A systematic review and meta-analysis of cognitive behavioural informed psychological interventions for psychiatric inpatients with psychosis

Lisa Wood

Claire Williams

Jo Billings

Sonia Johnson

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Abstract

Psychological interventions such as Cognitive Behavioural Therapy for psychosis (CBTp) are recommended by the National Institute of Health and Care Excellence (NICE) for delivery in the acute phase of people's mental health difficulties. However, the effectiveness of cognitive behaviourally informed psychological therapies for psychiatric inpatients is unknown. The aim of this review is to examine the type, quality and efficacy of cognitive behaviourally informed psychological interventions for psychiatric inpatients experiencing psychosis. A systematic review and meta-analysis was conducted of randomised controlled trials examining the efficacy of CBTp offered to acute psychiatric inpatients with psychosis on primary (positive symptoms) and secondary outcomes of interest. A total of 22 studies were identified reporting on 17 trials of interventions such as CBTp, Acceptance and Commitment Therapy (ACT) and Metacognitive Therapy (MCT). Cognitive Behavioural informed psychological interventions were found not be effective in reducing positive symptoms (primary outcome) at post-therapy and at follow-up but when a one study removed analysis was conducted a positive effect was found at both time points. In regard to secondary outcomes, cognitive behavioural interventions demonstrated a significant favourable effect on negative symptoms (post-therapy), total symptoms (post-therapy and follow-up), functioning (post-therapy and follow-up) and readmission (follow-up). These psychological interventions have potential to be effective for those admitted to psychiatric inpatient care and in acute crisis. However, findings are equivocal with evidence that these interventions have effect on some symptom measures but not others. Further examination of inpatient adapted cognitive behavioural informed psychological interventions is required.

Introduction

Cognitive behavioural psychological interventions are recommended by National Institute of Health and Clinical Excellence guidelines for those experiencing psychosis, particularly Cognitive Behavioural Therapy (CBT) (NICE, 2014). CBT for psychosis (CBTp), often considered as a second wave cognitive behavioural psychological intervention, is an intervention that aims to reduce distress, facilitate the development of coping strategies and improve quality of life by directly tackling negative appraisals and associated unhelpful coping behaviours (Morrison, 2001, Kingdon et al., 1994, Chadwick et al., 1996, Beck et al., 2008). A number of systematic reviews have demonstrated that CBTp is an effective treatment in reducing symptoms of psychosis and improving functioning and mood (Wykes et al., 2008, Dixon et al., 2010), even despite recent challenging evidence (Lynch et al., 2010, Jauhar et al., 2014). There is growing evidence demonstrating that CBT is evolving and a number of new third-wave approaches have developed with a developing but promising evidence base (Tai and Turkington, 2009), including approaches such as Metacognitive Therapy (MCT) and Acceptance and Commitment Therapy (ACT) (Yildiz, 2020, Lysaker et al., 2018). However, the vast majority of the evidence-base for both second and third wave cognitive behavioural interventions has been conducted in outpatient settings (Wykes et al., 2008), which leaves a gap in understanding what would be helpful for inpatient populations.

There is need to consider the specific needs of the acute psychiatric inpatient population as their needs are arguably different to that of outpatients. The presentations of psychiatric inpatients are more severe: they are more likely to pose high risk to themselves and others, to be acutely unwell, and to have multiple problems/dual diagnosis, cognitive difficulties (memory and concentration) and thought disorder. Thus they have different psychological needs from those in outpatient settings (Bowers et al., 2009) . Their acute presentations may

also make it more difficult for them to engage in routinely delivered cognitive behavioural psychological interventions (Wood et al., 2018). . For example, acute psychotic symptoms such as extreme emotional distress, thought disorder, and acute hallucinations or delusions can make the engagement in psychological therapy a challenge due to difficulties concentrating in sessions and finding the development of new relationships potentially threatening (Palmier-Claus et al., 2017, Clarke and Wilson, 2008). The primary aim of psychiatric inpatient care is to reduce risk, contain a crisis, and prevent relapse (Bowers et al., 2009), which is arguably different to longer-term outpatient recovery goals. Therapeutic interventions delivered in psychiatric inpatient settings also have different required competencies including, inclusion of the Multi-Disciplinary Team (MDT), involvement of family and carers in therapy, and flexible sessions, which are not traditional competencies of psychological interventions such as CBTp. Service users are living within a restricted inpatient environment, often under section of the Mental Health Act (MHA), therefore, the outpatient evidence base for cognitive behavioural psychological interventions is unlikely to be generalisable to this client group. The average length of admission is 32 days (NHS Benchmarking, 2018), which also makes the recommended 16-24 session unachievable in this context.

Randomised controlled trials (RCTs) of psychological therapies for psychosis with the acute inpatient population so far appears to be limited. Two recent systematic reviews have been conducted of inpatient psychological interventions; one scoping review (Jacobsen et al., 2018), and one systematic review and meta-analysis of both randomised and non-randomised studies (Paterson et al., 2018). Both concluded that psychological interventions show promise in this setting but there needs to be a standardised approach to the delivery and evaluation of interventions. There is yet to be a systematic review which has examined RCTs of cognitive

behavioural psychological interventions for psychiatric inpatients with psychosis, which is the highest quality of evidence (Higgins and Green, 2011). Thus there is a need for such a review to summarise and synthesise the current evidence base as a starting point for further research and service development. The aim of this study was to conduct a systematic review and meta-analysis of cognitive behavioural psychological interventions for those who experience psychosis in acute psychiatric inpatient settings. More specifically it will aim to:

- Examine the quality of available research evidence.
- Examine the type of interventions being offered to acute psychiatric inpatients with psychosis, and any adaptations made for the psychiatric inpatient setting.
- Examine the primary treatment targets/primary outcome of identified studies.
- Examine the efficacy of cognitive behavioural informed interventions on the primary outcome of positive psychotic symptoms.
- Examine the efficacy of cognitive behavioural informed interventions on secondary outcomes (readmission/rehospitalisation rates, change in total symptoms in psychosis, negative symptoms, general symptoms, self-esteem, depression, suicidality, hopelessness, shame, anxiety, recovery, quality of life, functioning, adverse events).

Methodology

Protocol registration and changes

This systematic review followed guidance from the Cochrane Collaboration on conducting systematic reviews (Higgins and Green, 2011). A review protocol was developed and published online prior to the review commencing (PROSPERO ID: CRD42017067982). Initially, due to the anticipated paucity of studies in this area, RCTs, uncontrolled studies, non-randomised studies, cohort studies, observational studies, case control studies, and qualitative studies were to be included. The initial aim was to conduct a narrative synthesis in order to meet all aims of the review (Popay et al., 2006) and for a meta-analysis to be conducted with available RCT data if the quantity and quality of data justified it. However, the searches identified sufficient RCTs for a systematic review and meta-analysis. Therefore this review only included RCTs, which are considered the gold standard of evidence (Higgins and Green, 2011).

Study inclusion and exclusion criteria

Sample criteria

This review included studies where: ≥ 50% of participants met criteria for a schizophrenia-spectrum diagnoses (schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, psychotic disorder not otherwise specified defined by any criteria), or met threshold for early intervention services (to allow for diagnostic uncertainty). The sample of the trials included ≥ 50% of participants who were psychiatric inpatients (under section of the MHA or informally) at the time of commencing the research trial. Participants in the study samples were aged 16 or older. The review excluded studies where: ≥ 50% of

participants had psychosis as a secondary diagnosis (e.g. to alcohol use, learning disability, dementia); ≥ 50% of participants were children and adolescents (participants aged below 16); people were experiencing psychosis secondary to other psychiatric diagnoses.

Intervention criteria

All studies evaluating cognitive behavioural psychological interventions, either in group or one-to-one format, for psychosis were included. The intervention had to have started during the acute psychiatric inpatient admission with at least half of the sessions being conducted in this setting. The intervention had to be offered by an appropriately trained professional (psychologist or therapist) or a professional in training (trainee psychologist or therapist). For the purposes of this review, a cognitive behavioural psychological intervention was defined as per NICE guidelines (NICE, 2014). The intervention was defined as a psychological intervention for people with psychosis "which follows a treatment manual so that people can establish links between their thoughts, feelings or actions and their current or past symptoms and/or functioning, and include the re-evaluation of people's perceptions, beliefs or reasoning relating to the target symptoms" (NICE, 2014). The cognitive behavioural intervention had to include at least one of the following components: "people monitoring their own thoughts, feelings or behaviours with respect to their symptoms or recurrence of symptoms, promoting alternative ways of coping with the target symptom, reducing distress, and improving function". No criteria was specified in relation to number of sessions. This allowed for the inclusion of third wave therapies, and interventions where a cognitive behavioural psychological intervention was a sub-component. Third wave interventions have been defined as therapies which focus on changing the person's relationship with the psychological events (i.e. cognitions and emotion) rather than directly targeting psychological events per se (Hayes et al., 2006). Third wave cognitive behavioural

psychological therapies emphasise issues such as mindfulness, emotions, acceptance, values, goals and metacognition (Hayes and Hofmann, 2017). These can be differentiated from traditional second-wave interventions, which are underpinned by Beck's model of CBT (Beck, 1979, Beck et al., 2008), and primarily target the content and psychological events themselves.

Outcomes

Examination of quality and feasibility of individual studies was explored by examining study design, consent rates, dropout rates, type of therapy offered, modality of therapy, average length of sessions, % of participants who received the full amount of sessions and length of sessions, and type of outcomes chosen to measure change.

The primary outcome was change in positive symptom severity at the end of treatment and at follow-up as this is the primary treatment target for Cognitive behavioural psychological interventions such as CBTp (Wykes et al., 2008). The following secondary outcomes were also examined: adverse events, readmission/rehospitalisation rates, change in total symptom severity in psychosis, negative symptom severity, general psychopathology, self-esteem, depression, suicidality, hopelessness, shame, anxiety, recovery, quality of life, and functioning.

Search Strategy

To examine the evidence base, a comprehensive search was conducted CINAHL, clinicaltrials.gov, PsycInfo, Embase and Medline. The search was conducted in June 2017 and further updated in January 2020. Reference lists of relevant reviews were also hand

searched for any further relevant studies (Paterson et al., 2018, Wykes et al., 2008, Whittington et al., in prep).

The following search terms were used to identify studies from the outlined search engines: [Schiz$ OR psychosis OR psychotic OR Delusions OR Voices OR Hallucination$] AND [Intervention OR Therapy OR Cognitive Therapy OR Behaviour$ Therapy OR Cognitive Behavioural Therapy OR CBT OR CFT OR ACT OR acceptance and commitment therapy OR mindful$ OR compassion focus$ed therapy] AND [inpatient$ OR acute OR crisis OR hospital OR relapse$ OR rehabilitat$ OR ward].

Study Selection and Data Extraction

The identification of studies followed procedures outlined by Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Liberati et al., 2009). Titles and abstract were initially screened for their relevance by LW (20% were cross checked by CW). From this search, potentially relevant studies were identified and full-texts examined (all examined by CW). Eligibility of final studies was determined in a face-to-face meeting by LW and CW.

Data was extracted from identified studies into tables by LW and crosschecked by CW. Study characteristics such as type of intervention, group or one-to one format, duration of treatment, session number, control condition, number of arms of study, diagnosis types, demographics (age, gender, ethnicity), data from each assessment time point (e.g. baseline, post therapy, follow-up points) were recorded.

Risk of Bias

A detailed examination of the risk of bias of studies was undertaken using the GRADE risk of bias tool (Higgins and Green, 2011). Studies were examined on selection bias, performance bias, attrition bias, and selective reporting bias. Quality assessments were carried out by LW and discussed in detail in supervision. 20% of quality assessments were cross checked by CW, no discrepancies were identified.

Analysis

Meta-analysis was conducting using Comprehensive Meta Analysis. A random effects model was adopted for all analyses, which is considered best practice for analysis of psychological therapies due to between study hetereogeneity (Higgins and Green, 2011). For continuous outcomes pooled standardised mean difference (SMD) was calculated with 95% confidence intervals. SMD was utilised in order to pool together means across studies utilising different outcome measures. Cohen's criteria for the interpretation of effects was utilised, 0.2 suggests a small effect, 0.5 a medium effect, and 0.8 for a large effect (Higgins and Green, 2011). Odds ratios and 95% confidence interviews were used for dichotomous outcomes. Efficacy on outcomes was assed post-therapy and at follow-up. Where more than one study timepoint contributed to each follow-up point, they were combined as recommended by Borenstein et al. (2009). Similarly, where studies had multiple subgroup comparisons (e.g. data presented by locality (Tarrier et al., 2004), studies with a shared control group (Lecomte et al., 1999, LeClerc et al., 2000)), all relevant groups were combined (Borenstein et al., 2009). For all outcomes with at least 10 studies contributing, publication bias was explored using the Trim and Fill method (Duval and Tweedie, 2000), as recommended (Borenstein et al., 2009). Hetereogenity was monitored and explored if moderate heterogeneity was over 50% (Borenstein et al., 2009).

Results

Study Selection

Study selection was undertaking following PRISMA guidance (Liberati et al., 2009), as outlined in figure 1. The initial search, after the removal of duplicates identified 1889 studies. After screening at title and abstract, 131 studies were retained for examination at full text. The full-texts were sourced and examined against the review inclusion and exclusion criteria. This led to a total of 16 studies being included from the database searches. Six further studies were identified from the four examined review papers (Paterson et al., 2018, Whittington et al., in prep, Wykes et al., 2008, Jacobsen et al., 2018), and one identified from already included study references. This led to a final 23 published papers being included in the analysis reporting on 18 RCTs (table 1).

[INSERT FIGURE 1 HERE]

[INSERT TABLE 1 HERE]

Risk of Bias

Figure 2 outlines the risk of bias ratings for all studies included within the review. Risk of bias was assessed for the 18 RCTs.

[INSERT FIGURE 2 HERE]

Selection bias refers to the researchers having knowledge or influencing the allocation of participants to treatment groups (Higgins et al., 2011). Selection bias was assessed through examination of random sequence generation and allocation concealment. Examination of

random sequence generation demonstrates that eight RCTs were at low risk, either were at unclear risk, and only two were at high risk due to the majority of studies using a computer-based system to generate random sequences. The large majority of trials (k=15) were at unclear risk of allocation concealment as they did not state who undertook the randomisation procedures. Performance bias refers to the systematic differences between groups in intervention provided (Higgins et al., 2011). Blinding of participants and research staff is an important strategy which minimises performance bias considerably. However, this is near impossible within trials of psychological interventions as participants and therapists will know what therapy is being delivered. As a consequence, all trials (k=18) were at high risk in regarding to blinding of participants. Just under half of trials had managed to blind their outcome assessors from treatment allocation (k=7). Attrition bias refers to withdrawals from the study which leads to incomplete outcome data. Over half of the trials demonstrated low (k=9) or unclear (k=3) risk of attrition bias post therapy or at follow-up, demonstrating that studies were able to engage psychiatric inpatients in a RCT. Finally, reporting bias, which is a bias referring to systematic differences between reported and unreported findings, was examined (Higgins et al., 2011). It was demonstrated that a large proportion of studies had selective reporting bias (k=13). In summary all RCTs had at least one area at high risk of bias, and seventeen RCTs had at least two. One RCT was deemed to be at high risk of bias across all six domains (Gaudiano and Herbert, 2006, Gaudiano et al., 2010). Given the limited number of trials, all trials were retained in the review but finding are tentative and should be interpreted with caution.

Study Intervention Characteristics

Individual study characteristic are outlined in table 1. The 23 included studies reported on 18 RCTs. All but one study (Boden et al., 2016) were able to recruit their target sample

demonstrating that participants who are currently psychiatric inpatients are willing and able to take part in a cognitive behaviourally informed psychological intervention trial within an acute psychiatric inpatient setting. None of the studies described the impact of acute symptoms as a barrier to the delivery of the interventions. The majority of studies were conducted in western countries, with a small number being conducted in Asia.

There was some consistency in the treatment target of therapy. Over half of RCTs (k = 10; 56%) focused on reducing psychotic symptoms as the primary target. Eight (44%) of the interventions focused solely on positive symptom reduction, two (11%) aimed at reducing psychotic symptoms alongside relapse prevention and functioning respectively, one (6%) focused on improving self-esteem, one (6%) focused on crisis management/reduction, two (12%) focused on reducing relapse and rehospitalisation, one (6%) aimed at improving social skills, one (6%) aimed to reduce internalised stigma, and two (12%) did not report its target. As described, only one of the interventions focused on reducing risk or crisis related to a psychiatric inpatient admission, which is arguably the main function of acute psychiatric inpatient care. All studies except one (Jacobsen et al., 2020) utilised a standard therapeutic protocol which was not explicitly described as being adapted to the needs and presentation of psychiatric inpatients (e.g. focusing on the reason for admission, risk reduction, adapting material for acutely unwell populations).

The intervention types varied including both traditional second-wave CBTp interventions and newer third-wave interventions. The most frequently used intervention was CBTp, a therapy which primarily aims to reduce psychotic symptoms through changes in cognitive appraisals of the psychotic experiences, which was utilised by six RCTs (33%). Five (28%) were based on the framework of Acceptance and Commitment Therapy (ACT), which is a therapeutic

model which encourages individuals to accept and experience internal events, such as psychotic symptoms, non-judgmentally (Hayes et al., 2006). Three (17%) utilised Meta Cognitive Therapy (MCT; Moritz & Woodward, 2007), which focuses on modifying common cognitive processes identified in psychosis such as jumping to conclusions, negative attribution biases, and improving memory. Of the remaining interventions, one (6%) utilised a combination of CBT and social skills training, one (6%) utilised CBT within an integrated care model, one (6%) utilised a coping programme, and one (6%) aimed to modify delusional beliefs.

The modality of intervention delivery also varied across RCTs but individual interventions were most dominant. Eleven (61%) were individual interventions, six (33%) utilised group interventions and two (12%) were a mixture of the both. Only one (6%) of the interventions included some involvement of members of the participant's network, e.g. family members (Habib et al., 2015). Seventeen interventions (94%) were solely carried out during inpatient admission, and one (6%) began the intervention during admission but continued following discharge into the community. Sessions offered to participants ranged from 1 to 60 sessions across a treatment window ranging from 2 to 52 weeks. Ten studies (56%) offered brief interventions of eight or less sessions, and remaining studies (k=8; 44%) offered nine and above. All available data demonstrated that session length ranged from 45 to 90 minutes. Sessions were mostly offered at a frequency or one or two per week (k=17, 94%) but one offered flexible sessions with a maximum of one per day (6%; Jacobsen et al., 2020). The time at which therapy started following from admission ranged from 3 to 40 days. Most studies reported some data on session attendance and dropouts which varied across the RCTs. Three studies reported average number of sessions attended which ranged from 6.45 to 11.9. Drop out from the intervention was reported in a variety of ways but overall cognitive

behavioural interventions seemed to be a therapeutic approach that participants were willing to engage in except for in one study where drop out rate was approximately 66% (Boden et al., 2016).

Comparator characteristics: The most common comparator utilised was treatment as usual or routine care, which did not include any psychological intervention (k=10; 56%). Six (33%) RCTs utilised an active control and two (12%) utilised a form of supportive counselling for their control arm.

Meta-analysis of primary and secondary outcomes

A meta-analysis was conducted on available data to examine the efficacy of cognitive behavioural interventions on the primary and secondary outcomes post-therapy and at follow-up, as shown in table 2. A total of 12 trials had useable data for the purposes of a meta-analysis (Aghotor et al., 2010, Bechdolf et al., 2004, Gaudiano and Herbert, 2006, Hall and Tarrier, 2003, Kumar et al., 2010, Lee et al., 2012, Moritz et al., 2011, Schaub et al., 2016, Wood et al., 2018, She et al., 2017, Haddock et al., 1999, Jacobsen et al., 2020). Six trials reported on a second-wave CBTp intervention and the remainder reported on a third wave intervention or a combined intervention (e.g. CBT and social skills training). Outcomes were examined when two or more trials contributed to an outcome.

[INSERT TABLE 2 HERE]

Figures 3 and 4 illustrate the meta-analysis for the primary outcome of positive symptoms post-therapy and at follow-up. A small effect of the cognitive behavioural interventions was found on the primary outcome of positive symptoms post-therapy (mean intervention length=

12.5; range= 8-20) and at follow-up (mean intervention length= 16 range= 12-20) but this was not significant. Heterogeneity was also high for the primary outcome post-therapy (I^2 = 74%). The removal of the one study, which strongly favoured the control and contradicted all other trials (Bechdolf et al., 2004), improved the SMD for positive symptoms leading to an effect at post-therapy (mean intervention length= 12; range= 8-20; SMD = -0.341; LI=-0.616 HI= -0.066; Z = -1.089, p = 0.015) and follow-up (mean intervention length= 16; range= 12-20, SMD = -0.270; LI=-0.520 HI= -0.020; Z=-2.177 p = 0.034). Narrowing the meta-analysis to just focus on trials which specifically aimed to reduce positive symptoms did not produce an effect post-therapy (mean intervention length= 11; range= 8-16; SMD = -0.036; LI=-0.671 HI= -0.598; Z = -0.112, p = 0.910) or at follow-up (mean intervention length= 14; range= 12-16; SMD = -0.136; LI=-0.414, HI= 0.142; Z = -0.9582, p = 0.338).

Sub group analysis demonstrated that RCTs with a treatment as usual control group had a small effect on positive symptoms favouring cognitive behavioural interventions with low heterogeneity (mean intervention length= 11.75; range= 7-20; SMD =-0.418; LI=-0.830 HI= -0.005; Z=-1.986, p = 0.015; Tau^2=0.054 Q(3) =4.122, p=0.249, I^2= 27.214%) and the trials with an active control group did not (mean intervention length= 13.25; range= 8-17; SMD=-0.050; LI=-0.668, HI=0.567, Z=-0.160, p=0.873; Tau^2=0.322, Q(3) =18.732, p=0.000, I^2= 83.984%). Moreover, therapy type (second wave: mean intervention length= 13.75; range= 7-20; SMD =-0.073; LI=-0.772 HI= 0.627; Z=-0.203 p = 0.839; Tau^2 =0.391 Q (3) =17.675, p=0.001, I^2= 83.027% vs. other interventions: mean intervention length= 11.25; range= 8-17; SMD =-0.311; LI=-0.895 HI= 0.054; Z=-1.737, p = 0.082; Tau^2 =0.129, Q(3) =7.174, p=0.067, I^2= 58.185%) did not demonstrate any between group difference post therapy. Subgroup analysis was not conducted at follow-up due to lack of data.

[INSERT FIGURES 3, 4 & 5 HERE]

Secondary outcomes

Secondary analysis was conducted for the outcomes of negative symptoms, general pathology, total symptoms, functioning, depression, anxiety, relapse and readmission (table 2). Other secondary outcomes (self-esteem, hopelessness, shame, quality of life, personal recovery, adverse events, relapse) could not be examined due to insufficient data.

Cognitive behavioural interventions were found to have a small significant effect on total symptoms and functioning post-therapy (mean intervention length= 11.28; range= 4-20 and mean intervention length= 10.75; range= 7-20 respectively) and follow-up (both mean intervention length= 16; range= 12-20), and negative symptoms and readmission at follow-up. Cognitive behavioural interventions were not found to be effective in improving the other secondary outcomes (figures 3 and 4). Heterogeneity was identified as ≤50% for a number of the non-significant secondary outcomes demonstrating that study variability makes the findings difficult to interpret.

Subgroup analysis

Subgroup analysis was conducted examining the impact on control condition (active vs. treatment as usual) and therapy type (second wave vs. others) where data allowed (at least two trials per subgroup). Sub-group analysis demonstrated that control condition did not demonstrate any between group difference post therapy for depression (TAU: SMD =-0.582; LI=-1.242, HI= 0.079; Z=-1.726 p = 0.084; Tau^2 =0.000; Q (1) =0.703, p=0.402, I^2= 0.000% vs. active control: SMD =-0.107; LI=-0.532, HI= 0.318; Z=-0.491, p = 0.623; Tau^2 =0.068,

Q(2) =3.759, p=0.153, I^2= 46.794) and anxiety (TAU: SMD =0.301; LI=-1.536, HI= 2.137; Z=0.321, p = 0.748; Tau^2 =1.513; Q (1) =7.221, p=0.007, I^2= 86.152% vs. active control: SMD =-0.178; LI=-0.639, HI= 0.282; Z=-0.759, p = 0.623; Tau^2 =0.063, Q(1) =2.134, p=0.144, I^2= 53.132%). However control condition did impact on the outcomes for negative symptoms (TAU: SMD =-0.320; LI=-0.592 HI= 0.048; Z=-2.304 p = 0.021; Tau^2 =0.000; Q (3) =2.769, p=0.429, I^2= 0.000% vs. active control: SMD =-0.181; LI=-0.471 HI= 0.109; Z=-1.255, p = 0.166; Tau^2 =0.068, Q(1) =2.812, p=0.094, I^2= 64.434%) and total symptoms (TAU: SMD =-0.348; LI=-0.653 HI= -0.043; Z=-2.234 p = 0.025; Tau^2 =0.015; Q (3) =3.427, p=0.330, I^2= 12.467% vs. active control: SMD =-0.181; LI=-0.471 HI= 0.109; Z=-1.255, p = 0.166; Tau^2 =0.023; Q (3) =3.777, p=0.287, I^2= 20.576%) with TAU controls trials having an effect favouring the cognitive behavioural intervention.

Therapy type was also explored and no difference between groups were identified post therapy for the majority of outcomes negative symptoms type (second wave: SMD =-0.156; LI=-0.622 HI= 0.310; Z=--0.656 p = 0.512; Tau^2 =0.128 Q (3) =17.950, p=0.047, I^2= 62.267% vs. other interventions: SMD =-0.181; LI=-0.471 HI= 0.109; Z=-1.255, p = 0.166; Tau^2 =0.000, Q(1) =0.040, p=0.842, I^2= 0.000%); functioning (second wave: SMD =-0.454; LI=-0.953 HI= 0.045; Z=-1.782 p = 0.075; Tau^2 =0.057 Q (1) =1.412, p=0.235, I^2= 29.183% vs. other interventions: SMD =-0.213; LI=-0.493 HI= 0.067; Z=-1.492, p = 0.136; Tau^2 =0.000, Q(1) =0.075, p=0.785, I^2= 0.000%); depression (second wave: SMD =-0.254; LI=-0.942 HI= 0.434; Z=-0.723 p = 0.470; Tau^2 =0.397 Q (2) =3.484, p=0.175, I^2= 42.596% vs. other interventions: SMD =-0.221; LI=-0.756, HI= 0.314; Z=-0.810, p = 0.418; Tau^2 =0.099, Q(1) =2.773, p=0.096, I^2= 63.932%); anxiety (second wave: SMD =0.301; LI=-1.536, HI= 2.137; Z=0.321 p = 0.748; Tau^2 =1.513, Q (1) =7.221, p=0.007, I^2= 86.512% vs. other interventions: SMD =-0.178; LI=-0.639, HI= 0.282; Z=-0.759, p = 0.448; Tau^2 =0.063, Q(1)

=2.134, p=0.144, I^2= 53.132%). However, the other interventions (e.g. third wave) were found more effective for total symptoms than second wave interventions (second wave: SMD =-0.207; LI=-0.742, HI= 0.328; Z=--0.758 p = 0.448; Tau^2 =0.155 Q (3) =6.446, p=0.092, I^2= 53.457% vs. other interventions: SMD =-0.276; LI=-0.510 HI= -0.041; Z=-2.299, p = 0.022; Tau^2 =0.000, Q(3) =1.201, p=0.753, I^2= 0.000%). Therapy type could not be compared at follow-up as there was inadequate data for analysis.

Discussion

This study aimed to conduct a systematic review and meta-analysis to examine the types, quality, and effectiveness of cognitive behavioural psychological interventions carried out in a psychiatric inpatient setting. A total of 23 studies were identified which examined 18 cognitive behavioural psychological interventions. Overall the studies demonstrated high risk of performance bias and selective reporting bias, but were most low in bias in the other three domains (selection bias, detection bias and attrition bias). Second-wave CBTp was the dominant intervention being utilised in the psychiatric inpatient setting followed by MCT, ACT and social skills based interventions. The interventions were diverse and varied greatly in therapeutic approach, session length, duration, and modality, also captured by the moderate hetereogeneity present within the meta-analysis.

The meta-analysis demonstrated that cognitive behavioural psychological interventions had a small effect on positive symptoms but only after the one conflicting study which favoured control was removed. Moreover, there was high hetereogeneity post-therapy and at follow-up. A small effect in reducing total symptoms (positive, negative and general psychopathology) (post therapy and follow-up), functioning (post-therapy but with high reported hetereogeneity) and depression (follow-up) was identified. The review has demonstrated that it is possible and feasible to undertake a RCT examining a cognitive behavioural psychological intervention with psychiatric inpatients. Although data was not reported in all trials, data which was available suggested that patients were willing to engage and undertake a cognitive behavioural psychological intervention within the acute psychiatric inpatient setting, as measured by low dropout rates from the trials.

Subgroup analysis demonstrated that therapy type (second vs third wave) and control condition did impact on findings for some outcomes. For the outcome of total symptoms, third wave interventions were favoured over second wave interventions, however for all other outcomes there was no identified difference. For the subgroup analysis examining control conditions, generally speaking, the TAU control arm trials found effects favouring cognitive behavioural interventions whereas trials with an active control arm did not identify any differences between conditions. Additionally, given the outcomes in which an effect was identified (negative symptoms, total symptoms, and functioning) are outcomes often improved through having therapeutic support broadly, it may not be possible to be conclude that cognitive behavioural interventions specifically are helpful. However, given the quality of the included studies and their lack of specificity it is very difficult to draw any firm conclusions about the specific effectiveness of the cognitive behavioural interventions.

The vast majority of interventions examined in the review focused on symptom reduction as the primary aim of their intervention. The review demonstrated that only one intervention focused on crisis reduction as their primary target of therapy (Jacobsen et al., 2020), and only two focused on preventing rehospitalisation (Bach and Hayes, 2002, She et al., 2017), which are arguably the primary foci of psychiatric inpatient treatment. High risk crisis presentations, risk to self or others, are one of the primary reason patients are admitted to psychiatric inpatient wards (Schromerus et al., 2015). As a consequence, reduction of admission triggers, such as risk reduction (e.g. reducing self-harm, suicidality and psychiatric symptoms which are maintaining risk), increasing a patient's safety, and reducing the likelihood of readmission, should be the primary foci of a psychiatric inpatient admission (Bowers et al., 2009). However, very few studies to date have explicitly explored this as the primary aim of their interventions. Moreover, the primary outcome of symptom reduction

utilised within the RCTs may not be appropriate to examine the efficacy of cognitive behavioural psychological interventions in psychiatric inpatient settings, and risk or crisis measures may be more suitable. It appears imperative for psychiatric inpatient cognitive behavioural psychological interventions to incorporate common admission risk triggers as a primary target if working with patients experiencing psychosis and in acute crisis, and utilised risk measures to measure the efficacy of interventions.

Only one of the included studies (Jacobsen et al., 2020) explicitly identified changes made to their cognitive behavioural psychological intervention protocol for adaptation to the psychiatric inpatient setting. As outlined in the introduction, psychiatric inpatient therapeutic interventions should involve competencies such as engaging the MDT and family in the therapeutic process, and be offered flexibly. Only one study included in the review demonstrated involvement of the patient's network in the intervention (Habib et al., 2015). Psychiatric inpatients regularly outline the importance of the inclusion of their network within the care offered during a psychiatric inpatient admission (Wood et al., 2019). A recent systematic review and thematic synthesis reported that patients felt that they or their families were not involved enough in their care highlighting the importance of incorporating this in any psychiatric inpatient intervention (Wood & Alsawy, 2016). Moreover none of the studies mentioned involvement with the multi-disciplinary team (MDT) regarding the implementation of the psychological intervention. It is widely documented that the inclusion of the psychiatric inpatient MDT is crucial to the success of any care planning or therapeutic intervention (Royal College of Psychiatrists, 2010). MDT inclusion may be crucial to the success of a cognitive behavioural psychological intervention in this setting.

The review demonstrated that second and third wave intervention trials were deliverable within the psychiatric inpatient setting. However, the majority of research available has either been conducted outside of the UK, a number of years ago, or within inpatient contexts which are not reflective of the current UK psychiatric inpatient context. Only three studies in the review examined the use of a brief intervention conducted within the current acute psychiatric inpatient context (Tyrberg et al., 2017, Wood et al., 2018, Jacobsen et al., 2020). As outlined, the current psychiatric inpatient context incorporates brief admissions of an average of four weeks, complex presentation, and high risk (to self and other) (The Kings Fund, 2017). Therefore, there is a requirement for future research trials to examine the efficacy of cognitive behavioural psychological interventions adapted to this current context.

There are a number of strengths to this review. It is the first systematic review and meta-analysis which has specifically examined the efficacy of cognitive behavioural psychological interventions for psychiatric inpatients with psychosis, an under researched area. It has followed robust guidance by PRISMA (Liberati et al., 2009), ensuring that bias in this review is minimal.

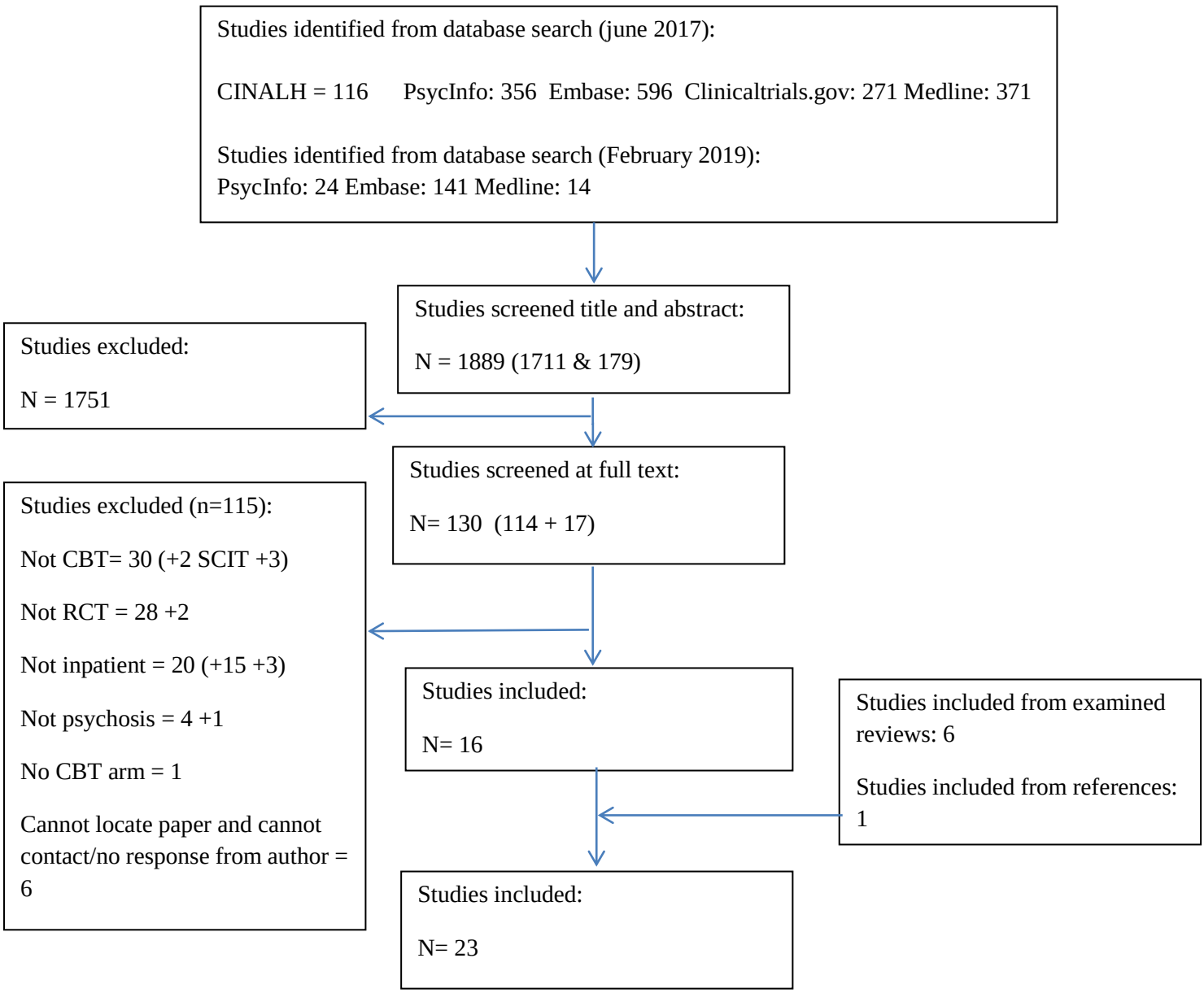
A limitation to the review was that the search strategy failed to identify seven RCTs, which were identified from the reference list of other review articles. This was because a number of cognitive behavioural psychological intervention RCTs utilised inpatient samples but do not explicitly describe this in their abstract or key words section, which meant they were not identifiable in our search strategy. Future inpatient research should ensure the sample population is clearly identified in their title, key words and abstract. A further limitation of the review is the moderate quality and high heterogeneity identified in the included RCTs. The studies included varied quite considerably in content, modality, and in length. Therefore,

findings from this review can only be interpreted tentatively. For example, some studies offered brief manualised interventions over 4 weeks whereas some offered extensive psychological input over 12 months. Moreover, there was a paucity of RCTs which prevented the examination of such factors through further subgroup analyses. In addition, the included studies had different targets for their intervention varying from positive symptoms to social skills, with some not explicitly identifying the target of their intervention at all. This means that not all included studies focused on reducing positive psychotic symptoms and therefore would not necessarily expect them to have a significant impact on this outcome which was the primary outcome for the review. However, positive psychotic symptoms was chosen as the primary outcome due to it being the most commonly used primary outcome in psychological therapy trials literature (Wykes et al., 2008, Van der Gaag et al., 2014). A final limitation is the multiple testing conducted on data through the sub-group analysis. Although the Cochrane handbook does not suggest any adjustments (Higgins et al., 2011), it is important that results are tentatively interpreted.

In summary, the results of this review demonstrate a small effect for cognitive behavioural psychological interventions on improving positive symptoms, negative symptoms, total symptoms (positive symptoms, negative symptoms and general psychopathology collectively), and functioning in people with psychosis who are also psychiatric inpatients. The majority of studies did not explicitly adapted their intervention for acute psychiatric inpatients, and outcomes of symptomatology may not be appropriate to examine change in the inpatient population. There is a need to adapt cognitive behavioural psychological interventions trials to meet the specific needs of psychiatric inpatients and improve their effectiveness with this population. Further definitive trials of cognitive behavioural

psychological interventions, which have been adapted for its use with psychiatric inpatients, are warranted.

Figure 1 – PRISMA diagram of study inclusion



Trial	Treatment	Therapy target	No of sessions offered	Frequency	Treatment window	Treatment commencement	Modality	Number randomised	Follow-ups	Country	Baseline characteristics			
											Age	**Gender (% male)**	**% psychosis**	**Session attendance**
Aghotor2010	MCT	Positive symptoms	8 1hr	2/wk	4 weeks	NR	Group	16	1	Germany	28.9 (8.3)	12/16	100	13/16 did not miss one session
	NRG		4 1hr	1/wk			Group	14			26.3 (3.6)	8/6	100	9/14 did not miss one session
Bach2002 (Bach2012; Bach2013)*	ACT	Rehospitalisation	4 45-50m	2/wk	2 weeks	72 hours after consent	Individual	40	4, 24	USA	39.2	27/40	100	NR
	TAU							40			39.5	24/40	100	
Bechdolf2004 (Bechdolf2005; Bechdolf2010) *	CBT	Positive symptoms	16 60-90m	2/wk	8 weeks	14 days admission	Group	40	2, 6, 24	Germany	32.2 (9.9)	18/40	100	Average 11.9(4.1)
	PE		8 60-90m	1/wk	8 weeks		Group	48			31.4 (10.6)	22/48	100	6.4(1.8)
Boden (2016)	ACT	NR	4 1-hr (standalone)	NR	NR	NR	Individual	12	NR	USA	53.4 (17.5)	18/18	100	2.8 (1.6) session attendance
	TAU							6						
Gaudiano2006 (Gaudiano, 2010)*	ACT	Positive symptom & rehospitalisation	4 1-hr (standalone)	NR	NR	NR	Individual	19	4, 12		**40 (10)**	**64% male**	**100**	NR
	ETAU		15m daily					21						
Habib2015	CA-CBT	Positive symptoms	16 1-hr	2/wk	4-6 months	NR	Individual plus family sessions	21	6	Pakistan	21 (10.5)	11/21	100	NR
	TAU							21			21 (6.7)	14/21	100	
Haddock1999	CBT	Positive symptoms	10.2 (5.1)		5 weeks	10 working days	Individual	10	4	UK	28.1 (7.24)	9/9	100	1withdrew after 3 sessions
	SC		9.1 (4.36)				Individual	11			30.0 (7.9)	9/11	100	
Hall2003	CBT	Low self-esteem	7 1-hr	1/wk	NR	NR	Individual	12		UK	**38 (9.97)**	**12/25**	**100**	NR
	TAU							13						
Jacobsen2020	MCBI	Crisis management/ reduction	Up to 5 (standalone)	Ad hoc	During admission	NR	Individual	26	6, 12	UK	35	17/26	100	3 (1-5)
	SAT							24			33			
Klingberg2001	CBT	Positive symptoms	40 inpatient, 20 outpatient	4/wk	8 week stabilisation, 1 year outpatient care		Individual and group	63	Post-therapy	Germany	33.1 (9.7)	49%	100	NR
	ST							61						

Kumar2010	MCT	Positive symptoms	8 1-hr	2/wk	4 weeks	14 days	Group	8		India	31.50 (7.98)	8/8	100	NR
	TAU							8			34.13 (8.20)	8/8	100	
Lee2012	CBSST	Social skills	12			NR	Individual	12 (4 drop out)		Korea	51.76 (5.4)	3/8	100	NR
	TAU							13 (1 drop out)			52.67 (6.1)	5/12		
Milton1978	BM	Delusions	5 1hr	NR	NR	NR	Individual	8		UK	NR	NR	100	NR
	C		5 1hr					8						
Moritz 2011	MCT	NR	9 45-60m group & 8 1:1		4 weeks	NR	Individual & Group	24		Germany	32.63 (12.48)	17/24	100	NR
	CogPack		8				Individual	24			35.46 (9.10)	14/10	100	
Schaub 2016	COP	Psychotic symptoms functioning	12 75m (6.45)	1-2/wk	8 weeks	40.7 (30.7) days	Group (6-10)	100		Germany	**33.6 (11.3)**	**104/196**	100	At least 6 sessions of COP (72%)
	SUP		12 75m	1-2/wk	8 weeks			96					100	
She 2017	IC	Clinical Relapse	20 45m	1-2/wk	12-weeks	NR	Group	86		China	31.27 (8.02)	51/86	100	NR
	MA							84			33.45 (8.49)	56/84	100	NR
Tyrberg 2017	ACT	NR	Up to 4 45m	NR	4 months	NR	Individual	12		Sweden	42.5 (13.4)	5/11	100	NR
	TAU							10			39 (11)	8/10	100	
Wood2017	CBT	Internalised stigma	2 1hr	1/wk	2 weeks	NR	Individual	15		UK			100	2
	PE		2 1hr	1/wk	2 weeks		Individual	15						2

AYT – Activity to provide informal support, BM – Belief Modification, C- Confrontation, CA-CBT – Culturally Adapted Cognitive Behavioural Therapy, CBT – Cognitive Behavioural Therapy, COP – Coping Oriented Program, CSM – Coping Skills Module, ETAU – Enhanced Treatment as Usual, IC – Integrated Care, MA – Medication Alone, MCT – Metacognitive Therapy, NR – Not Reported, NRG – Newspaper Reading Group, NS – Not specified, PE – psychoeducation, RC – Routine Care, SAT – Social Activity Therapy, SC – Supportive Counselling, SCIT – Social Cognition and Interaction Training, ST – Standard Treatment, SUP – Supportive Therapy Program, UK – United Kingdom, USA – United States of America, * used the same control group.

Figure 2 – Assessment of Risk of Bias

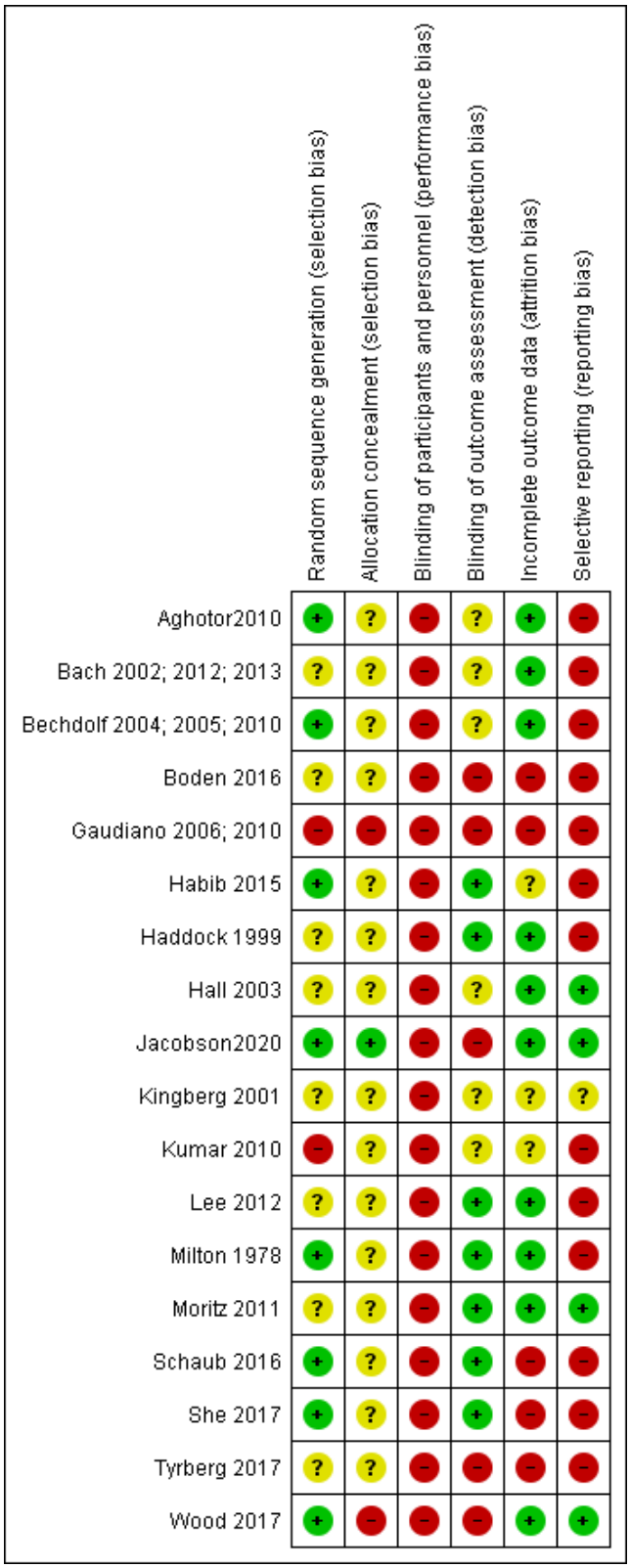


Table 3 – Meta-analysis of primary and secondary outcomes

Outcome	Time point	Study N	Sample N	Statistical Method	Effect Size	CI	Z	P	Heterogeneity statistics
Primary outcome:									
Positive symptoms	ET	8	535	SMD	-0.238	LI: -0.624; HI: 0.148	-1.209	0.227	Tau^2=0.200; Q (7)=26.995, p=0.000; I^2=74.069%
	FU (12 mo)	3	319		-0.201	LI: -0.421; HI: 0.020	-1.782	0.075	Tau^2=0.000; Q (2)=1.433, p=0.488; I^2=0.000%
Secondary outcomes:									
Negative symptoms	ET	6	461	SMD	-0.155	LI: -0.421; HI: 0.111	-1.145	0.252	Tau^2=0.038; Q (5)=8.024, p=0.155; I^2=37.687%
	FU (12 mo)	3	319		**-0.249**	**LI: -0.470; HI: -0.028**	**-2.204***	**0.027**	**Tau^2=0.000; Q (2)=1.980, p=0.372; I^2=0.000%**
General psychopathology	ET	4	273	SMD	0.034	LI: -0.728; HI: 0.795	0.087	0.931	Tau^2=0.476; Q (3)=20.086, p=0.000; I^2=85.064%
	FU(12 mo)	2	189		-0.022	LI: -0.809; HI: 0.766	-0.054	0.957	Tau^2=0.277; Q (1)=6.944, p=0.008; I^2=85.599%
Total Symptoms	ET	8	499	SMD	**-0.252**	**LI: -0.449; HI: -0.055**	**-2.502***	**0.012**	**Tau^2=0.009; Q (7)=7.796, p=0.351; I^2=10.208%**
	FU (12mo)	2	248		**-0.530**	**LI: -0.784 HI: -0.277**	**-4.098***	**0.000**	**Tau^2=0.000; Q (1)=0.269, p=0.604; I^2=0.000%**
Functioning	ET	4	374	SMD	**-0.291**	**LI: -0.496; HI -0.087**	**-2.794***	**0.005**	**Tau^2=0.000; Q (3)=2.124, p=0.547; I^2=0.000%**
	FU	2	248		**-0.482**	**LI: -0.800; HI -0.164**	**-2.973***	**0.003**	**Tau^2=0.019; Q (1)=1.575, p=0.209; I^2=36.512%**
Depression	ET	5	275	SMD	-0.219	LI: -0.582; HI: 0.144	-1.181	0.238	Tau^2=0.063; Q (4)=6.410, p=0.171; I^2=37.599%
	FU (12mo)	2	171		-0.275	LI: -1.054; HI: 0.504	-0.692	0.489	Tau^2=0.254; Q (1)=4.907, p=0.027; I^2=79.619%

Anxiety	ET	4	275	SMD	-0.036	LI: -0.621; HI: 0.549	-0.122	0.903	Tau^2=0.233; Q (3)=10.096, p=0.018; I^2=70.284%
	FU (12mo)	2	171		-0.433	LI: -0.934; HI: 0.067	-1.696	0.090	Tau^2=0.073; Q (1)=2.125, p=0.145; I^2=52.938%
Readmission	FU	4	228	OR	0.47	LI: 0.24 ; HI: 0.92	2.22	0.03	Q (2)=3.07, p=0.38; I^2=2%

ET-End of Treatment, FU – Follow-up, OR – Odds ratio, SMD – Standardised Mean Difference

Figure 3 – Effect of CBTp on positive symptoms end of therapy

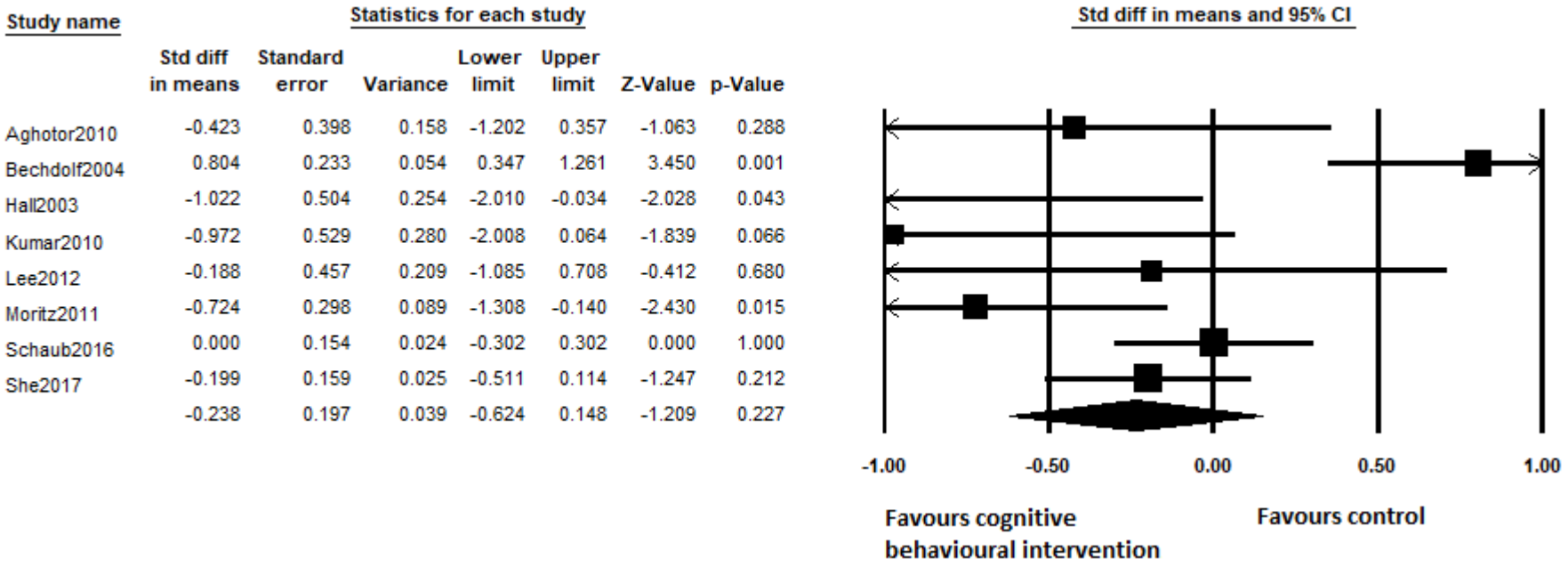
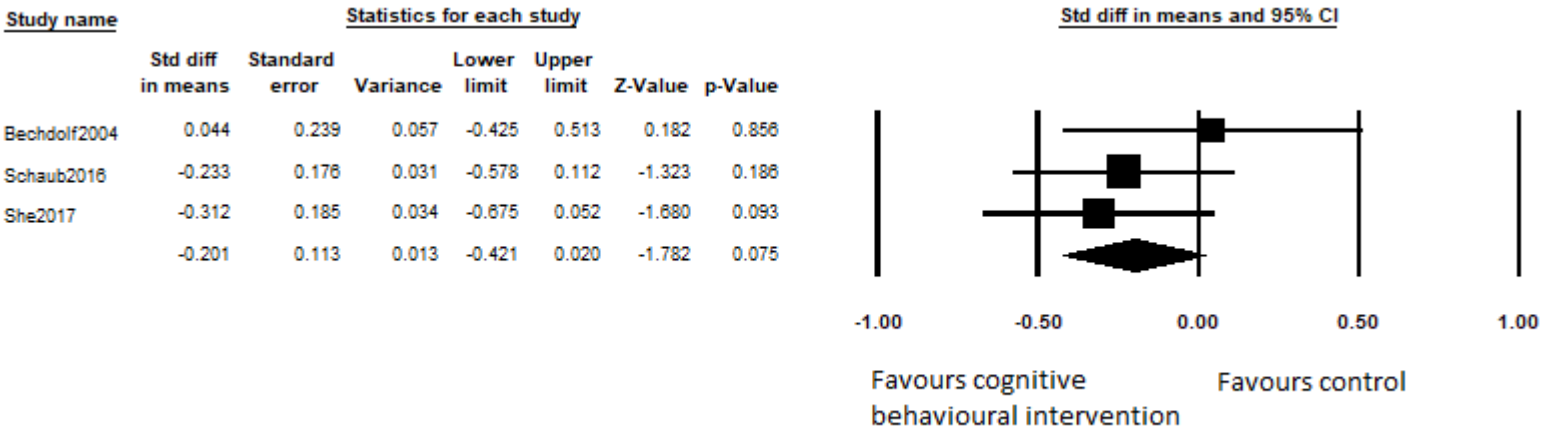


Figure 4 – Effect of CBTp on positive symptoms at follow-up



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