.0, 37.5)	0 (0.0)	32.9 (9.2)	31.0 (26.0, 39.0)	1 (1.1)
Cather *et al.* (2005)[62]	PANSS	36.9 (9.8)	34.0 (30.5, 39.5)	0 (0.0)	36.4 (10.3)	33.0 (29.0, 42.0)	0 (0.0)	36.6 (9.9)	33.5 (30.0, 40.5)	0 (0.0)
Haddock *et al.* (2009)[77]	PANSS	32.1 (6.8)	32.0 (28.0, 35.8)	0 (0.0)	32.9 (7.2)	33.0 (27.5, 38.5)	0 (0.0)	32.5 (7.0)	32.0 (28.0, 37.0)	0 (0.0)
Li *et al.* (2015)[83]	PANSS	37.0 (7.0)	36.0 (33.0, 41.2)	0 (0.0)	36.3 (5.7)	36.0 (32.8, 40.0)	0 (0.0)	36.6 (6.4)	36.0 (33.0, 40.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS	35.2 (6.6)	34.0 (31.5, 38.0)	0 (0.0)	35.5 (6.2)	37.0 (31.0, 38.8)	0 (0.0)	35.4 (6.4)	36.0 (31.0, 38.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS	45.1 (9.7)	44.0 (38.0, 52.0)	0 (0.0)	46.0 (9.3)	44.0 (39.0, 51.0)	0 (0.0)	45.6 (9.5)	44.0 (39.0, 52.0)	0 (0.0)
Valmaggia *et al.* (2005)[100]	PANSS	36.2 (12.2)	30.0 (28.0, 44.0)	0 (0.0)	38.8 (8.1)	41.5 (36.8, 43.5)	0 (0.0)	37.0 (10.8)	36.0 (28.0, 44.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Anxiety scores at baseline

TABLE 34 Baseline anxiety scores for nine studies (this outcome was not recorded in two studies)

Anxiety		CBT arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Cather *et al.* (2005)[62]	PANSS G2	3.3 (1.5)	3.0 (3.0, 5.0)	0 (0.0%)	3.3 (1.0)	3.0 (3.0, 4.0)	0 (0.0)	3.3 (1.3)	3.0 (3.0, 4.2)	0 (0.0)
Haddock *et al.* (1999)[76]	BPRS anxiety item	3.0 (1.0)	3.0 (3.0, 4.0)	0 (0.0%)	2.7 (2.0)	2.0 (1.0, 4.5)	0 (0.0)	2.9 (1.6)	3.0 (1.8, 4.0)	0 (0.0)
Haddock *et al.* (2009)[77]	PANSS G2	2.4 (1.2)	2.5 (1.0, 3.0)	0 (0.0%)	2.7 (1.3)	3.0 (1.5, 3.0)	0 (0.0)	2.5 (1.3)	3.0 (1.0, 3.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	BAI	32.1 (10.4)	28.0 (24.0, 37.0)	7 (15.2%)	33.3 (8.9)	32.5 (25.2, 38.0)	8 (17.4)	32.7 (9.7)	30.0 (25.0, 37.0)	15 (16.3)
Li *et al.* (2015)[83]	PANSS G2	2.7 (1.3)	3.0 (1.0, 4.0)	0 (0.0%)	2.7 (1.1)	3.0 (2.0, 3.0)	0 (0.0)	2.7 (1.2)	3.0 (2.0, 3.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS G2	3.6 (0.8)	3.0 (3.0, 4.0)	0 (0.0%)	3.4 (1.1)	3.0 (3.0, 4.0)	0 (0.0)	3.5 (0.9)	3.0 (3.0, 4.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS G2	3.7 (1.4)	4.0 (3.0, 5.0)	0 (0.0%)	3.7 (1.2)	4.0 (3.0, 4.2)	1 (1.0)	3.7 (1.3)	4.0 (3.0, 5.0)	1 (0.5)
Valmaggia *et al.* (2005)[100]	ZBV	52.2 (13.9)	51.0 (45.0, 59.0)	0 (0.0%)	61.8 (10.2)	57.0 (56.0, 62.8)	0 (0.0)	55.2 (13.3)	56.0 (50.0, 59.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS anxiety item	4.5 (1.6)	5.0 (3.0, 6.0)	0 (0.0%)	4.7 (1.5)	5.0 (4.0, 6.0)	0 (0.0)	4.6 (1.5)	5.0 (3.0, 6.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile; ZBV, Zelf-Beoordelings-Vragenlijst (a Dutch translation of the State-Trait Anxiety Inventory).

Depression scores at baseline

TABLE 35 Baseline depression scores for 10 studies (this outcome was not recorded in 1 study)

Depression score		CBT arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Cather *et al.* (2005)[62]	BDI	15.1 (9.0)	18.0 (8.5, 22.0)	0 (0.0%)	19.2 (8.2)	18.5 (13.5, 25.5)	1 (7.7)	16.9 (8.7)	18.0 (12.0, 23.5)	1 (3.6)
Haddock *et al.* (1999)[76]	BPRS depression item	2.8 (1.5)	3.0 (1.0, 4.0)	0 (0.0%)	2.7 (1.8)	3.0 (1.0, 4.5)	0 (0.0)	2.8 (1.7)	3.0 (1.0, 4.0)	0 (0.0)
Haddock *et al.* (2009)[77]	PANSS G6	2.6 (1.4)	3.0 (1.0, 4.0)	0 (0.0%)	2.8 (1.4)	3.0 (1.5, 4.0)	0 (0.0)	2.7 (1.4)	3.0 (1.0, 4.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	BDI	14.6 (11.6)	12.0 (6.0, 21.0)	1 (2.2%)	14.6 (9.3)	15.0 (8.0, 19.5)	3 (6.5)	14.6 (10.4)	12.5 (6.0, 21.0)	4 (4.3)
Li *et al.* (2015)[83]	PANSS G6	2.4 (1.3)	3.0 (1.0, 3.0)	0 (0.0%)	2.3 (1.2)	2.0 (1.0, 3.0)	0 (0.0)	2.4 (1.2)	3.0 (1.0, 3.0)	0 (0.0)
Penadés *et al.* (2006)	PANSS G6	2.5 (1.4)	2.5 (1.0, 3.0)	0 (0.0%)	2.2 (1.2)	2.0 (1.0, 3.0)	0 (0.0)	2.4 (1.3)	2.0 (1.0, 3.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	PANSS G6	3.4 (1.5)	4.0 (2.0, 4.0)	0 (0.0%)	3.6 (1.5)	4.0 (3.0, 5.0)	1 (1.0)	3.5 (1.5)	4.0 (3.0, 4.0)	1 (0.5)
Turkington *et al.* (2008)[99]	MADRS	9.5 (4.9)	8.5 (6.0, 12.5)	0 (0.0%)	10.3 (4.4)	10.0 (6.2, 13.5)	0 (0.0)	9.9 (4.7)	9.5 (6.0, 13.0)	0 (0.0)
Valmaggia *et al.* (2005)[100]	BDI	18.8 (12.3)	14.0 (11.0, 23.0)	0 (0.0%)	28.8 (16.7)	29.5 (18.8, 39.5)	0 (0.0)	21.8 (13.9)	17.0 (11.0, 32.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS depression item	3.4 (1.7)	4.0 (2.0, 5.0)	0 (0.0%)	3.6 (1.6)	4.0 (2.0, 5.0)	0 (0.0)	3.5 (1.6)	4.0 (2.0, 5.0)	0 (0.0)

LQ, lower quartile; MADRS, Montgomery–Asberg Depression Rating Scale; SD, standard deviation; UQ, upper quartile.

Specific diagnostic subgroup

TABLE 36 Specific diagnostic subgroup data in seven studies (this variable was not available for four studies)

Citation	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	32 (80.0)	8 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	35 (72.9)	9 (18.8)	3 (6.2)	0 (0.0)	1 (2.1)	0 (0.0)	67 (76.1)	17 (19.3)	3 (3.4)	0 (0.0)	1 (1.1)	0 (0.0)
Cather *et al.* (2005)[62]	8 (53.3)	7 (46.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (69.2)	4 (30.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	17 (60.7)	11 (39.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haddock *et al.* (2009)[77]	34 (89.5)	4 (10.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	35 (89.7)	4 (10.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	69 (89.6)	8 (10.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lecomte *et al.* (2008)[82]	18 (39.1)	5 (10.9)	0 (0.0)	8 (17.4)	2 (4.3)	13 (28.3)	17 (37.0)	4 (8.7)	1 (2.2)	10 (21.7)	3 (6.5)	11 (23.9)	35 (38.0)	9 (9.8)	1 (1.1)	18 (19.6)	5 (5.4)	24 (26.1)
Li *et al.* (2015)[83]	96 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	96 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	192 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tarrier *et al.* (2004)[97]	34 (33.7)	17 (16.8)	50 (49.5)	0 (0.0)	0 (0.0)	0 (0.0)	47 (44.8)	8 (7.6)	50 (47.6)	0 (0.0)	0 (0.0)	0 (0.0)	81 (39.3)	25 (12.1)	100 (48.5)	0 (0.0)	0 (0.0)	0 (0.0)
Valmaggia *et al.* (2005)[100]	35 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	23 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	58 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Phase of illness (first episode vs. not first episode)

TABLE 37 First episode vs. not first episode data in nine studies (this variable was not available for two studies)

Phase of illness	CBT arm		AC arm		Both arms	
Citation	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**
Bechdolf *et al.* (2010)[60]	13 (32.5)	0 (0.0)	13 (27.1)	0 (0.0)	26 (29.5)	0 (0.0)
Cather *et al.* (2005)[62]	2 (13.3)	0 (0.0)	1 (7.7)	0 (0.0)	3 (10.7)	0 (0.0)
Lecomte *et al.* (2008)[82]	46 (100.0)	0 (0.0)	46 (100.0)	0 (0.0)	92 (100.0)	0 (0.0)
Li *et al.* (2015)[83]	35 (36.5)	0 (0.0)	35 (36.5)	0 (0.0)	70 (36.5)	0 (0.0)
Penadés *et al.* (2006)	14 (70.0)	6 (30.0)	20 (100.0)	0 (0.0)	34 (85.0)	6 (15.0)
Tarrier *et al.* (2004)[97]	85 (84.2)	0 (0.0)	86 (81.9)	0 (0.0)	171 (83.0)	0 (0.0)
Turkington *et al.* (2008)[99]	8 (17.0)	0 (0.0)	7 (16.3)	0 (0.0)	15 (16.7)	0 (0.0)
Valmaggia *et al.* (2005)[100]	9 (25.7)	3 (8.6)	6 (26.1)	2 (8.7)	15 (25.9)	5 (8.6)
Velligan *et al.* (2015)[104]	5 (13.5)	13 (35.1)	2 (6.1)	9 (27.3)	7 (10.0)	22 (31.4)

Illness duration

TABLE 38 Illness duration data in eight studies (this variable was not available for three studies)

Illness duration	CBT arm			AC arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Bechdolf *et al.* (2010)[60]	4.7 (5.5)	3.0 (0.8, 6.7)	0 (0.0)	4.2 (4.9)	2.0 (0.4, 7.2)	0 (0.0)	4.4 (5.1)	2.5 (0.5, 7.0)	0 (0.0)
Cather *et al.* (2005)[62]	17.0 (11.7)	17.0 (8.0, 25.0)	0 (0.0)	19.2 (15.0)	14.0 (6.0, 32.0)	0 (0.0)	18.0 (13.1)	16.5 (6.8, 28.0)	0 (0.0)
Li *et al.* (2015)[83]	7.6 (6.5)	6.8 (2.0, 11.0)	0 (0.0)	8.8 (8.1)	6.5 (2.0, 14.2)	0 (0.0)	8.2 (7.3)	6.8 (2.0, 12.0)	0 (0.0)
Penadés *et al.* (2006)	14.3 (6.5)	13.5 (9.8, 19.8)	0 (0.0)	13.2 (5.4)	11.0 (9.0, 16.2)	0 (0.0)	13.8 (5.9)	12.0 (9.0, 19.2)	0 (0.0)
Tarrier *et al.* (2004)[97]	0.8 (1.6)	0.2 (0.1, 0.7)	16 (15.8)	0.9 (2.1)	0.2 (0.1, 0.8)	21 (20.0)	0.8 (1.8)	0.2 (0.1, 0.8)	37 (18.0)
Turkington *et al.* (2008)[99]	10.7 (6.8)	9.0 (6.0, 15.0)	2 (4.3)	11.1 (7.8)	10.0 (4.5, 15.0)	0 (0.0)	10.9 (7.3)	9.0 (5.0, 15.0)	2 (2.2)
Velligan *et al.* (2015)[104]	16.2 (11.7)	18.0 (5.2, 22.2)	13 (35.1)	17.1 (11.6)	15.0 (6.8, 28.0)	9 (27.3)	16.6 (11.5)	16.0 (6.0, 26.2)	22 (31.4)
Valmaggia *et al.* (2005)[100]	7.6 (5.2)	6.5 (3.0, 10.0)	3 (8.6)	10.2 (8.9)	8.0 (3.0, 15.0)	2 (8.7)	8.6 (7.0)	7.0 (3.0, 12.0)	5 (8.6)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Duration of untreated psychosis

TABLE 39 Duration of untreated psychosis data in 1 study (this variable was not available for 10 studies)

DUP	CBT arm			AC arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Tarrier *et al.* (2004)[97]	0.8 (1.6)	0.2 (0.1, 0.9)	0 (0.0)	0.8 (1.9)	0.2 (0.1, 0.7)	0 (0.0)	0.8 (1.7)	0.2 (0.1, 0.8)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Number of antipsychotic medications at baseline

TABLE 40 Number of antipsychotic medications data in three studies (this variable was not available for eight studies)

Number of antipsychotic medications	CBT arm			AC arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Bechdolf *et al.* (2010)[60]	1.3 (0.5)	1.0 (1.0, 1.0)	2 (5.0)	1.3 (0.4)	1.0 (1.0, 1.5)	5 (10.4)	1.3 (0.5)	1.0 (1.0, 1.0)	7 (8.0)
Cather *et al.* (2005)[62]	2.1 (1.0)	2.0 (1.0, 3.0)	2 (13.3)	1.6 (0.8)	1.0 (1.0, 2.0)	1 (7.7)	1.8 (0.9)	2.0 (1.0, 2.0)	3 (10.7)
Lecomte *et al.* (2008)[82]	2.5 (1.0)	2.0 (2.0, 3.0)	8 (17.4)	2.3 (1.1)	2.0 (2.0, 3.0)	9 (19.6)	2.4 (1.1)	2.0 (2.0, 3.0)	17 (18.5)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Specific intervention characteristics

TABLE 41 Data pertaining to treatment duration (study-level variable available for 11 studies), number of sessions offered in the trial (study-level variable available for 11 studies), and number of sessions attended (individual-level variable available for 7 studies that provided relevant IPD)

Citation	Treatment duration (years)	Number of sessions offered	CBT sessions attended			Therapist training and competence	Competency check	Manualised intervention	Formulation-based intervention	Individual or group	Intended target/trial primary outcome[a]
			Mean (SD)	Median (LQ, UQ)	*N* missing (%)						
Bechdolf *et al.* (2010)[60]	0.15	20	–	–	–	1	0	0	0	NA	Overall psychotic symptom severity, readmission to hospital
Cather *et al.* (2005)[62]	0.31	16	16.9 (4.3)	20.0 (14.0, 20.0)	0 (0.0%)	1	0	1	1	0	Overall psychotic symptom severity, hallucinations severity, delusion severity, social and occupational functioning
Haddock *et al.* (1999)[76]	0.12	20	11.9 (5.2)	12.0 (7.0, 14.0)	0 (0.0%)	1	1	1	1	0	Overall psychotic symptom severity
Haddock *et al.* (2009)[77]	0.5	25	14.3 (4.8)	14.5 (13.2, 16.8)	24 (63.2%)	1	1	1	1	0	NA
Lecomte *et al.* (2008)[82]	0.25	24	12.3 (8.6)	14.0 (4.0, 20.8)	12 (26.1%)	0	1	1	0	1	Overall psychotic symptom severity
Li *et al.* (2015)[83]	0.46	15	–	–	–	0	0	1	0	0	Overall psychotic symptom severity
Penadés *et al.* (2006)	0.33	40	–	–	–	–	0	–	–	0	NA
Tarrier *et al.* (2004)[97]	0.10	20	15.2 (5.5)	17.0 (12.0, 19.0)	7 (6.9%)	1	1	1	1	0	Overall psychotic symptom severity
Turkington *et al.* (2008)[99]	0.75	20	18.5 (7.3)	19.5 (15.0, 22.5)	5 (10.6%)	0	1	1	1	0	Overall psychotic symptom severity, hallucinations severity, delusion severity
Valmaggia *et al.* (2005)[100]	0.42	16	15.1 (3.1)	16.0 (16.0, 16.0)	3 (8.6%)	1	1	1	1	0	Overall psychotic symptom severity, hallucinations severity, delusion severity
Velligan *et al.* (2015)[104]	0.75	38	–	–	–	0	0	1	1	0	Overall psychotic symptom severity, social and occupational functioning

a Coded according to the originally planned primary and secondary outcome analyses of the IMPART project.
LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Appendix 9 Descriptive statistics of treatment effect modifiers tested for the cognitive–behavioural therapy plus additional elements of other therapies versus treatment as usual treatment comparison

Participant demographic characteristics

Age at entry to trial

TABLE 42 Baseline data for age at entry to trial in 14 studies

Age	CBT+ arm			TAU arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Baker *et al.* (2006)[55]	38.1 (11.1)	38.0 (30.0, 46.0)	0 (0.0)	36.8 (11.2)	36.0 (29.0, 44.0)	0 (0.0)	37.5 (11.1)	37.0 (29.0, 45.0)	0 (0.0)
Baker *et al.* (2006)[56]	28.4 (8.9)	25.0 (21.0, 36.0)	0 (0.0)	29.2 (11.4)	26.0 (20.0, 35.0)	0 (0.0)	28.8 (10.2)	25.5 (21.0, 35.8)	0 (0.0)
Barrowclough *et al.* (2010)[58]	37.4 (9.4)	36.8 (30.6, 44.6)	0 (0.0)	38.3 (10.0)	38.4 (30.4, 45.1)	0 (0.0)	37.9 (9.7)	37.4 (30.6, 44.8)	0 (0.0)
Barrowclough *et al.* (2014)[59]	24.5 (5.4)	23.8 (20.1, 28.1)	0 (0.0)	23.4 (3.8)	22.7 (20.8, 26.0)	0 (0.0)	24.2 (5.0)	23.4 (20.3, 27.2)	0 (0.0)
Chadwick *et al.* (2016)[63]	41.5 (11.6)	42.0 (33.5, 51.0)	0 (0.0)	40.2 (10.6)	42.0 (32.2, 48.0)	0 (0.0)	40.8 (11.1)	42.0 (32.8, 49.0)	0 (0.0)
Favrod *et al.* (2014)[65]	36.8 (10.4)	35.0 (29.2, 44.0)	0 (0.0)	36.6 (9.8)	36.0 (29.5, 44.8)	0 (0.0)	36.7 (10.0)	35.0 (29.0, 44.2)	0 (0.0)
Fowler *et al.* (2009)[67]	27.8 (6.1)	26.0 (24.0, 30.5)	0 (0.0)	30.0 (7.2)	29.0 (25.0, 34.0)	0 (0.0)	29.0 (6.8)	27.0 (24.0, 33.0)	0 (0.0)
Granholm *et al.* (2005)[72]	54.5 (7.0)	54.0 (49.0, 58.0)	0 (0.0)	53.1 (7.5)	52.0 (46.0, 58.0)	0 (0.0)	53.8 (7.2)	52.5 (48.0, 58.0)	0 (0.0)
Palma-Sevillano *et al.* (2011)[91]	24.0 (4.3)	24.0 (21.0, 26.0)	0 (0.0)	23.8 (4.0)	23.0 (21.0, 25.0)	0 (0.0)	23.9 (4.1)	23.5 (21.0, 26.0)	0 (0.0)
Steel *et al.* (2020)[96]	42.6 (9.9)	43.0 (34.0, 49.0)	0 (0.0)	43.4 (11.2)	43.0 (34.0, 54.0)	0 (0.0)	43.0 (10.6)	43.0 (34.0, 52.0)	0 (0.0)
Turkington *et al.* (2002)[98]	40.1 (11.0)	40.0 (31.0, 48.0)	1 (0.4)	42.0 (10.8)	41.0 (34.0, 50.0)	2 (1.2)	40.8 (11.0)	40.0 (32.5, 49.0)	3 (0.7)
van den Berg *et al.* (2015)[101]	40.4 (11.3)	43.0 (31.5, 48.0)	0 (0.0)	40.3 (9.7)	40.0 (32.0, 48.0)	0 (0.0)	40.4 (10.5)	42.0 (32.0, 48.0)	0 (0.0)
van der Gaag *et al.* (2012)[103]	40.9 (12.0)	38.0 (32.5, 50.0)	0 (0.0)	41.2 (12.0)	39.5 (32.0, 50.5)	0 (0.0)	41.1 (11.9)	38.0 (32.0, 50.0)	0 (0.0)
Velligan *et al.* (2015)[104]	41.7 (9.3)	44.0 (34.5, 48.0)	3 (8.6)	41.1 (9.9)	43.5 (32.8, 50.0)	1 (2.7)	41.4 (9.6)	44.0 (33.0, 48.2)	4 (5.6)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Gender

TABLE 43 Baseline data for gender in 14 studies

Gender	CBT+ arm		TAU arm		Both arms	
Citation	*N* male (%)	*N* missing (%)	*N* male (%)	*N* missing (%)	*N* male (%)	*N* missing (%)
Baker *et al.* (2006)[55]	71 (48.3)	0 (0.0)	85 (56.3)	0 (0.0)	156 (52.3)	0 (0.0)
Baker *et al.* (2006)[56]	49 (75.4)	0 (0.0)	52 (80.0)	0 (0.0)	101 (77.7)	0 (0.0)
Barrowclough *et al.* (2010)[58]	146 (89.0)	0 (0.0)	137 (84.0)	0 (0.0)	283 (86.5)	0 (0.0)
Barrowclough *et al.* (2014)[59]	68 (90.7)	0 (0.0)	30 (85.7)	0 (0.0)	98 (89.1)	0 (0.0)
Chadwick *et al.* (2016)[63]	27 (50.0)	0 (0.0)	26 (48.1)	1 (1.9)	53 (49.1)	1 (0.9)
Favrod *et al.* (2014)[65]	17 (65.4)	0 (0.0)	17 (65.4)	0 (0.0)	34 (65.4)	0 (0.0)
Fowler *et al.* (2009)[67]	25 (71.4)	0 (0.0)	30 (71.4)	0 (0.0)	55 (71.4)	0 (0.0)
Granholm *et al.* (2005)[72]	26 (70.3)	0 (0.0)	30 (76.9)	0 (0.0)	56 (73.7)	0 (0.0)
Palma-Sevillano *et al.* (2011)[91]	16 (76.2)	0 (0.0)	11 (84.6)	0 (0.0)	27 (79.4)	0 (0.0)
Steel *et al.* (2020)[96]	34 (69.4)	0 (0.0)	41 (80.4)	0 (0.0)	75 (75.0)	0 (0.0)
Turkington *et al.* (2002)[98]	174 (67.7)	0 (0.0)	104 (63.0)	0 (0.0)	278 (65.9)	0 (0.0)
van den Berg *et al.* (2015)[101]	25 (45.5)	0 (0.0)	23 (48.9)	0 (0.0)	48 (47.1)	0 (0.0)
van der Gaag *et al.* (2012)[103]	21 (53.8)	0 (0.0)	19 (50.0)	0 (0.0)	40 (51.9)	0 (0.0)
Velligan *et al.* (2015)[104]	19 (54.3)	0 (0.0)	20 (54.1)	0 (0.0)	39 (54.2)	0 (0.0)

Ethnicity

TABLE 44 Baseline data for ethnicity (defined as proportion of Caucasian participants) in six studies

Ethnicity	CBT+ arm		TAU arm		Both arms	
Citation	***N* Caucasian (%)**	***N* missing (%)**	***N* Caucasian (%)**	***N* missing (%)**	***N* Caucasian (%)**	***N* missing (%)**
Baker *et al.* (2006)[56]	65 (100.0)	0 (0.0)	63 (96.9)	0 (0.0)	128 (98.5)	0 (0.0)
Barrowclough *et al.* (2014)[59]	69 (92.0)	0 (0.0)	33 (94.3)	0 (0.0)	102 (92.7)	0 (0.0)
Chadwick *et al.* (2016)[63]	52 (96.3)	1 (1.9)	50 (92.6)	0 (0.0)	102 (94.4)	1 (0.9)
Granholm *et al.* (2005)[72]	29 (78.4)	0 (0.0)	31 (79.5)	0 (0.0)	60 (78.9)	0 (0.0)
Turkington *et al.* (2002)[98]	221 (86.0)	0 (0.0)	137 (83.0)	0 (0.0)	358 (84.8)	0 (0.0)
van den Berg *et al.* (2015)[101]	34 (61.8)	0 (0.0)	27 (57.4)	0 (0.0)	61 (59.8)	0 (0.0)

Participant clinical characteristics

Positive and Negative Syndrome Scale: total scores at baseline

TABLE 45 Baseline PANSS total scores for 10 studies (this outcome was not recorded in 4 studies)

PANSS score		CBT+ arm			TAU arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Baker *et al.* (2006)[55]	BPRS	32.9 (8.0)	31.0 (27.0, 37.0)	0 (0.0)	35.2 (11.5)	32.0 (27.0, 40.0)	1 (0.7)	34.1 (10.0)	31.0 (27.0, 38.0)	1 (0.3)
Baker *et al.* (2006)[56]	BPRS	36.5 (14.0)	32.0 (29.0, 38.0)	0 (0.0)	35.5 (10.9)	32.0 (28.0, 40.0)	0 (0.0)	36.0 (12.5)	32.0 (28.2, 39.0)	0 (0.0)
Barrowclough *et al.* (2010)[58]	PANSS	63.7 (14.3)	63.0 (56.0, 72.2)	0 (0.0)	61.2 (13.3)	62.0 (52.0, 71.0)	0 (0.0)	62.4 (13.8)	63.0 (52.0, 72.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	PANSS	64.1 (13.3)	64.0 (54.0, 73.0)	2 (2.7)	61.3 (12.4)	62.0 (52.0, 69.0)	2 (5.7)	63.2 (13.0)	63.0 (53.2, 72.8)	4 (3.6)
Chadwick *et al.* (2016)[63]	PSYRATS auditory hallucinations subscale	30.6 (5.6)	31.0 (28.0, 34.0)	5 (9.3)	30.3 (7.2)	32.0 (27.0, 34.2)	2 (3.7)	30.5 (6.4)	32.0 (28.0, 34.0)	7 (6.5)
Fowler *et al.* (2009)[67]	PANSS	57.6 (11.5)	57.0 (49.5, 64.0)	0 (0.0)	55.9 (10.2)	55.0 (48.5, 62.0)	0 (0.0)	56.7 (10.8)	55.0 (49.0, 64.0)	0 (0.0)
Granholm *et al.* (2005)[72]	PANSS	51.5 (13.2)	49.0 (41.0, 61.0)	0 (0.0)	56.1 (14.8)	57.0 (43.0, 66.0)	0 (0.0)	53.8 (14.2)	53.0 (42.8, 63.5)	0 (0.0)
Palma-Sevillano *et al.* (2011)[91]	PANSS	116.3 (37.7)	115.0 (90.0, 145.0)	0 (0.0)	119.2 (52.8)	95.0 (85.0, 164.0)	0 (0.0)	117.4 (43.3)	110.0 (85.0, 156.2)	0 (0.0)
Turkington *et al.* (2002)[98]	CPRS	25.4 (14.7)	22.0 (15.0, 34.0)	0 (0.0)	27.7 (14.9)	26.0 (14.0, 39.0)	0 (0.0)	26.3 (14.8)	23.0 (15.0, 36.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS	60.6 (9.9)	61.0 (54.0, 66.0)	0 (0.0)	63.1 (12.6)	64.0 (55.0, 72.0)	0 (0.0)	61.9 (11.3)	61.0 (54.8, 69.5)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: positive symptoms scores at baseline

TABLE 46 Baseline PANSS positive symptoms scores for six studies (this outcome was not recorded in eight studies)

PANSS positive symptoms		CBT+ arm			TAU arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2010)[58]	PANSS	15.9 (5.2)	16.0 (12.8, 19.0)	0 (0.0)	16.1 (5.5)	16.0 (12.0, 20.0)	0 (0.0)	16.0 (5.3)	16.0 (12.0, 19.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	PANSS	15.1 (4.6)	15.0 (12.0, 18.0)	0 (0.0)	14.9 (3.1)	15.0 (12.0, 17.0)	0 (0.0)	15.0 (4.2)	15.0 (12.0, 17.8)	0 (0.0)
Favrod *et al.* (2014)[65]	PANSS	19.3 (5.3)	20.5 (15.0, 22.8)	0 (0.0)	18.8 (4.7)	18.5 (15.0, 22.8)	0 (0.0)	19.1 (5.0)	19.5 (15.0, 23.0)	0 (0.0)
Fowler *et al.* (2009)[67]	PANSS	12.5 (4.1)	12.0 (10.0, 14.0)	0 (0.0)	12.0 (3.6)	12.5 (9.0, 15.0)	0 (0.0)	12.2 (3.8)	12.0 (9.0, 15.0)	0 (0.0)
Granholm *et al.* (2005)[72]	PANSS	11.8 (4.5)	11.0 (8.0, 14.0)	0 (0.0)	13.7 (5.2)	14.0 (9.0, 17.0)	0 (0.0)	12.8 (4.9)	12.0 (8.8, 16.0)	0 (0.0)
Steel *et al.* (2020)[96]	PANSS	18.5 (5.9)	18.0 (15.0, 22.0)	0 (0.0)	18.4 (6.0)	19.0 (14.0, 23.0)	0 (0.0)	18.4 (5.9)	19.0 (14.0, 23.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: negative symptoms scores at baseline

TABLE 47 Baseline PANSS negative symptoms for five studies (this outcome was not recorded in nine studies)

PANSS negative symptoms		CBT+ arm			TAU arm			Both arms		
	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Barrowclough *et al.* (2010)[58]	PANSS	14.5 (4.8)	14.0 (11.0, 18.0)	0 (0.0)	13.4 (4.1)	13.0 (10.5, 15.5)	0 (0.0)	14.0 (4.5)	13.0 (11.0, 16.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	PANSS	14.1 (4.5)	14.0 (10.0, 16.5)	0 (0.0)	14.1 (5.4)	13.0 (10.5, 16.5)	0 (0.0)	14.1 (4.8)	13.0 (10.0, 16.8)	0 (0.0)
Fowler *et al.* (2009)[67]	PANSS	13.9 (3.9)	14.0 (11.0, 17.0)	0 (0.0)	13.4 (3.5)	13.0 (11.0, 15.8)	0 (0.0)	13.6 (3.7)	13.0 (11.0, 16.0)	0 (0.0)
Granholm *et al.* (2005)[72]	PANSS	14.3 (5.1)	13.0 (11.0, 17.0)	0 (0.0)	15.2 (5.7)	14.0 (10.5, 18.5)	0 (0.0)	14.7 (5.4)	13.0 (11.0, 18.0)	0 (0.0)
Steel *et al.* (2020)[96]	PANSS	16.7 (4.9)	17.0 (13.0, 20.0)	0 (0.0)	17.9 (5.4)	18.0 (14.0, 22.0)	0 (0.0)	17.3 (5.1)	17.0 (13.0, 21.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: general psychopathology

TABLE 48 Baseline PANSS general psychopathology scores for 4 studies (this outcome was not recorded in 10 studies)

PANSS general psychopathology		CBT+ arm			TAU arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Barrowclough *et al.* (2010)[58]	PANSS	33.2 (8.0)	33.0 (28.0, 38.0)	0 (0.0)	31.6 (7.5)	31.0 (26.0, 37.0)	0 (0.0)	32.4 (7.8)	32.0 (27.0, 37.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	PANSS	34.7 (7.2)	35.0 (30.0, 40.0)	0 (0.0)	32.7 (6.8)	33.0 (27.5, 38.5)	0 (0.0)	34.1 (7.1)	35.0 (28.2, 39.0)	0 (0.0)
Fowler *et al.* (2009)[67]	PANSS	31.2 (6.4)	32.0 (25.5, 35.0)	0 (0.0)	30.6 (5.6)	31.5 (27.0, 33.8)	0 (0.0)	30.9 (5.9)	32.0 (26.0, 34.0)	0 (0.0)
Granholm *et al.* (2005)[72]	PANSS	25.4 (7.3)	24.0 (19.0, 29.0)	0 (0.0)	27.2 (7.2)	25.0 (22.0, 33.0)	0 (0.0)	26.3 (7.2)	25.0 (20.0, 32.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Anxiety scores at baseline

TABLE 49 Baseline anxiety scores for 14 studies (this outcome was not recorded in 6 studies)

Anxiety		CBT+ arm			TAU arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Baker *et al.* (2006)[55]	BPRS anxiety item	2.4 (1.3)	2.0 (1.0, 3.0)	0 (0.0)	2.4 (1.5)	2.0 (1.0, 3.0)	1 (0.7)	2.4 (1.4)	2.0 (1.0, 3.0)	1 (0.3)
Baker *et al.* (2006)[56]	BPRS anxiety item	2.4 (1.3)	2.0 (2.0, 3.0)	0 (0.0)	1.8 (0.8)	2.0 (1.0, 2.0)	0 (0.0)	2.1 (1.1)	2.0 (1.0, 3.0)	0 (0.0)
Barrowclough *et al.* (2010)[58]	PANSS G2	3.2 (1.6)	3.0 (2.0, 5.0)	0 (0.0)	3.0 (1.5)	3.0 (2.0, 4.0)	0 (0.0)	3.1 (1.5)	3.0 (2.0, 5.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	BAI	18.6 (12.2)	17.5 (9.0, 25.8)	1 (1.3)	14.8 (10.9)	15.0 (8.0, 20.0)	0 (0.0)	17.4 (11.9)	16.0 (8.0, 24.0)	1 (0.9)
Chadwick *et al.* (2016)[63]	HADS	13.3 (3.7)	14.0 (11.0, 16.0)	0 (0.0)	13.6 (3.7)	13.5 (11.2, 16.0)	0 (0.0)	13.4 (3.7)	14.0 (11.0, 16.0)	0 (0.0)
Fowler *et al.* (2009)[67]	BAI	16.9 (13.5)	15.0 (6.5, 23.5)	0 (0.0)	17.0 (11.8)	15.0 (7.5, 25.5)	3 (7.1)	17.0 (12.6)	15.0 (7.0, 24.0)	3 (3.9)
van der Gaag *et al.* (2012)[103]	BAI	20.5 (12.5)	20.0 (9.8, 29.0)	3 (7.7)	23.0 (16.4)	17.5 (10.8, 33.0)	2 (5.3)	21.7 (14.6)	19.0 (10.0, 31.0)	5 (6.5)
Velligan *et al.* (2015)[104]	BPRS anxiety item	3.7 (1.6)	4.0 (3.0, 5.0)	0 (0.0)	4.1 (1.7)	4.0 (3.0, 5.0)	0 (0.0)	3.9 (1.7)	4.0 (3.0, 5.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Depression scores at baseline

TABLE 50 Baseline depression scores for 14 studies (this outcome was not recorded in 3 studies)

Depression		CBT+ arm			TAU arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Baker *et al.* (2006)[55]	BDI	14.4 (12.1)	11.0 (4.0, 23.0)	15 (10.2)	17.9 (14.7)	15.0 (6.0, 25.0)	10 (6.6)	16.2 (13.6)	13.0 (5.0, 24.0)	25 (8.4)
Baker *et al.* (2006)[56]	BDI	22.4 (12.9)	22.0 (12.0, 33.0)	0 (0.0)	13.2 (11.0)	12.0 (4.0, 18.0)	0 (0.0)	17.8 (12.8)	16.0 (7.0, 27.8)	0 (0.0)
Barrowclough *et al.* (2010)[58]	CDSS	6.4 (5.1)	6.0 (2.0, 10.0)	0 (0.0)	5.1 (5.0)	5.0 (0.0, 9.0)	0 (0.0)	5.8 (5.1)	5.0 (0.0, 9.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	CDSS	7.5 (4.2)	7.0 (4.0, 11.0)	0 (0.0)	5.7 (5.5)	5.0 (1.0, 9.0)	0 (0.0)	7.0 (4.7)	7.0 (3.0, 10.0)	0 (0.0)
Chadwick *et al.* (2016)[63]	HADS	9.7 (4.9)	9.5 (6.0, 13.0)	0 (0.0)	10.3 (4.5)	10.0 (7.0, 14.0)	0 (0.0)	10.0 (4.7)	10.0 (6.0, 14.0)	0 (0.0)
Fowler *et al.* (2009)[67]	BDI	21.1 (13.9)	20.5 (11.5, 30.0)	1 (2.9)	22.6 (13.8)	21.0 (13.0, 32.5)	3 (7.1)	21.9 (13.7)	21.0 (12.0, 32.0)	4 (5.2)
Granholm *et al.* (2005)[72]	MADRS	13.5 (9.0)	9.0 (8.0, 19.0)	0 (0.0)	14.2 (8.7)	11.0 (7.5, 21.5)	0 (0.0)	13.8 (8.8)	10.5 (7.8, 20.0)	0 (0.0)
Steel *et al.* (2020)[96]	BDI	30.6 (10.3)	31.0 (23.0, 39.0)	0 (0.0)	30.3 (9.8)	30.0 (22.0, 39.0)	0 (0.0)	30.4 (10.0)	30.0 (22.0, 39.0)	0 (0.0)
van den Berg *et al.* (2015)[101]	BDI	28.2 (11.6)	27.0 (22.5, 36.5)	0 (0.0)	29.7 (12.4)	31.0 (21.5, 39.0)	0 (0.0)	28.9 (11.9)	28.0 (22.2, 38.0)	0 (0.0)
van der Gaag *et al.* (2012)[103]	BDI	21.1 (13.9)	20.0 (10.5, 30.2)	3 (7.7)	23.5 (15.2)	24.5 (8.8, 35.5)	2 (5.3)	22.3 (14.5)	21.5 (9.0, 32.0)	5 (6.5)
Velligan *et al.* (2015)[104]	BPRS depression item	3.5 (1.6)	4.0 (2.0, 4.5)	0 (0.0)	3.5 (1.6)	4.0 (2.0, 5.0)	0 (0.0)	3.5 (1.6)	4.0 (2.0, 5.0)	0 (0.0)

CDSS, Calgary Depression Scale for Schizophrenia; LQ, lower quartile; MADRS, Montgomery–Asberg Depression Rating Scale; SD, standard deviation; UQ, upper quartile.

Specific diagnostic subgroup

TABLE 51 Specific diagnostic subgroup data in 10 studies

Diagnostic subgroup		CBT+ arm							TAU arm						Both arm				
Citation	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)
Baker *et al.* (2006)[56]	39 (60.0)	5 (7.7)	10 (15.4)	11 (16.9)	0 (0.0)	0 (0.0)	43 (66.2)	12 (18.5)	5 (7.7)	5 (7.7)	0 (0.0)	0 (0.0)	82 (63.1)	17 (13.1)	15 (11.5)	16 (12.3)	0 (0.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	36 (48.0)	10 (13.3)	26 (34.7)	0 (0.0)	3 (4.0)	0 (0.0)	18 (51.4)	3 (8.6)	11 (31.4)	0 (0.0)	3 (8.6)	0 (0.0)	54 (49.1)	13 (11.8)	37 (33.6)	0 (0.0)	6 (5.5)	0 (0.0)
Chadwick *et al.* (2016)[63]	32 (59.3)	6 (11.1)	4 (7.4)	4 (7.4)	0 (0.0)	8 (14.8)	31 (57.4)	8 (14.8)	5 (9.3)	5 (9.3)	0 (0.0)	5 (9.3)	63 (58.3)	14 (13.0)	9 (8.3)	9 (8.3)	0 (0.0)	13 (12.0)
Favrod *et al.* (2014)[65]	22 (84.6)	4 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	22 (84.6)	4 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	44 (84.6)	8 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fowler *et al.* (2009)[67]	23 (65.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	12 (34.3)	27 (64.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	15 (35.7)	50 (64.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	27 (35.1)
Granholm *et al.* (2005)[72]	25 (67.6)	12 (32.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	23 (59.0)	16 (41.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	48 (63.2)	28 (36.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palma-Sevillano *et al.* (2011)[91]	16 (76.2)	3 (14.3)	0 (0.0)	2 (9.5)	0 (0.0)	0 (0.0)	12 (92.3)	1 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	28 (82.4)	4 (11.8)	0 (0.0)	2 (5.9)	0 (0.0)	0 (0.0)
Turkington *et al.* (2002)[98]	254 (98.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	163 (98.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	417 (98.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)
van den Berg *et al.* (2015)[101]	34 (61.8)	15 (27.3)	3 (5.5)	3 (5.5)	0 (0.0)	0 (0.0)	30 (63.8)	13 (27.7)	1 (2.1)	3 (6.4)	0 (0.0)	0 (0.0)	64 (62.7)	28 (27.5)	4 (3.9)	6 (5.9)	0 (0.0)	0 (0.0)
van der Gaag *et al.* (2012)[103]	29 (74.4)	3 (7.7)	4 (10.3)	0 (0.0)	0 (0.0)	3 (7.7)	25 (65.8)	2 (5.3)	8 (21.1)	0 (0.0)	0 (0.0)	3 (7.9)	54 (70.1)	5 (6.5)	12 (15.6)	0 (0.0)	0 (0.0)	6 (7.8)

Phase of illness (first episode vs. not first episode)

TABLE 52 First episode vs. not first episode data in 11 studies (this variable was not available for 3 studies)

Phase of illness	CBT+ arm		TAU arm		Both arms	
Citation	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**	**First episode (%)**	***N* missing (%)**
Baker *et al.* (2006)[55]	11 (7.5)	0 (0.0)	11 (7.3)	0 (0.0)	22 (7.4)	0 (0.0)
Baker *et al.* (2006)[56]	17 (26.2)	0 (0.0)	26 (40.0)	0 (0.0)	43 (33.1)	0 (0.0)
Barrowclough *et al.* (2010)[58]	24 (14.6)	0 (0.0)	25 (15.3)	0 (0.0)	49 (15.0)	0 (0.0)
Barrowclough *et al.* (2014)[59]	63 (84.0)	0 (0.0)	28 (80.0)	0 (0.0)	91 (82.7)	0 (0.0)
Chadwick *et al.* (2016)[63]	15 (27.8)	9 (16.7)	14 (25.9)	9 (16.7)	29 (26.9)	18 (16.7)
Fowler *et al.* (2009)[67]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	24 (31.2)	0 (0.0)
Granholm *et al.* (2005)[72]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palma-Savillano *et al.*, (2011)	21 (100.0)	0 (0.0)	13 (100.0)	0 (0.0)	34 (100.0)	0 (0.0)
Turkington *et al.* (2002)[98]	48 (18.7)	2 (0.8)	21 (12.7)	3 (1.8)	69 (16.4)	5 (1.2)
van den Berg *et al.* (2015)[101]	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
Velligan *et al.* (2015)[104]	3 (8.6)	13 (37.1)	3 (8.1)	15 (40.5)	6 (8.3)	28 (38.9)

Illness duration

TABLE 53 Illness duration data in nine studies (this variable was not available for five studies)

Illness duration	CBT+ arm			TAU arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Baker *et al.* (2006)[55]	15.1 (10.1)	14.0 (6.0, 21.8)	1 (0.7)	13.8 (9.8)	12.0 (6.0, 18.0)	1 (0.7)	14.4 (10.0)	13.0 (6.0, 20.2)	2 (0.7)
Baker *et al.* (2006)[56]	9.1 (7.9)	7.0 (3.0, 12.0)	0 (0.0)	9.9 (10.7)	7.0 (2.0, 16.0)	0 (0.0)	9.5 (9.4)	7.0 (2.0, 14.8)	0 (0.0)
Barrowclough *et al.* (2014)[59]	1.6 (1.2)	1.3 (0.7, 2.0)	0 (0.0)	1.8 (1.4)	1.4 (0.6, 2.7)	0 (0.0)	1.6 (1.3)	1.3 (0.7, 2.3)	0 (0.0)
Chadwick *et al.* (2016)[63]	10.4 (10.5)	8.0 (2.0, 15.0)	9 (16.7)	9.7 (8.2)	7.0 (3.0, 14.0)	9 (16.7)	10.0 (9.4)	7.5 (2.2, 14.8)	18 (16.7)
Fowler *et al.* (2009)[67]	4.9 (2.2)	5.0 (3.5, 7.0)	0 (0.0)	4.8 (2.4)	4.5 (3.0, 6.8)	0 (0.0)	4.8 (2.3)	5.0 (3.0, 7.0)	0 (0.0)
Granholm *et al.* (2005)[72]	28.1 (10.5)	28.0 (21.0, 36.0)	0 (0.0)	28.3 (10.5)	29.0 (22.5, 35.5)	0 (0.0)	28.2 (10.4)	29.0 (21.0, 36.2)	0 (0.0)
Turkington *et al.* (2002)[98]	12.6 (9.8)	10.0 (4.0, 19.0)	2 (0.8)	14.1 (10.4)	12.0 (6.0, 20.0)	3 (1.8)	13.2 (10.1)	10.0 (5.0, 19.0)	5 (1.2)
van den Berg *et al.* (2015)[101]	18.2 (11.7)	20.0 (6.5, 26.5)	0 (0.0)	15.7 (10.5)	12.0 (8.5, 22.0)	0 (0.0)	17.1 (11.2)	16.5 (7.0, 24.0)	0 (0.0)
Velligan *et al.* (2015)[104]	16.0 (10.1)	17.5 (7.2, 23.0)	13 (37.1)	13.0 (7.0)	13.5 (6.8, 18.0)	15 (40.5)	14.5 (8.7)	15.5 (6.8, 20.0)	28 (38.9)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Duration of untreated psychosis

TABLE 54 Duration of untreated psychosis data in 2 studies (this variable was not available for 12 studies)

DUP	CBT+ arm			TAU arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Barrowclough *et al.* (2014)[59]	1.0 (1.7)	0.4 (0.1, 1.1)	36 (48.0)	0.4 (0.7)	0.2 (0.1, 0.4)	15 (42.9)	0.8 (1.4)	0.3 (0.1, 0.8)	51 (46.4)
Palma-Sevillano *et al.* (2011)[91]	0.8 (1.1)	0.3 (0.2, 0.7)	0 (0.0)	1.7 (1.7)	0.7 (0.4, 3.7)	1 (7.7)	1.1 (1.4)	0.5 (0.2, 1.4)	1 (2.9)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Number of antipsychotic medications at baseline

TABLE 55 Number of antipsychotic medications data in six studies (this variable was not available for eight studies)

Number of antipsychotic medications	CBT+ arm			TAU arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Baker *et al.* (2006)[55]	2.0 (1.0)	2.0 (1.0, 3.0)	0 (0.0)	1.9 (1.1)	2.0 (1.0, 2.0)	0 (0.0)	1.9 (1.1)	2.0 (1.0, 2.0)	0 (0.0)
Baker *et al.* (2006)[56]	1.3 (0.9)	1.0 (1.0, 2.0)	0 (0.0)	1.2 (0.8)	1.0 (1.0, 2.0)	0 (0.0)	1.3 (0.9)	1.0 (1.0, 2.0)	0 (0.0)
Chadwick *et al.* (2016)[63]	1.4 (0.7)	1.0 (1.0, 2.0)	0 (0.0)	1.4 (0.8)	1.0 (1.0, 2.0)	2 (3.7)	1.4 (0.8)	1.0 (1.0, 2.0)	2 (1.9)
Granholm *et al.* (2005)[72]	1.1 (0.2)	1.0 (1.0, 1.0)	0 (0.0)	1.1 (0.3)	1.0 (1.0, 1.0)	0 (0.0)	1.1 (0.3)	1.0 (1.0, 1.0)	0 (0.0)
Turkington *et al.* (2002)[98]	1.4 (0.6)	1.0 (1.0, 2.0)	0 (0.0)	1.3 (0.6)	1.0 (1.0, 2.0)	0 (0.0)	1.3 (0.6)	1.0 (1.0, 2.0)	0 (0.0)
van den Berg *et al.* (2015)[101]	3.3 (2.0)	3.0 (2.0, 4.0)	0 (0.0)	3.2 (2.0)	3.0 (2.0, 4.0)	0 (0.0)	3.3 (2.0)	3.0 (2.0, 4.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Specific intervention characteristics

TABLE 56 Data pertaining to treatment duration (study-level variable available for 14 studies), number of sessions offered in the trial (study-level variable available for 13 studies), and number of sessions attended (individual-level variable available for 11 studies that provided relevant IPD)

Citation	Treatment duration (years)	Number of sessions offered	Sessions attended			Therapist training and competence	Competency check	Manualised intervention	Formulation-based intervention	Individual or group	Intended target/ trial primary outcome[a]
			Mean (SD)	Median (LQ, UQ)	*N* missing (%)						
Baker *et al.* (2006)[55]	0.19	8.0	6.2 (2.2)	7.0 (5.0, 8.0)	0 (0.0)	0	0	1	0	0	NA
Baker *et al.* (2006)[56]	0.29	10.0	7.8 (3.7)	10.0 (5.0, 10.0)	0 (0.0)	0	0	1	1	0	NA
Barrowclough *et al.* (2010)[58]	1	26	9.0 (8.1)	8.5 (1.0, 14.2)	136 (82.9)	1	1	1	1	0	Readmission to hospital
Barrowclough *et al.* (2014)[59]	0.75	24	NA	NA	75 (100.0)	1	1	1	1	0	NA
Chadwick *et al.* (2016)[63]	0.33	12.0	8.0 (4.3)	10.0 (5.5, 11.0)	3 (5.6)	0	0	1	1	1	NA
Favrod *et al.* (2014)[65]	0.15	8.0	7.0 (1.9)	8.0 (7.0, 8.0)	0 (0.0)	0	0	1	0	0	Delusions severity
Fowler *et al.* (2009)[67]	0.75	NA	NA	NA	35 (100.0)	0	0	1	1	0	Social and occupational functioning
Granholm *et al.* (2005)[72]	0.50	24.0	19.9 (6.7)	22.1 (19.9, 24.0)	0 (0.0)	0	1	1	0	0	Social and occupational functioning
Palma-Sevillano *et al.* (2011)[91]	1.00	34	15.2 (1.5)	16.0 (15.0, 16.0)	0 (0.0)	1	0	0	0	0	Overall psychotic symptom severity
Steel *et al.* (2020)[96]	0.25	12.0	9.0 (3.0)	10.0 (8.0, 11.0)	0 (0.0)	0	0	1	0	0	Depression
Turkington *et al.* (2002)[98]	0.39	6.0	5.6 (1.0)	6.0 (6.0, 6.0)	0 (0.0)	0	0	1	1	0	Overall psychotic symptom severity
van den Berg *et al.* (2015)[101]	0.19	8.0	6.6 (2.6)	8.0 (7.0, 8.0)	0 (0.0)	1	1	1	0	0	NA
van der Gaag *et al.* (2012)[103]	0.17	7.0	5.2 (3.1)	7.0 (3.5, 7.0)	0 (0.0)	0	1	1	0	0	Depression
Velligan *et al.* (2015)[104]	0.75	38	NA	NA	35 (100.0)	0	0	1	1	0	Overall psychotic symptom severity, social and occupational functioning

a Coded according to the originally planned primary and secondary outcome analyses of the IMPART project.
LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Appendix 10 Descriptive statistics of treatment effect modifiers tested for the cognitive–behavioural therapy plus additional elements of other therapies versus active control treatment comparison

Participant demographic characteristics

Age at entry to trial

TABLE 57 Baseline data for age at entry to trial in three studies

Age	CBT+ arm			AC arm			Both arms		
Citation	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	55.3 (5.8)	55.0 (50.3, 60.2)	0 (0.0%)	54.7 (7.4)	51.9 (49.1, 60.6)	0 (0.0%)	55.0 (6.6)	52.5 (49.7, 60.6)	0 (0.0%)
Granholm *et al.* (2014)[74]	41.1 (10.4)	41.7 (35.1, 47.4)	0 (0.0%)	41.6 (9.2)	42.3 (37.3, 47.7)	0 (0.0%)	41.4 (9.8)	41.9 (35.3, 47.4)	0 (0.0%)
Velligan *et al.* (2015)[104]	41.7 (9.3)	44.0 (34.5, 48.0)	3 (8.6%)	43.5 (10.7)	44.5 (37.8, 52.0)	1 (3.0%)	42.6 (10.0)	44.0 (34.8, 50.2)	4 (5.9%)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Gender

TABLE 58 Baseline data for gender in three studies

Gender	CBT+ arm		AC arm		Both arms	
Citation	***N* male (%)**	***N* missing (%)**	***N* male (%)**	***N* missing (%)**	**N male (%)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	16 (51.6)	0 (0.0)	19 (57.6)	0 (0.0)	35 (54.7)	0 (0.0)
Granholm *et al.* (2014)[74]	46 (63.0)	0 (0.0)	53 (69.7)	0 (0.0)	99 (66.4)	0 (0.0)
Velligan *et al.* (2015)[104]	19 (54.3)	0 (0.0)	18 (54.5)	0 (0.0)	37 (54.4)	0 (0.0)

Ethnicity

TABLE 59 Baseline data for ethnicity (defined as proportion of Caucasian participants) in three studies

Ethnicity	CBT+ arm		AC arm		Both arms	
Citation	***N* Caucasian (%)**	***N* missing (%)**	***N* Caucasian (%)**	***N* missing (%)**	***N* Caucasian (%)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	18 (58.1)	0 (0.0)	24 (72.7)	0 (0.0)	42 (65.6)	0 (0.0)
Granholm *et al.* (2014)[74]	41 (56.2)	0 (0.0)	44 (57.9)	0 (0.0)	85 (57.0)	0 (0.0)
Velligan *et al.* (2015)[104]	14 (40.0)	0 (0.0)	8 (24.2)	0 (0.0)	22 (32.4)	0 (0.0)

Participant clinical characteristics

Positive and Negative Syndrome Scale: total scores at baseline

TABLE 60 Baseline values of primary outcome PANSS for three studies

PANSS		CBT+ arm			AC arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	PANSS	63.7 (19.9)	63.0 (50.0, 74.0)	0 (0.0)	66.4 (18.1)	68.0 (52.0, 80.0)	0 (0.0)	65.1 (18.9)	64.5 (51.8, 79.0)	0 (0.0)
Granholm *et al.* (2014)[74]	PANSS	70.4 (19.0)	72.0 (59.0, 83.0)	0 (0.0)	73.3 (20.0)	74.0 (56.5, 84.0)	0 (0.0)	71.8 (19.5)	73.0 (58.0, 84.0)	0 (0.0)
Velligan *et al.* (2015)[104]	BPRS	60.6 (9.9)	61.0 (54.0, 66.0)	0 (0.0)	62.1 (12.9)	61.0 (54.0, 70.0)	0 (0.0)	61.3 (11.4)	61.0 (53.8, 68.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: positive symptoms scores at baseline

TABLE 61 Baseline PANSS positive symptoms scores for two studies

Positive symptoms		CBT+ arm			AC arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	PANSS	18.3 (8.1)	17.0 (12.0, 23.0)	0 (0.0)	17.8 (6.3)	17.0 (14.0, 20.0)	0 (0.0)	18.0 (7.2)	17.0 (12.8, 22.0)	0 (0.0)
Granholm *et al.* (2014)[74]	PANSS	19.0 (6.4)	20.0 (15.0, 23.0)	0 (0.0)	20.2 (6.7)	21.0 (14.0, 25.2)	0 (0.0)	19.6 (6.6)	20.0 (15.0, 24.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: negative symptoms scores at baseline

TABLE 62 Baseline PANSS negative symptoms for two studies (this outcome was not recorded in one study)

Negative symptoms		CBT+ arm			AC arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	PANSS	14.1 (5.3)	11.0 (10.0, 18.0)	0 (0.0)	15.7 (6.7)	13.0 (11.0, 19.0)	0 (0.0)	14.9 (6.1)	12.0 (10.0, 19.0)	0 (0.0)
Granholm *et al.* (2014)[74]	PANSS	34.7 (10.3)	34.0 (28.0, 43.0)	0 (0.0)	35.9 (10.7)	36.5 (26.0, 42.2)	0 (0.0)	35.3 (10.5)	35.0 (27.0, 43.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Positive and Negative Syndrome Scale: general psychopathology scores at baseline

TABLE 63 Baseline PANSS general psychopathology scores for two studies (this outcome was not recorded in one study)

PANSS general psychopathology		CBT+ arm			AC arm			Both arms		
Citation	**Original scale**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**	**Mean (SD)**	**Median (LQ, UQ)**	***N* missing (%)**
Granholm *et al.* (2013)[73]	PANSS	31.6 (9.6)	32.0 (25.0, 38.5)	0 (0.0)	31.8 (9.1)	33.0 (25.0, 38.0)	0 (0.0)	31.7 (9.3)	32.0 (25.0, 38.2)	0 (0.0)
Granholm *et al.* (2014)[74]	PANSS	34.7 (10.3)	34.0 (28.0, 43.0)	0 (0.0)	35.9 (10.7)	36.5 (26.0, 42.2)	0 (0.0)	35.3 (10.5)	35.0 (27.0, 43.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Anxiety scores at baseline

TABLE 64 Baseline anxiety scores for three studies

Baseline anxiety		CBT+ arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Granholm *et al.* (2013)[73]	BAI	16.4 (12.7)	16.0 (5.5, 28.0)	0 (0.0)	14.5 (12.1)	11.0 (5.0, 21.0)	0 (0.0)	15.4 (12.3)	13.5 (5.0, 25.5)	0 (0.0)
Granholm *et al.* (2014)[74]	BAI	16.0 (10.6)	15.0 (8.0, 21.5)	2 (2.7)	17.1 (12.7)	17.0 (6.0, 24.0)	0 (0.0)	16.5 (11.7)	16.0 (7.0, 23.5)	2 (1.3)
Velligan *et al.* (2015)[104]	BPRS anxiety item	3.7 (1.6)	4.0 (3.0, 5.0)	0 (0.0)	4.7 (1.5)	5.0 (4.0, 6.0)	0 (0.0)	4.2 (1.6)	5.0 (3.0, 5.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Depression scores at baseline

TABLE 65 Baseline depression scores for three studies

Baseline depression		CBT+ arm			AC arm			Both arms		
Citation	Original scale	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Granholm *et al.* (2013)[73]	BDI	16.3 (9.8)	14.0 (9.5, 23.5)	0 (0.0)	16.4 (13.5)	14.0 (4.0, 26.0)	0 (0.0)	16.4 (11.7)	14.0 (6.8, 25.0)	0 (0.0)
Granholm *et al.* (2014)[74]	BDI	17.4 (9.7)	17.0 (9.0, 24.2)	1 (1.4)	17.2 (11.5)	18.0 (7.5, 25.0)	1 (1.3)	17.3 (10.6)	17.0 (9.0, 25.0)	2 (1.3)
Velligan *et al.* (2015)[104]	BPRS depression item	3.5 (1.6)	4.0 (2.0, 4.5)	0 (0.0)	3.6 (1.6)	4.0 (2.0, 5.0)	0 (0.0)	3.5 (1.6)	4.0 (2.0, 5.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Specific diagnostic subgroup

TABLE 66 Specific diagnostic subgroup data in three studies

Diagnostic subgroup	CBT+ arm						AC arm						Both arms					
Citation	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)	Schizophrenia (%)	Schizoaffective (%)	Other psychosis (%)	Other affective psychosis (%)	Substance-induced psychosis (%)	*N* missing (%)
Granholm *et al.* (2013)[73]	22 (71.0)	7 (22.6)	0 (0.0)	2 (6.5)	0 (0.0)	0 (0.0)	29 (87.9)	4 (12.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	51 (79.7)	11 (17.2)	0 (0.0)	2 (3.1)	0 (0.0)	0 (0.0)
Granholm *et al.* (2014)[74]	59 (80.8)	13 (17.8)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	56 (73.7)	19 (25.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	115 (77.2)	32 (21.5)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
Velligan *et al.* (2015)[104]	NA	NA	NA	NA	NA	35 (100.0)	NA	NA	NA	NA	NA	33 (100.0)	NA	NA	NA	NA	NA	68 (100.0)

Phase of illness (first episode vs. not first episode)

TABLE 67 First episode vs. not first episode data in three studies

Phase of illness	CBT+ arm		AC arm		Both arms	
Citation	First episode (%)	*N* missing (%)	First episode (%)	*N* missing (%)	First episode (%)	*N* missing (%)
Granholm *et al.* (2013)[73]	2 (6.5)	10 (32.3)	0 (0.0)	3 (9.1)	2 (3.1)	13 (20.3)
Granholm *et al.* (2014)[74]	5 (6.8)	0 (0.0)	3 (3.9)	0 (0.0)	8 (5.4)	0 (0.0)
Velligan *et al.* (2015)[104]	3 (8.6)	13 (37.1)	2 (6.1)	9 (27.3)	5 (7.4)	22 (32.4)

Illness duration

TABLE 68 Illness duration data in three studies

Illness duration	CBT+ arm			AC arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Granholm *et al.* (2013)[73]	25.6 (13.1)	27.2 (16.5, 34.4)	10 (32.3)	32.0 (11.6)	32.9 (25.8, 39.1)	3 (9.1)	29.4 (12.5)	30.0 (22.0, 38.9)	13 (20.3)
Granholm *et al.* (2014)[74]	21.4 (11.5)	21.2 (12.5, 28.2)	0 (0.0)	21.4 (10.6)	21.4 (14.9, 27.1)	0 (0.0)	21.4 (11.0)	21.3 (13.2, 28.2)	0 (0.0)
Velligan *et al.* (2015)[104]	16.0 (10.1)	17.5 (7.2, 23.0)	13 (37.1)	17.1 (11.6)	15.0 (6.8, 28.0)	9 (27.3)	16.6 (10.8)	16.0 (7.0, 25.0)	22 (32.4)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Duration of untreated psychosis

No CBT+ versus AC studies provided relevant data to the estimation of DUP.

Number of antipsychotic medications at baseline

TABLE 69 Number of antipsychotic medications data in two studies (this variable was not available for one study)

Number of antipsychotic medications	CBT+ arm			AC arm			Both arms		
Citation	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)	Mean (SD)	Median (LQ, UQ)	*N* missing (%)
Granholm *et al.* (2013)[73]	1.3 (0.7)	1.0 (1.0, 2.0)	0 (0.0)	1.0 (0.6)	1.0 (1.0, 1.0)	0 (0.0)	1.1 (0.6)	1.0 (1.0, 1.2)	0 (0.0)
Granholm *et al.* (2014)[74]	1.5 (0.7)	1.0 (1.0, 2.0)	0 (0.0)	1.5 (0.8)	1.0 (1.0, 2.0)	0 (0.0)	1.5 (0.8)	1.0 (1.0, 2.0)	0 (0.0)

LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

Specific intervention characteristics

TABLE 70 Data pertaining to treatment duration (study-level variable available for three studies), number of sessions offered in the trial (study-level variable available for three studies), and number of sessions attended (in this treatment comparison, no relevant IPD were available)

Citation	Treatment duration (years)	Number of sessions offered	Sessions attended			Therapist training and competence	Competency check	Manualised intervention	Formulation-based intervention	Individual or group	Intended target/trial primary outcome[a]
			Mean (SD)	Median (LQ, UQ)	*N* missing (%)						
Granholm *et al.* (2013)[73]	0.75	36	–	–	–	0	1	1	0	0	Social and occupational functioning
Granholm *et al.* (2014)[74]	0.75	36	–	–	–	0	1	1	0	0	Social and occupational functioning
Velligan *et al.* (2015)[104]	0.75	38	–	–	–	0	0	1	1	0	Overall psychotic symptom severity, social and occupational functioning

a Coded according to the originally planned primary and secondary outcome analyses of the IMPART project.
LQ, lower quartile; SD, standard deviation; UQ, upper quartile.

EME
HSDR
HTA
PGfAR
PHR

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