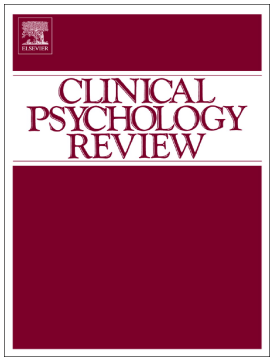

Psychological interventions for acute psychiatric inpatients with schizophrenia-spectrum disorders: A systematic review and meta-analysis

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Psychological interventions for acute psychiatric inpatients with schizophrenia-spectrum disorders: A systematic review and meta-analysis

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Abstract

Background. Acute inpatient psychiatric wards are important yet challenging environments in which to implement psychological interventions for people with schizophrenia-spectrum disorders. No meta-analysis to date has evaluated whether psychological interventions are effective in this context.

Methods. We systematically searched Embase, Medline and PsycInfo databases for randomised controlled trials (RCTs) of psychological interventions implemented in acute inpatient psychiatric settings with individuals with schizophrenia-spectrum disorders. We conducted random effects meta-analyses of between-groups outcomes at post-intervention and relapse/re-hospitalisation rates by follow-up.

Results. Twenty-nine trials were suitable for meta-analysis. Psychological interventions improved post-intervention positive symptoms, social functioning and treatment compliance and reduced the risk of relapse/ re-hospitalisation, relative to control conditions. Analyses of specific intervention effects found positive effects of psychoeducation on several key outcomes (power > 80%) and preliminary evidence for positive effects of acceptance and commitment therapy (ACT), cognitive behaviour therapy (CBT) and metacognitive training (MCT) on some outcomes (power < 80%).

Conclusion. Psychological interventions can be helpful for acute inpatients with schizophrenia-spectrum disorders. However, risk of bias was often high or unclear, and some analyses were underpowered. Further research should use more rigorous RCT designs and publish meta-analysable data on positive symptoms, general psychopathology, relapse/ re-hospitalisation, social functioning and treatment compliance.

Schizophrenia; Psychotherapy; Inpatients; Randomised Controlled Trial

Psychological interventions for acute psychiatric inpatients with schizophrenia-spectrum disorders: A systematic review and meta-analysis

Acute inpatient psychiatric wards offer treatment to individuals experiencing mental health crises that cannot be safely managed in the community (The Commission to Review the Provision of Acute Psychiatric Care for Adults, 2015). In the USA and Europe, between 3 and 37% of inpatients are admitted involuntarily under legal compulsion, as they are deemed by mental health professionals to pose an unacceptable level of risk to self, others or both (Salize, Dressing, & Peitz, 2002; Substance Abuse and Mental Health Services Administration, 2016). Acute inpatient psychiatric wards have been criticised as overly focussed on risk management and the medical model, with patients primarily treated using medication rather than psychological interventions (McCulloch, Ryrie, Williamson, & St John, 2005; Slemon, Jenkins, & Bungay, 2017). Investigations of nursing activity have found that although nursing staff spend up to 50% of their time in contact with inpatients, just 4-20% of this time is used to provide therapeutic interventions (Sharac et al., 2010), with the majority of their time focussed on dispensing medication, attending to physical health needs and resolving social problems such as access to housing or welfare payments (Lloyd-Evans, 2010). This is despite a recent UK Care Quality Commission survey (Care Quality Commission, 2009) which showed that half of psychiatric inpatients would like access to psychological therapy. Similarly, the Commission on Acute Adult Psychiatric Care found that UK inpatients and carers desire a wider range of therapies to be made available, including psychological therapies (Crisp, Smith, & Nicholson, 2016). The report emphasised the need for acute mental health services to "deliver a full range of evidence-based biopsychosocial and physical interventions which focus on the patient's recovery" (p. 57).

This shortfall in provision of psychological therapy may stem from a number of factors which make the acute inpatient psychiatric ward a particularly difficult environment

in which to deliver psychological interventions. A major challenge stems from the typically very brief duration of inpatient stays, ranging from 4 to 11 days in the USA depending on diagnosis (Substance Abuse and Mental Health Services Administration, 2016), and slightly longer but still brief in European countries, ranging from 13 to 52 days (Salize et al., 2002). This allows very little time to build a therapeutic relationship, develop an understanding of the inpatient's psychological difficulties, or conduct therapy sessions (Clarke & Wilson, 2009; Leibenluft, Tasman, & Green, 1993; Sayles, Ayoub, & van Schalkwyk, 2019). Additionally, high levels of emotional exhaustion and 'burnout' are reported by psychiatric inpatient staff (Jenkins & Elliott, 2004), contributed to by staff shortages and by pressure to release beds and tackle administrative duties whilst handling inpatient crises involving high levels of risk (Bowers et al., 2005; Campbell, 2016; Crisp et al., 2016; Killaspy, 2006; Quirk, Lelliott, & Seale, 2004). This may lead staff to deprioritise psychological work and to feel that they lack the time and emotional energy to deliver psychological interventions.

A further important consideration in delivering psychological interventions in the acute inpatient setting is that individuals experiencing acute mental health crises may find it difficult to engage with traditional psychotherapy (Bowers, 2005; Clarke & Wilson, 2009; Quirk & Lelliot, 2001). In particular, across the UK, USA, Europe and New Zealand, between 28 and 44% of acute mental health inpatients are diagnosed with a schizophrenia-spectrum disorder, and patients with this diagnosis have a two-fold increase in the odds of involuntary rather than voluntary hospitalisation, relative to patients with other psychiatric disorders (Newman, Harris, Evans, & Beck, 2018; Preti et al., 2009; Saba, Levit, & Elixhauser, 2008; Walker et al., 2019; Wheeler, Robinson, & Robinson, 2005). Psychotherapy may present particular challenges for individuals experiencing acute exacerbation of psychotic symptoms, as paranoid delusional ideation may make it very difficult for the patient to develop trusting therapeutic relationships, whilst increased

preoccupation with hallucinatory and delusional content, with a concomitant increase in the cognitive and attentional deficits characteristic of schizophrenia, may make it very difficult for the patient to concentrate on what the therapist is saying, to process and retain information, or to communicate coherently (Freeman & Garety, 2006; Park, Püschel, Sauter, Rentsch, & Hell, 2002; Roth & Pilling, 2013; Sharp, Gulati, Barker, & Barnicot, 2018). Additionally, there is concern that conducting psychotherapy with acutely unwell individuals experiencing high levels of emotional arousal can in some cases worsen rather than relieve emotional distress (Moos, 2012). Whilst it is now increasingly recognised that certain psychological treatments can be effective in this patient group (Hazell, Hayward, Cavanagh, & Strauss, 2016; Pilling et al., 2002) and it is recommended that interventions such as cognitive behaviour therapy for psychosis and family therapy should be implemented both in acute inpatient and community settings (National Institute for Health and Care Excellence, 2014), such interventions have usually been developed for use in outpatient settings and it is unclear how effective they are when delivered to inpatients.

Our systematic search has identified no prior meta-analytic synthesis of the evidence on the effectiveness of psychological interventions for schizophrenia-spectrum disorders in acute mental health care settings. We have identified only one meta-analysis of psychological interventions in acute inpatient settings, which pooled data across diagnostic groups, and concluded that psychological interventions may be helpful in this context (Paterson et al., 2018). However, this analysis was limited by merging of data across randomised controlled trials (RCTs) and non-RCTs, across multiple types of interventions and across multiple diagnostic groups, potentially leading to biased or misleading effect estimates and contrary to Cochrane Collaboration guidance (Deeks, Higgins, & Altman, 2011; Reeves, Deeks, Higgins, & Wells, 2011), as well as prohibiting evaluation of which specific interventions are effective for which groups of patients.

Our systematic review and meta-analysis therefore aimed to answer the following question: For people with schizophrenia-spectrum disorders who are treated in acute psychiatric inpatient mental health settings, are psychological interventions effective for improving patients' mental health and social outcomes?

Methods

Design

A systematic review and meta-analysis of the effectiveness of psychological interventions for people with schizophrenia-spectrum disorders treated in acute adult inpatient psychiatric settings.

Study Inclusion Criteria

Randomised controlled trials in which the authors evaluated the implementation of a psychological intervention in an adult acute psychiatric inpatient ward were eligible for inclusion in the review, if:

1) The "psychological intervention" conformed to the following definition given by the American Psychological Association: "the informed and intentional application of clinical methods and interpersonal stances derived from established psychological principles for the purpose of assisting people to modify their behaviors, cognitions, emotions, and/or other personal characteristics in directions that the participants deem desirable." (American Psychological Association, 2013). Computer-mediated interventions, which are inherently minimally interpersonal, were included if they fulfilled the rest of these criteria. Non-directive interventions were not considered to meet this definition.

2) The "acute psychiatric inpatient ward" conformed to the following definition: A hospital ward specialising in treating patients experiencing an acute exacerbation of mental illness, on an inpatient basis, and typically with a short length of stay (< 90 days). The length

of stay criterion was based on data showing that in the UK, 90% of acute inpatient stays are shorter than 90 days (Thompson et al., 2004).

3) One hundred percent of the sample met diagnostic criteria for a schizophrenia-spectrum disorders as encompassed by category F2 Schizophrenia spectrum and other primary psychotic disorders (schizophrenia, schizoaffective disorder, delusional disorder, schizophreniform disorder, brief psychotic disorder, psychosis associated with substance use or medical conditions) in ICD-11 (World Health Organization, 2018).

4) The authors presented outcome data on any outcome relevant to patients' mental health or social functioning, including general psychopathology, psychotic symptoms, re-hospitalisation, relapse, depression, anxiety, hopelessness, social functioning, cognitive functioning, illness insight, medication adherence, and episodes of self-harm, violence, physical restraint, and seclusion.

5) The control condition consisted of treatment-as-usual (TAU) alone, a non-psychological intervention, a non-directive psychological intervention or a psychological intervention.

Both English and non-English language papers were included.

Study Exclusion Criteria

Studies were excluded from the review if: 1) The setting was a specialist residential facility for treating specific disorders (e.g., substance misuse or eating disorders) or a forensic facility; 2) The participants were predominantly adolescents (aged under 18 years) or older adults (aged 65 years or older); 3) The intervention applied was exclusively pharmacological or biological; 4) The intervention applied was predominantly non-verbal; for example, art therapy or music therapy; 5) The study was published only as a conference abstract; 6) The study was not published in a peer-reviewed journal.

Search Strategy

The databases Embase, PsycInfo and Medline were searched in June 2015, and updated searches were performed in January 2016, August 2018 and October 2019, using a combination of article title and abstract search terms describing the study setting ("inpatient" or "hosp*"), the patient group ("psychiatr*" or "mental"), and the intervention ("psycho*" or "therap*" or "train*" or "group*" or "interven*"). The updated searches in August 2018 and October 2019 also included an additional set of search terms describing the acute nature of the inpatient setting ("acute" or "brief" or "short"). In addition, the reference lists of included studies were searched in order to identify any additional eligible studies.

Study Screening and Selection

Following identification and removal of duplicate search results, article titles were screened, and the abstracts and full texts of potentially eligible studies were then screened independently by two review authors in order to determine whether each met the review inclusion or exclusion criteria, using a standardised inclusion and exclusion criteria spreadsheet. Non-English language papers were translated by native or fluent speakers of the publication language. Any disagreements regarding eligibility were then resolved through discussion between the review authors. Where the full texts were not available, or where the information needed to determine study eligibility was not present in the publication, the authors of the publication were contacted and asked to provide this.

Data Synthesis and Meta-Analysis

Additional information on study characteristics and outcome data were extracted from the included studies by authors CM and ET using a standardised extraction spreadsheet. Meta-analysis was conducted for outcomes for which meta-analysable data was reported in at least five RCTs, increasing the likelihood of sufficient statistical power to detect treatment effects (Jackson & Turner, 2017). The eligible outcome variables were general psychopathology, positive symptoms of schizophrenia, relapse/ re-hospitalisation, social

functioning and treatment compliance. The metan command in STATA was used to conduct random effects meta-analysis. This computes risk ratios (RRs) for dichotomous outcomes and Cohen's standardised mean differences (SMDs) for continuous outcomes. Where a scale measuring an outcome differed in directionality from those used in other studies, mean scores for this scale were multiplied by -1, as recommended by the Cochrane Collaboration (Deeks et al., 2011). In instances where some studies presented only absolute scores and others only change scores, these were combined as unstandardised weighted mean differences (WMDs) (Deeks et al., 2011). In instances where studies had not published post-intervention means/standard deviations, the study authors were contacted to request this data. First, data was pooled across all intervention types, and the effect of any psychological intervention, relative to the control condition, was analysed. Next, subgroup analysis by type of control condition (treatment-as-usual alone, or an alternative intervention), was conducted. Finally, separate meta-analyses for each type of psychological intervention were conducted. For each analysis, the percentage of the variance in an effect estimate due to heterogeneity across studies rather than sampling error was estimated using the I^2 statistic (Deeks et al., 2011). Additionally, for each analysis where the outcome variable was a continuous measure, a power calculator for random effects meta-analysis was used to determine statistical power to detect small (SMD = 0.2), medium (SMD = 0.5) or large (SMD = 0.8) effects at small, medium and high levels of between-study heterogeneity and at alpha = .05 (Quintana & Tiebel, 2018; Valentine et al., 2010). For dichotomous risk ratio data, trial sequential analysis software was used to determine whether the total sample size had less than or over 80% power to detect a medium effect (RR = 0.5) at medium heterogeneity at alpha = .05 (Thorlund et al., 2017). For both types of outcome, where power was under 80%, the number of additional participants required to detect a medium effect at medium heterogeneity at alpha = .05 at 80% power was calculated (Exact power is not provided by this software). Finally,

narrative synthesis was used to summarise the findings of included RCTs that did not provide data suitable for meta-analysis.

The Cochrane Collaboration's Tool for Assessing Risk of Bias (Higgins, Altman, & Sterne, 2011) was used to assess risk of bias in individual studies. For the two outcomes for which the largest number of RCTs provided data for meta-analysis – general psychopathology and relapse/ re-hospitalisation – Egger's test was conducted and a funnel plot constructed in order to evaluate the potential presence of publication bias, pooling data across intervention types.

Results

The numbers of potentially eligible articles identified at each stage of the review process are shown in Figure 1. Thirty-four eligible studies were identified as suitable for narrative synthesis. Thirty were in English language, two in German, and two in Mandarin. Within the eligible studies, nine types of psychological intervention were evaluated: acceptance and commitment therapy, cognitive behaviour therapy, cognitive remediation therapy, eye movement and desensitisation reprocessing therapy, interpersonal psychotherapy, metacognitive training, motivational interventions, psychoeducation and social skills training. Five outcomes were evaluated in at least five trials: general psychopathology, positive symptoms of schizophrenia, relapse/ re-hospitalisation, social functioning and treatment compliance. Twenty-nine trials published or provided upon request post-intervention means and standard deviations for at least one of these outcomes. The authors of ten studies who collected but did not publish meta-analysable data on one or more of these outcomes were contacted, and two provided data (Pitschel-Walz et al., 2006; 2013).

Using the Cochrane Collaboration's Tool for Assessing Risk of Bias (Higgins et al., 2011), the method of randomisation was judged adequate in all included studies; the method

of allocation concealment used was judged adequate in six studies, inadequate in one and unclear in 27; outcome assessments were blinded in 12 studies, unblinded in six, and unspecified in 16; attrition bias was judged low in 17 studies, high in six and unclear in 11; and reporting bias was judged low in two studies and unclear in 32 due to lack of a pre-published trial protocol. Many criteria were rated unclear as the authors did not publish sufficient information to enable a judgement to be made. The Cochrane Collaboration recommends designating any trial as at high overall risk of bias if one or more criteria are deemed high risk; at low overall risk only if all criteria are rated as low risk; and at unclear overall risk if the criteria are rated unclear or a mix of unclear and low risk (Higgins et al., 2011). As blinding of study participants to allocation is not possible in studies of psychological interventions (Berger, 2016), this criterion was discounted, resulting in 11 studies being rated as at overall high risk of bias, one study being rated as overall low risk, and the remaining 22 as unclear risk. Since studies posing an unclear risk of bias may potentially in reality pose a high risk of bias, all but one of the included studies may potentially be considered to pose a high risk of bias. Study characteristics and risk of bias ratings are summarised in Table 1 below.

Figure 1. PRISMA Flow Diagram for study screening and selection

[Insert Figure 1 about here]

Intervention	Intervention sub-type	Study	Sample size	Control	Risk of bias ratings					
					a	b	d	e	f	Overall
ACT	ACT	Bach and Hayes (2002)	I = 40, C = 40	TAU alone	L	U	L	U	U	U
ACT	ACT	Gaudiano and Herbert (2006)	I = 19, C = 21	Non-directive SC	L	H	H	L	U	H
ACT	ACT	Tyrberg, Calrbring, and Lundgren (2017)	I = 12, C = 10	TAU alone	L	U	H	H	U	H
ACT	Morita therapy	Wang et al. (2000)	I = 33, C = 33	TAU alone	L	U	U	U	U	U
CBT	Cognitive therapy	Zhang, Yao, and Fang (1999)	I = 30, C = 30	Non-directive SC	L	U	U	U	U	U
CBT	CBT for internalised stigma	Wood, Byrne, Enache, and Morrison (2018)	I = 15, C = 15	Psycho-education	L	L	H	L	L	H
CBT	CBT for low self-esteem	Hall and Tarrier (2003)	I = 12, C = 13	TAU alone	L	L	U	L	U	U
CBT	CBT for psychosis	Bechdolf et al. (2004)	I = 40, C = 48	Psycho-education	L	L	U	L	U	U
CBT	CBT for psychosis	Haddock et al. (1999)	I = 10, C = 11	Non-directive SC + Psycho-education	L	U	U	L	U	U
CBT	CBT for psychosis	Habib, Dawood, Kingdon, and Naeem (2015)	I = 21, C = 21	TAU alone	L	U	L	U	U	U
CBT	CBT for psychosis	Startup, Jackson, and Bendix (2004)	I = 47, C = 43	TAU alone	L	L	H	L	U	H
CRT	Cognitive remediation therapy	Pitschel-Walz et al. (2013)	I = 59, C = 57	TAU alone	L	U	L	L	U	U
CRT	Cognitive remediation therapy	Sanchez et al. (2014)	I = 38, C = 54	Leisure group (NP)	L	U	L	L	U	U
CRT	Cognitive remediation therapy	Van der Gaag, Kern, van den Bosch, and Liberman (2002)	I = 21, C = 21	TAU alone	L	U	U	L	U	U
EMDR	EMDR	Kim et al. (2010)	I = 15, C = 15	TAU alone	L	U	L	L	U	U

Intervention	Intervention sub-type	Study	Sample size	Control	Risk of bias ratings					
					a	b	d	e	f	Overall
Interpersonal	Interpersonal therapy	Kanas, Rogers, Kreth, Patterson, and Campbell (1980)	I = 40, C = 46	Activity group (NP)	L	U	U	H	U	H
MCT	Metacognitive training	Aghotor, Pfueller, Moritz, Weisbrod, and Roesch-Ely (2010)	I = 16, C = 14	Discussion group (NP)	L	U	L	L	U	U
MCT	Metacognitive training	Kumar et al. (2010)	I = 8, C = 8	TAU alone	L	U	U	U	U	U
MCT	Metacognitive training	Moritz, Veckenstedt, Randjbar, Vitzthum, and Woodward (2011)	I = 24, C = 24	CRT	L	U	L	L	U	U
Motivational	Compliance therapy	Kemp, Hayward, Applewhaite, Everitt, and David (1996)	I = 25, C = 22	Non-directive SC	L	U	L	L	U	U
Motivational	Motivational interviewing	Hayashi, Yamashina, Igarashi, and Kazamatsuri (2001)	I = 25, I = 25	TAU alone	L	U	H	L	U	H
Psycho-education	Patient-based psycho-education	Bechdolf et al. (2004)*	I = 40, C = 48	CBT for psychosis	L	L	U	L	U	U
Psycho-education	Patient-based psycho-education	Chan, Lee, and Chan (2007)	I = 44, C = 37	Occupational therapy (NP)	L	U	U	U	U	U
Psycho-education	Patient-based psycho-education with video self-observation	Davidoff, Forester, Ghaemi, and Bodkin (1998)	I = 9, C = 9	Patient-based psychoeducation with comedy video (NP)	L	U	L	H	U	H
Psycho-education	Patient-based psycho-education	Klingberg, Wiedemann, and Buchkremer (2001)	I = 63, C = 61	TAU alone	L	U	U	U	U	U
Psycho-education	Patient-based psychoeducation	Pitschel-Walz et al. (2006)	I = 125, C = 111	TAU alone	L	L	L	L	U	U

Intervention	Intervention sub-type	Study	Sample size	Control	Risk of bias ratings					
					a	b	d	e	f	Overall
Psycho-education	Patient-based psycho-education	Wallace and Liberman (1985)	I = 14, C = 14	Social skills training	L	U	U	U	U	U
Psycho-education	Patient-based psycho-education	Wang et al. (2015)	I = 14, C = 13	TAU alone	L	U	H	H	U	H
Psycho-education	Patient-based psycho-education	Wood, Byrne, Enache, and Morrison (2018)*	I = 15, C = 15	CBT for internalised stigma	L	L	H	L	L	H
Psycho-education	Multiple family psycho-education	McFarlane et al. (1995)	I = 83, C = 29	Single family psycho-education	L	U	U	H	U	H
Psycho-education	Single family psycho-education	Haas, Glick, Clarkin, Spencer, and Lewis (1988)	I = 37, C = 55	TAU alone	L	U	U	U	U	U
Psycho-education	Single family psycho-education	Vickar, North, Downs, and Marshall (2000)	I = 26, I = 31	TAU alone	L	U	L	H	U	H
Psycho-education	Individualised occupational therapy	Shimada et al. (2018, 2019)	I = 68, C = 68	TAU alone	L	L	L	L	L	L
Social Skills	Social skills training	Wallace and Liberman (1985)*	I = 14, C = 14	Psychoeducation	L	U	U	U	U	U

Key. ACT = Acceptance and commitment therapy; C = Control condition; CBT = Cognitive behavioural therapy; CRT = Cognitive remediation therapy; EMDR = Eye movement desensitisation and reprocessing; Family = Family therapy; I = Intervention condition; MCT = metacognitive training; Non-directive SC or Nd-SC = Non-directive supportive counselling; NP = Non-psychological; TAU = Treatment as usual. * Study has been double-entered as control condition comprised a psychological intervention of interest. Risk of bias key a = randomisation method; b= allocation concealment; c= blinding of participants and personnel (omitted); d = blinding of outcome assessments; e = attrition bias; f = selective outcome reporting; H = high risk; L = low risk; U = unclear risk.

Table 1. Summary of included studies

Meta-analysis was conducted for outcomes for which meta-analysable data was reported in at least five RCTs, increasing the likelihood of sufficient statistical power to detect treatment effects (Jackson & Turner, 2017). The five outcomes evaluated were: general psychopathology, positive symptoms of schizophrenia, relapse/ re-hospitalisation, social functioning and treatment compliance. Analysis findings for the effect of any psychological intervention on these outcomes (i.e. pooled across different intervention types), are reported below, followed by a breakdown of analysis findings and a narrative review of other outcomes for specific types of intervention. For each analysis, the estimated power to detect a medium effect (SMD = 0.5 or RR = 0.5) at medium between-studies heterogeneity and alpha = .05, is given. The references of the included studies are listed in Appendix A. The measures used in each study are described in Appendix B. Detailed results of the meta-analyses and power calculations for different effect sizes and degrees of heterogeneity are shown in Appendix C.

Any psychological intervention

General psychopathology

Seventeen trials reported or provided upon request post-intervention means and standard deviations for general psychopathology. One trial was omitted from the main analysis due to reporting only pre-post change scores (Aghotor et al., 2010) but is included in the analysis of specific interventions. A further four trials reported non-meta-analysable data on general psychopathology and their findings are summarised in the review of individual psychological treatments below. Meta-analysis found no overall effect of psychological interventions on general psychopathology (SMD = -0.14, 95% CI -0.31 to 0.04, p = .12, N = 1144, power 100%); subgroup analysis found a significant effect when the comparator was treatment-as-usual (SMD = -0.27, 95% CI -0.46 to -0.08, p = .01, N = 676, power 99%) but not when the

comparator was an alternative intervention (SMD = 0.02, 95% CI -0.27 to 0.31, p = .91, N = 468, power 96%) (Figure 2; Table C.1). However, meta-regression showed no significant effect of control condition (TAU alone vs. alternative intervention) on effect size (β = 0.20, 95% CI -0.08 to 0.66, p = .12).

Positive symptoms of schizophrenia

Twelve trials reported or provided upon request post-intervention means and standard deviations for positive symptoms. One trial was omitted from the main analysis due to reporting only pre-post change scores (Aghotor et al., 2010) but is included in the analysis of specific interventions. A further two trials reported non-analysable data on positive symptoms and their findings are summarised in the review of individual psychological treatments below. Meta-analysis found an overall beneficial effect of psychological interventions versus control treatments on positive symptoms (SMD = -0.28, 95% CI -0.51 to -0.06, p = .01, N = 703, power 100%); subgroup analysis found a significant effect when the comparator was treatment-as-usual (SMD = -0.32, 95% CI -0.61 to -0.04, p = .03, N = 483, power 97%) but not when the comparator was an alternative intervention (SMD = -0.23, 95% CI -0.56 to 0.11, p = .32, N = 246, power 73%) (Figure 3; Table C.2). Meta-regression showed no significant effect of control condition (TAU alone vs. alternative intervention) on effect size (β = 0.11, 95% CI -0.47 to 0.69, p = .68).

Relapse/ re-hospitalisation

Thirteen trials reported, or provided upon request, relapse or re-hospitalisation rates over post-discharge follow-up periods ranging from 4 months to 2 years. (Re-hospitalisation was used as a proxy for relapse where relapse data was not available). Meta-analysis found an overall beneficial effect of psychological interventions versus control treatments on preventing relapse/ re-hospitalisation (pooled RR = 0.50, 95% CI 0.40 to 0.61, p < .01, N = 898, power >80%); subgroup analysis found significant effects both when the comparator

was treatment-as-usual (pooled RR = 0.46, 95% CI 0.32 to 0.66, *N* = 488, *p* < .01, power > 80%) and when the comparator was an alternative intervention (pooled RR = 0.58, 95% CI 0.41 to 0.82, *p* < .01, *N* = 410, power > 80%) (Figure 4; Table C.3). Meta-regression showed no effect of control condition (TAU alone vs. alternative intervention) on effect size (β = 0.05, 95% CI -0.51 to 0.60, *p* = .86).

Social functioning

Eleven trials reported or provided upon request post-intervention means and standard deviations for social functioning. A further four trials reported non-meta-analysable data and their findings are summarised in the review of individual psychological treatments below. Meta-analysis found an overall beneficial effect of psychological interventions versus control treatments on social functioning (SMD = 0.43, 95% CI 0.21 to 0.64, *p* < .01, *N* = 824, power 100%); subgroup analysis found a significant effect when the comparator was treatment-as-usual (SMD = 0.66, 95% CI 0.31 to 1.00, *p* < .01, *N* = 512, power 98%) but not when the comparator was an alternative intervention (SMD = 0.21, 95% CI -0.02 to 0.43, *p* = .07, *N* = 312, power 87%) (Figure 5; Table C.4). Meta-regression showed no significant effect of control condition (TAU alone vs. alternative intervention) on effect size (β = -0.42, 95% CI -0.91 to 0.07, *p* = .09).

Treatment compliance

Five trials reported or provided upon request post-interventions means and standard deviations for treatment compliance. A further two trials reported non-meta-analysable data and their findings are summarised in the review of individual psychological treatments below. Meta-analysis found an overall beneficial effect of psychological interventions versus control treatments on treatment compliance (SMD = 0.46, 95% CI 0.29 to 0.64, *p* < .01, *N* = 530, power 98%); subgroup analysis found a significant effect both when the comparator was treatment-as-usual (SMD = 0.44, 95% CI 0.24 to 0.64, *p* < .01, *N* = 395, power 93%) and when the comparator was an alternative intervention (SMD = 0.59, 95% CI 0.06 to 1.13, *p* =

.03, *N* = 135, power 53%) (Figure 6; Table C.5). Meta-regression showed no effect of control condition (TAU alone vs. alternative intervention) on effect size (β = 0.11, 95% CI -0.57 to 0.78, *p* = .65).

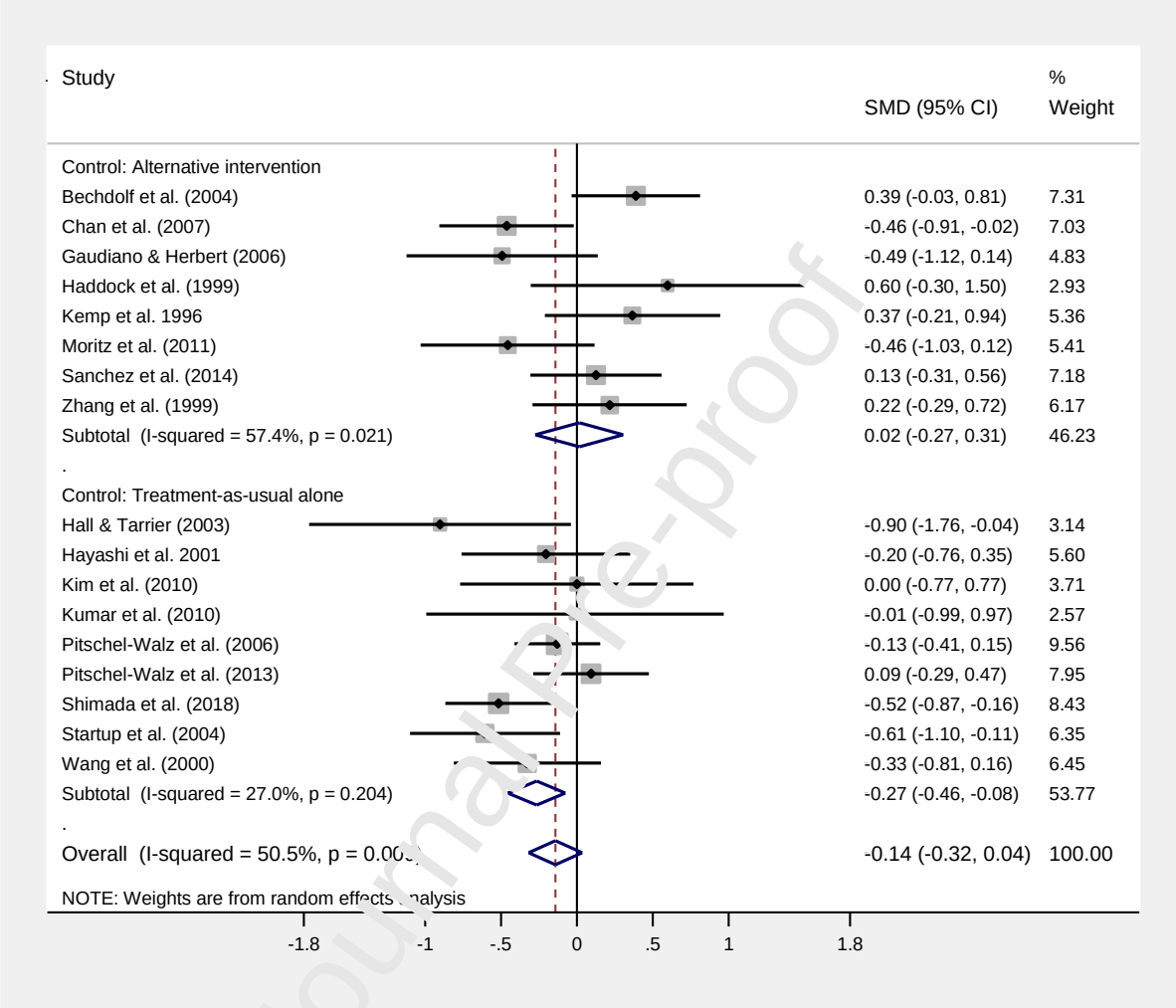

Figure 2. Meta-analysis of psychological interventions versus control treatment for post-intervention general psychopathology

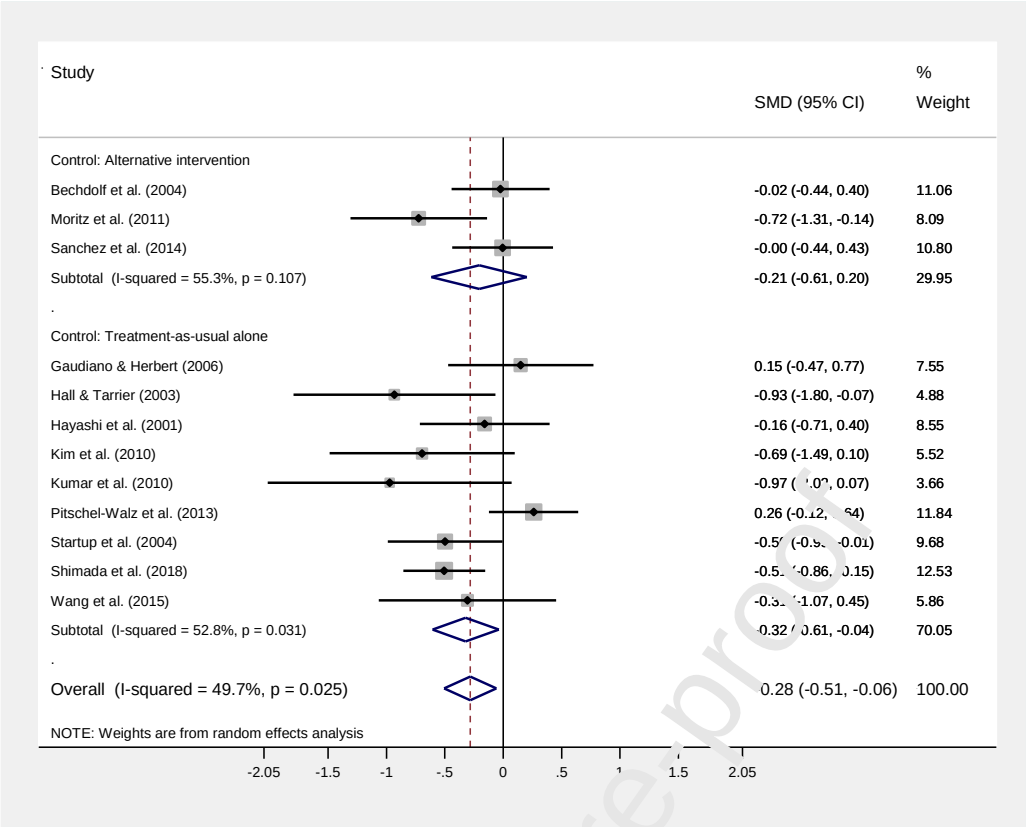

Figure 3. Meta-analysis of psychological interventions versus control treatment for post-intervention positive symptoms

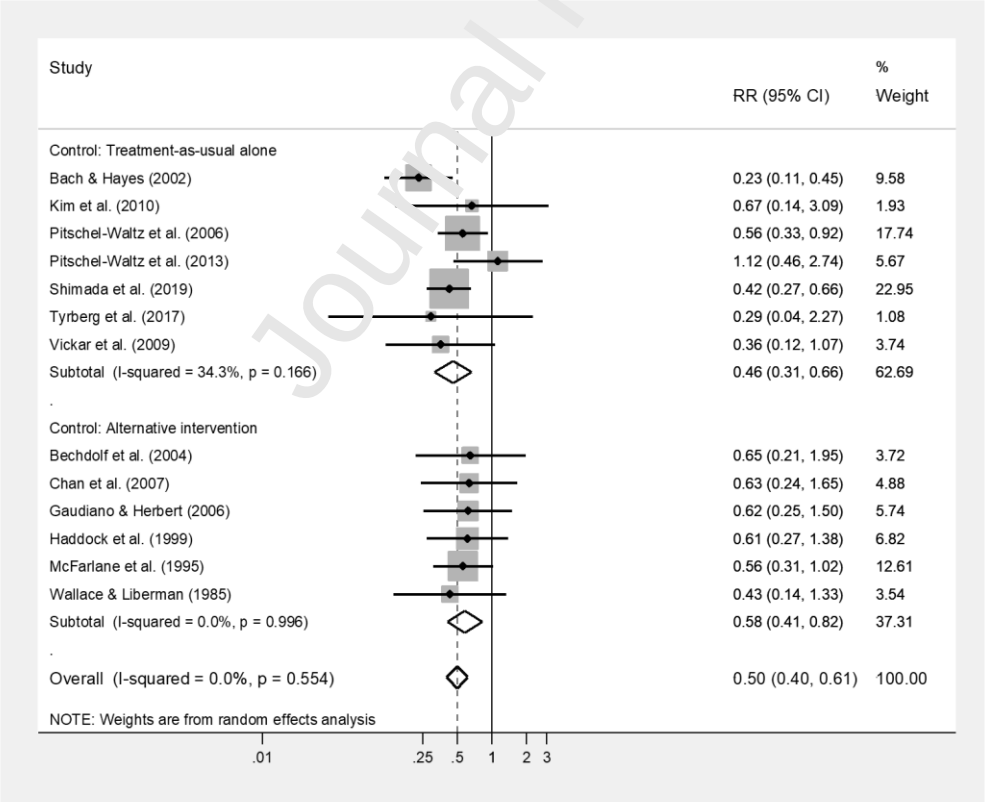

Figure 4. Meta-analysis of psychological interventions versus control treatment for relapse/ re-hospitalisation by follow-up

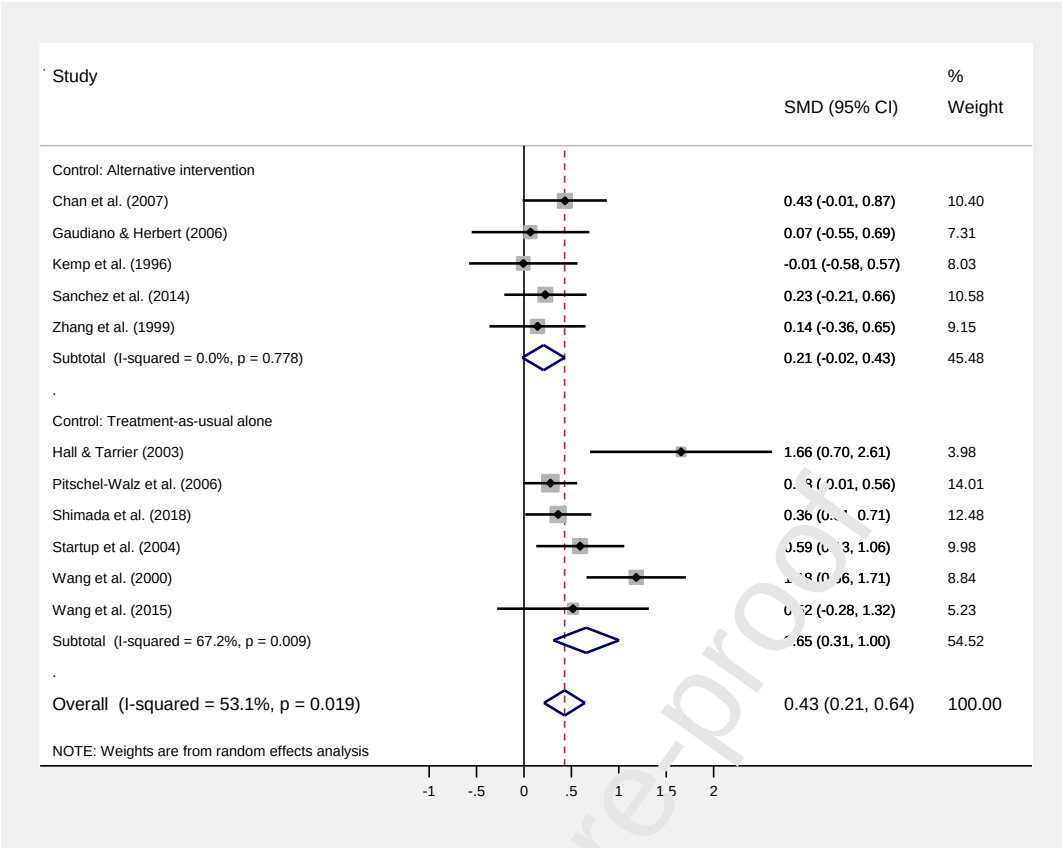

Figure 5. Meta-analysis of psychological interventions versus control treatment for post-intervention social functioning

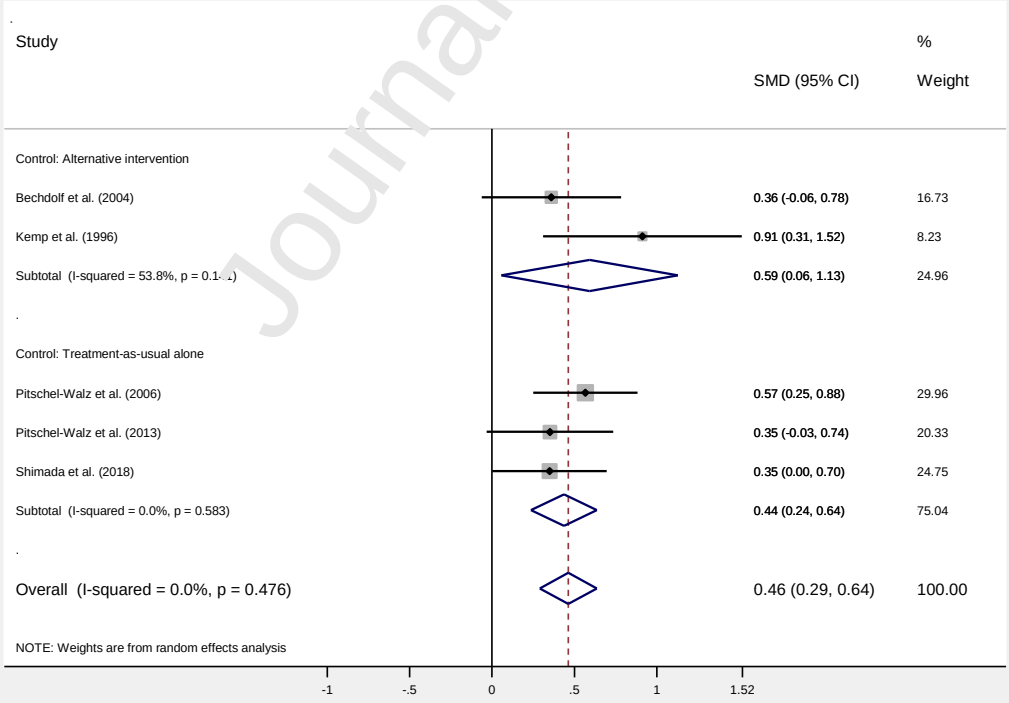

Figure 6. Meta-analysis of psychological interventions versus control treatment for post-intervention treatment compliance

Acceptance and commitment (Morita) therapies

Acceptance and commitment therapy (ACT) is "based on the view that many maladaptive behaviors are produced by unhealthy attempts to avoid or suppress thoughts, feelings, or bodily sensations… patients are taught to identify and abandon internally oriented control strategies and accept the presence of difficult thoughts or feelings" (Bach & Hayes, 2002, p. 1130). Morita therapy has been argued to bear striking similarities to ACT and was therefore placed in the same intervention category (Hofmann, 2008). Four RCTs were identified (see Table 1): three of ACT and one of Morita therapy.

General psychopathology

Meta-analysis of two trials found significantly lower post-intervention general psychopathology relative to the control conditions (SMD = -0.39, 95% CI -0.77 to -0.01, p = .04, N = 106, power 43%).

Positive symptoms of schizophrenia

In a single trial, there was no significant difference in post-intervention frequency of positive symptoms relative to the control treatment (SMD = 0.15, 95% CI -0.47 to 0.77, p = .64, N = 40, power 34%). A second RCT also found no post-intervention difference in frequency of symptoms but did not report meta-analysable data (Bach & Hayes, 2002); a third collected data on this outcome but did not analyse it due to large amounts of missing data (Tyrberg et al., 2017).

Relapse/ re-hospitalisation

Across three RCTs of ACT there was a significant reduction in the risk of re-hospitalisation by follow-up, relative to the control condition (RR = 0.34, 95% CI 0.17 to 0.70, p < .01. N = 141, power < 80%).

Social functioning

Across two RCTs of ACT there was no difference in post-intervention social functioning relative to the control condition (SMD = 0.64, 95% CI -0.45 to 1.73, p = .25, power 43%).

Treatment compliance

Bach and Hayes (2002) reported no difference in compliance between patients receiving ACT and those receiving TAU alone. The data was reported as percentage with good compliance rather than mean scores and hence could not be included in meta-analysis.

Other outcomes

Wang et al. (2000) found negative symptoms of schizophrenia were lower at post-intervention in patients receiving morita therapy than those receiving TAU alone. One RCT found positive symptoms caused patients less distress following ACT than following the control treatment (Gaudiano & Herbert, 2006) but another found no difference on this outcome (Bach & Hayes, 2002).

Cognitive behavioural therapy (CBT)

CBT "aims to reduce distressing emotional experiences or problematic behaviour by changing the way in which the individual appraises, interprets and evaluates their experiences." (Jones et al., 2018, p. 7). Seven RCTs evaluating four CBT sub-types were identified (cognitive therapy, CBT for internalised stigma, CBT for low self-esteem and CBT for psychosis; see Table 1).

General psychopathology

Meta-analysis of five RCTs showed no significant overall difference in general psychopathology at post-intervention relative to control treatments (SMD = -0.03, 95% CI -0.24 to 0.25, p = .86, N = 284, power 83%). A sixth trial reported a significant post-

intervention difference in favour of CBT but could not be included in the analysis as means and standard deviations were not reported (Habib et al., 2015).

Positive symptoms of schizophrenia

Meta-analysis of three RCTs showed no significant difference in positive symptoms at post-intervention relative to control treatments (SMD = -0.39, 95% CI -0.86 to 0.09, p = .11, N = 203, power 70%). A fourth RCT also reported no significant difference in post-intervention positive symptoms whilst a fifth reported a significant post-intervention difference in favour of CBT but these could not be included in the analysis as meta-analysable data was not reported (Habib et al., 2015; Haddock et al., 1999).

Relapse/ re-hospitalisation

Meta-analysis of two RCTs showed no significant overall reduction in the risk of relapse relative to alternative psychological interventions (RR = 0.62, 95% CI 0.32 to 1.20, p = .16, N = 91, power < 80%).

Social functioning

Meta-analysis of three RCTs showed superior social functioning at post-intervention relative to TAU alone (SMD = 0.68, 95% CI 0.01 to 1.36, p = .04, N = 158, power 59%).

Treatment compliance

A single RCT found no difference in post-intervention treatment compliance relative to psychoeducation (SMD = 0.36, 95% CI -0.06 to 0.78, p = .10, power 37%).

Other outcomes

Hall and Tarrier (2003) found superior outcomes for CBT compared to TAU alone for post-intervention depression, self-esteem and negative symptoms but no difference in anxiety. Wood et al. (2018) found superior outcomes for CBT compared to psychoeducation for post-intervention self-esteem but no differences in depression, internalised stigma, perceived external stigma or personal recovery.

Cognitive remediation therapy (CRT)

CRT is "a behavioral training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition)… with a further goal that improved cognition will affect community functioning" (Wykes et al., 2011, p. 472). Three RCTs were identified (see Table 1).

General psychopathology

Meta-analysis of two RCTs found no difference in post-intervention general psychopathology relative to control treatment (SMD = 0.11, 95% CI -0.29 to 0.47, p = .46, N = 190, power 67%).

Positive symptoms of schizophrenia

Meta-analysis of two RCTs found no difference in post-intervention positive symptoms relative to control treatment (SMD = 0.14, 95% CI – 0.14 to 0.43, p = .32, N = 190, power 67%).

Relapse/ re-hospitalisation

A single RCT found no difference in the risk of re-hospitalisation by follow-up relative to the control treatment (RR = 0.43, 95% CI 0.14 to 1.33, p = .80, N = 88, power < 80%).

Social functioning

A single RCT found no difference in post-intervention social functioning relative to the control treatment (SMD = 0.23, 95% CI – 0.21 to 0.66, p = .31, N = 84, power 36%).

Treatment compliance

A single RCT found no difference in post-intervention treatment compliance relative to the control treatment (SMD = 0.35, 95% CI – 0.03 to 0.74, p = .07, N = 106, power 43%).

Other outcomes

Pitschel-Walz et al. (2013) found no difference in post-intervention global cognitive functioning relative to the control treatment. Sanchez et al. (2014) found no post-intervention differences on any outcome but did find greater pre-post improvements in processing speed, verbal memory, verbal fluency, working memory, executive functioning, negative symptoms, disorganisation and emotional distress relative to the control treatment. Van der Gaag et al. (2002) found greater pre-post improvements in emotion matching, emotion labelling and verbal learning relative to the control treatment.

Eye movement desensitization reprocessing (EMDR)

EMDR "conceptualizes insufficiently processed memories of disturbing or traumatic experiences as the primary source of all psychopathology not caused by organic deficit. The processing of these memories is posited to lead to resolution through the reconsolidation and assimilation within the larger adaptive memory networks." (Oren & Solomon, 2012, p. 198). One RCT was identified (see Table 1).

General psychopathology

A single RCT found no difference in post-intervention general psychopathology relative to control treatment (SMD = 0.00, 95% CI -0.76 to 0.77, p = 1.00, power 19%).

Positive symptoms of schizophrenia

A single RCT found no difference in post-intervention positive symptoms relative to control treatment (SMD = -0.69, 95% CI -1.49 to 0.09, p = .09, power 19%).

Relapse/ re-hospitalisation

A single RCT found no difference in re-hospitalisation by follow-up relative to control treatment (RR = 0.67, 95% CI 0.14 to 1.33, p = .60, power < 80%).

Social functioning; Treatment compliance

Not reported.

Other outcomes

Kim et al. (2010) found no benefits over TAU for anxiety or depression.

Interpersonal psychotherapy

Interpersonal psychotherapy aims to "help patients gain insight into intrapsychic and intrapersonal difficulties by focussing on here-and-now group interactions and expression of feelings" (Kanas et al., 1980, p. 488). One RCT was identified (see Table 1).

General psychopathology

In an RCT including subgroup data for patients meeting criteria for schizophrenia-spectrum disorders, general psychiatric symptoms were reported to be no better and on some measures were worse in patients receiving interpersonal group therapy than in patients participating in a non-psychological activity group (Kanas et al., 1980). This study could not be included in the analysis as meta-analysable data was not reported.

Positive symptoms of schizophrenia; Relapse/ re-hospitalisation; Social functioning; Treatment compliance; Other outcomes

Not reported.

Metacognitive training (MCT)

MCT aims at "changing the 'cognitive infrastructure' of delusional ideation by bringing metacognitive impairments to the attention of patients" (Aghotor et al., 2010, p. 208). Three RCTs were identified (see Table 1).

General psychopathology

General psychopathology outcomes were reported as post-intervention means in some trials and as pre-post change scores in others and have therefore been combined using unstandardized weighted mean differences as recommended by the Cochrane Collaboration (Deeks et al., 2011, section 9.5.1). Meta-analysis of three RCTs showed no significant overall

difference in general psychopathology outcomes relative to an alternative psychological intervention/TAU alone (WMD = -3.22, 95% CI -8.84 to 2.21, p = .26, N = 90, power 38%).

Positive symptoms of schizophrenia

Positive symptom outcomes were reported as post-intervention means in some trials and as pre-post change scores in others and have therefore been combined using unstandardized weighted mean differences as recommended by the Cochrane Collaboration (Deeks et al., 2011, section 9.5.1). Meta-analysis of three RCTs showed significantly lower positive symptoms at post-intervention relative to control treatments (WMD = -2.29, 95% CI -4.07 to -0.51, p = .01, power 40%).

Relapse/ re-hospitalisation; Social functioning; Treatment compliance

Not reported.

Other outcomes

Two RCTs (Kumar et al., 2010; Moritz et al., 2011) found that the strength of patients' belief in their delusions was significantly lower following MCT than following an alternative psychological intervention/TAU alone. Two RCTs found no effect of MCT on jumping to conclusions at post-intervention (Aghotor et al., 2010; Moritz et al., 2011).

Motivational Interventions

Motivational interventions "have the overarching goal of addressing and enhancing motivation to change" (Tevyaw & Monti, 2004, p. 63). Two RCTs were identified of motivational interventions targeting patients' compliance with treatment: One of compliance therapy and one of motivational interviewing (see Table 1).

General psychopathology

Meta-analysis of two RCTs showed no significant overall difference in general psychopathology at post-intervention relative to a non-directive psychological intervention/TAU alone (SMD = 0.08, 95% CI -0.48 to 0.64, p = .79, N = 72, power 31%).

Positive symptoms of schizophrenia

A single RCT found no difference in post-intervention positive symptoms relative to the control treatment (SMD = -0.16, 95% CI -0.71 to 0.40, p = .58, N = 50, power 23%).

Relapse/ re-hospitalisation

Kemp et al. (1998) reported a significantly longer time to re-hospitalisation by follow-up, relative to the control condition; however, re-hospitalisation rates were not reported.

Social functioning

A single RCT found no difference in post-intervention social functioning relative to the control treatment (SMD = -0.01, 95% CI -0.57 to 0.57, p = .98, N = 47, power 22%).

Treatment compliance

A single RCT found superior treatment compliance at post-intervention relative to the control treatment (SMD = 0.91, 95% CI 0.31 to 1.52, p < .01, N = 47, power 22%).

Other outcomes

Illness insight was significantly better at post-intervention in one RCT (Kemp et al., 1996) but not the other (Hayashi et al., 2001), relative to the control treatments.

Psychoeducation

Psychoeducation aims to "increase patients' knowledge and understanding of their illness and treatment…. (to) enable people with schizophrenia to cope more effectively with their illness" (Xia, Merinder, & Belgamwar, 2011, p. 6). Eleven RCTs were identified (see Table 1), including the only trial in this review deemed to pose a low risk of bias (Shimada et al., 2018). Eight of the studied trials were patient-based (i.e., included patients but not their

families) and three were family-based (i.e., the patients' families attended psychoeducation sessions together with the inpatient).

General psychopathology

Meta-analysis of four RCTs found significantly lower post-intervention general psychopathology relative to control treatments (SMD = -0.33, 95% CI -0.53 to -0.14, p < .01, *N* = 492, power 97%). A fifth RCT found significantly greater improvement in general psychopathology following psychoeducation with video self-observation versus psychoeducation with a non-psychological video (Davidoff et al., 1998), whilst a sixth reported no difference in post-intervention general psychopathology relative to the control treatment (Haas et al., 1988); however, meta-analysable data was not reported.

Positive symptoms of schizophrenia

Meta-analysis of three RCTs found no difference in post-intervention positive symptoms, relative to the control condition (SMD = -0.41, 95% CI -0.99 to 0.17, *p* = .17, *N* = 244, power 78%).

Relapse/ re-hospitalisation

Meta-analysis of seven RCTs found a significantly lower risk of relapse/ re-hospitalisation by follow-up, relative to the control treatment (pooled RR = 0.63, 95% CI 0.43 to 0.94, *p* = .02, *N* = 657, power > 80%).

Social functioning

Meta-analysis of four RCTs found significantly better post-intervention social functioning relative to the control treatment (SMD = 0.35, 95% CI 0.15 to 0.54, *p* < .01. *N* = 429, power 95%). Conversely, both Klingberg et al. (2001) and Haas et al. (1988) found no difference in post-intervention social functioning relative to the control treatment, whilst Wallace and Liberman (1985) found patients receiving psychoeducation were rated by their

families as showing poorer post-intervention social adjustment than patients receiving social skills training. These trials did not report meta-analysable data on these outcomes.

Treatment compliance

Meta-analysis of three RCTs found no difference in post-intervention treatment compliance relative to the control treatment (SMD = 0.20, 95% CI -0.31 to 0.71, p = .44, N = 377, power 92%). A fourth RCT also reported no effect on treatment compliance but did not report meta-analysable data (Klingberg et al., 2001).

Other outcomes

Two RCTs examined the effect of psychoeducation versus non-psychological interventions on illness insight at post-intervention, with one finding significantly greater improvement in insight following psychoeducation with video self-observation (Davidoff et al., 1998) and another finding no significant difference on this outcome (Chan et al., 2007). For cognitive functioning, one RCT found significantly better post-intervention cognitive functioning relative to TAU alone (Shimada et al., 2018). For depression severity, one RCT found no significant difference following psychoeducation versus CBT for internalised stigma (Wood et al., 2018). For negative symptoms, one RCT found lower negative symptoms following multiple family group psychoeducation than following single family psychoeducation (McFarlane et al., 1995). For quality of life, one RCT found significantly greater improvement following psychoeducation versus TAU alone (Wang et al., 2015).

Social skills training

Social skills training "consists of a package of techniques including modeling, behavioral rehearsal and role playing, feedback, coaching, and positive reinforcement" to improve patients' social skills (Wallace & Liberman, 1985, p. 239). One RCT was identified (Table 1).

Relapse/ re-hospitalisation

A single RCT found no difference in the rate of relapse by follow-up relative to the control condition (RR = 0.43, 95% CI 0.14 to 1.33, p = .14, N = 28, power < 80%).

Social functioning

A single RCT reported greater pre-post improvements in self-ratings of assertiveness, family ratings of social adjustment and observer ratings of social competence, compared to the control treatment (Wallace & Liberman, 1985). This study did not report meta-analysable data.

General psychopathology; Positive symptoms of schizophrenia; Treatment compliance; Other outcomes

Not reported.

Publication Bias

Publication bias for general psychopathology outcomes

Egger's test indicated no evidence of publication bias in RCTs publishing meta-analysable data on general psychopathology outcomes at post-intervention (bias coefficient = 0.09, 95% CI -2.34 to 2.52, p = .94). The funnel plot (Figure 7) indicates relatively even distribution of trials finding positive and negative effects across a range of sample sizes.

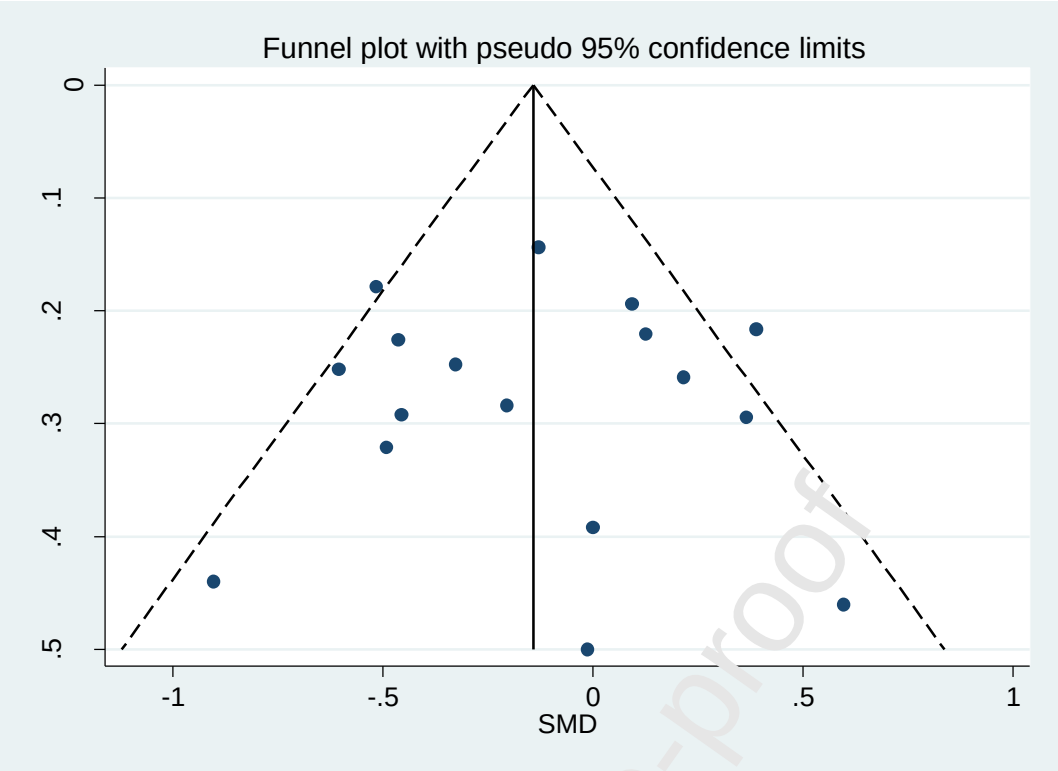

Figure 7. Funnel plot of SMD against standard error for general psychopathology outcomes (17 RCTs)

Publication bias for relapse/ re-hospitalisation

Egger's test indicated no evidence of significant publication bias in RCTs publishing meta-analysable data on relapse / re-hospitalisation rates at follow-up (bias coefficient = 0.35, 95% CI -1.24 to 1.93, $p = .64$). The funnel plot (Figure 8) indicates relatively even distribution of trials finding positive and negative effects across a range of sample sizes.

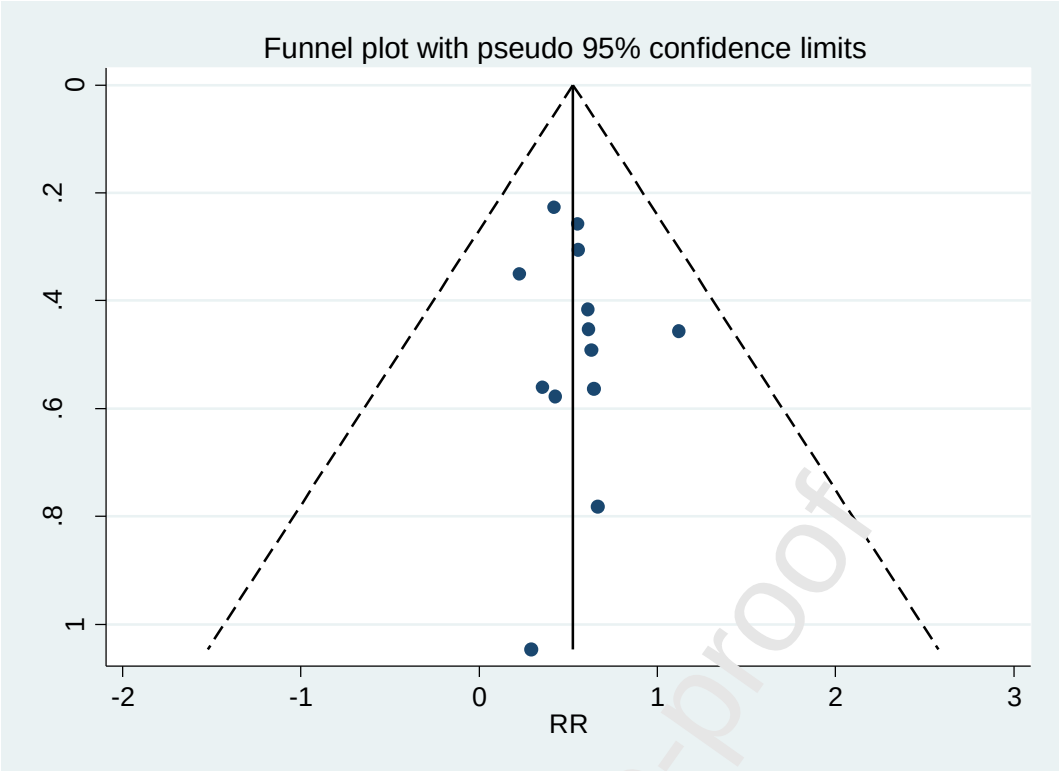

Figure 8. Funnel plot of risk ratio (RR) against standard error of log RR for relapse/ re-hospitalisation (13 RCTs)

Discussion

We reviewed 34 randomised controlled trials of psychological interventions for patients with schizophrenia-spectrum disorders in acute inpatient psychiatric settings, of which 29 published or provided data suitable for meta-analysis. Psychoeducational interventions have been most frequently evaluated, followed by CBT. There have been fewer trials of alternative approaches such as ACT, CRT, MCT, motivational or psychodynamic therapies. In random effects meta-analyses pooled across intervention types, psychological interventions improved post-intervention positive symptoms, social functioning and treatment compliance, and reduced the risk of relapse/ re-hospitalisation, but did not improve general psychopathology, relative to control conditions. Highly powered (>80%) sub-group analyses showed positive intervention effects for several outcomes (general psychopathology, positive symptoms, and social functioning) where the control condition was treatment-as-usual but not when it was an

alternative intervention; however, all meta-regression analyses found no significant effect of control condition on effect size. Further highly powered sub-group analyses (>80%) of specific intervention effects showed that psychoeducation improved several key outcomes (general psychopathology, relapse/ re-hospitalisation and social functioning, but not positive symptoms or treatment compliance) but did not support the effectiveness of cognitive behaviour therapy for improving general psychopathology. Preliminary underpowered analyses (<80%) also showed positive intervention effects of ACT for reducing general psychopathology and relapse/ re-hospitalisation, CBT for improving social functioning, and MCT for reducing positive symptoms. Further preliminary analyses found no effect of ACT, CBT, CRT or MCT on any of the other evaluated outcomes; however, these analyses were underpowered (<80%) due to small sample sizes. Separate meta-analyses of EMDR, interpersonal therapy and social skills training effects could not be conducted as they were evaluated only in single trials. Risk of bias was high or unclear in all but one of the included studies, primarily due to inadequate allocation concealment, non-blinding of outcome assessments and/ or incomplete outcome reporting. Analysis of data on the two most frequently studied outcomes - general psychopathology and relapse/ re-hospitalisation - revealed no evidence of publication bias.

Interpretation of Findings and Comparison to Previous Research

To our knowledge there has been no other meta-analysis of psychological interventions in the acute inpatient psychiatric setting focussed on patients with schizophrenia-spectrum disorders. Our findings broadly concur with those of Paterson and colleagues (2018), who synthesised data across intervention types and a range of diagnostic groups, concluding overall that psychological interventions are effective for reducing positive symptoms, readmissions, depression, and anxiety in acute inpatients. However, they were

unable to reach a conclusion about which interventions might be particularly effective or ineffective for which patient groups. Our work follows Cochrane guidance by reducing the heterogeneity of included studies through focussing on a single diagnostic patient group (Deeks et al., 2011), and – where the total sample size of analysable studies was sufficient to give adequate power to do so - allowing us to reach focussed conclusions about which specific interventions have evidence for effectiveness amongst acute inpatients with schizophrenia-spectrum disorders, and which do not. Additionally, our work improves upon the previous meta-analysis by including only RCT evidence, rather than merging RCT and non-RCT data which can lead to biased and potentially over-inflated effect size estimates (Reeves et al., 2011).

Our findings that receiving psychoeducation was associated with lower general psychopathology, better social functioning and a reduced risk of relapse/ re-hospitalisation are in line with a Cochrane review focussed mainly on outpatient studies, which identified superiority of psychoeducation over treatment-as-usual for improving general psychopathology, social functioning and medication compliance and reducing the risk of relapse in patients with schizophrenia (Xia et al., 2011). One possibility is that psychoeducation may have been particularly beneficial as the tested programmes were often explicitly developed for acute inpatient settings, covering a broad range of relevant topics such as the role of medication, managing stress and identifying signs of relapse, whereas other types of intervention were often developed first in outpatient settings and subsequently adapted. Psychoeducation is often employed as an active control in trials of psychological interventions, and indeed was used as a control condition in four of the trials included in this review, with the explicit or implicit hypothesis that patients receiving psychoeducation would achieve poorer outcomes. Yet our analysis and others show that it can be an effective psychological intervention in its own right.

Our findings with regards to the second-most frequently evaluated intervention, CBT, were on the whole disappointing. Whilst we did find a positive effect on social functioning, we found no effect on general psychopathology, positive symptoms or treatment compliance. This stands in contrast to recent large meta-analyses based primarily on CBT conducted among outpatients with schizophrenia, which found reductions in post-intervention general psychopathology and positive symptoms compared to control treatments (Eichner & Berna, 2016; Jauhar et al., 2014; Pilling et al., 2002; Turner, van der Gaag, Karyotaki, & Cuijpers, 2014). However, whilst our analysis of the effect of CBT on general psychopathology was highly powered (>80%) to detect a medium intervention effect at medium heterogeneity, our analyses of other outcomes were based on small numbers of studies and were therefore underpowered. Of particular note, the analysis of the effect of CBT on positive symptoms comprised just three trials; two of which evaluated CBT for psychosis, with the primary aim of improving positive symptoms, and one of which evaluated CBT for low self-esteem. Given the small number of trials, of which only two had a primary focus on improving positive symptoms, it is unsurprising that the findings were non-significant. A further two small trials of CBT did not publish nor provide upon request analysable data on positive symptoms; it is unclear how inclusion of this data would have affected the findings. By contrast, a meta-analysis of 33 trials of primarily outpatient CBT for patients with schizophrenia-spectrum disorders found a significant intervention effect on positive symptoms (Jauhar et al. 2014). Our analysis yielded a standardised mean difference of -0.39, similar to Jauhar and colleagues' finding of a standardised mean difference of -0.25; had we been able to include further trials in our comparison it is possible that the confidence interval would have narrowed sufficiently to generate statistical significance.

Conversely, despite also being based on small numbers of studies, our analyses did yield preliminary support for the effectiveness of two interventions which draw on CBT

principles but aim to enhance their value by incorporating ideas from other therapeutic paradigms: ACT and MCT. Our findings on the effectiveness of these interventions are in accordance with meta-analytic evidence spanning both in- and outpatient trials (Normann & Morina, 2018; Tonarelli, Pasillas, Alvarado, Dwivedi, & Cancellare, 2016). Both these approaches differ from traditional CBT in that they do not directly challenge patients' dysfunctional beliefs, but instead target maintaining cognitive and affective processes – MCT by modifying the cognitive biases thought to underlie and maintain delusional thinking in schizophrenia (e.g., jumping to conclusions, resistance to changing beliefs) (Moritz et al., 2011) – and ACT by teaching patients to recognise that their thoughts are products of mental events rather than the self, and encouraging patients to mindfully and non-judgementally observe their thoughts and hallucinatory experiences rather than trying to suppress them (Gaudiano & Herbert, 2006). It is possible that this focus on changing patients' cognitive and affective response to their thoughts may be particularly helpful for inpatients experiencing acute psychotic symptoms, who may be resistant to more direct challenges to their beliefs.

Limitations

As detailed above, whilst our analyses of the overall effects of psychological interventions, our subgroup analyses by control condition, and our analyses of psychoeducation trials were large and adequately powered, we had limited power to discern the effects of other less frequently evaluated types of psychological intervention. Furthermore, several of the trials included in the narrative review could not be included in the meta-analyses, as some omitted key outcomes such as positive symptoms, general psychopathology and relapse, and others failed to report data in a usable way and were not responsive to requests for this data. For the majority of studies, risk of bias was either high due to inadequate allocation concealment, lack of blinded assessments, high attrition and/or failure to pre-publish planned outcome measures, or risk of bias was unclear as study authors

did not provide sufficient information to evaluate these criteria. Our use of non-disorder-specific search terms – "psychiatric" and "mental" - was intended to generate comprehensive search results. Whilst a sensitivity analysis replacing the non-disorder-specific terms with disorder-specific ones did not identify any omitted trials, we nonetheless cannot guarantee that we did not miss additional relevant trials which used disorder-specific terms and did not use our non-disorder-specific terms.

Implications for Clinical Practice and Further Research

On the basis of our findings, clinicians can be confident that, in general, psychological interventions can be effective and are worthwhile implementing in acute inpatient settings for patients with schizophrenia-spectrum disorders. When deciding which specific interventions to implement, clinicians may find it helpful to know that psychoeducation currently has the best evidence base, with preliminary emerging evidence based on smaller numbers of trials for ACT and MCT. Clinicians should utilise caution in judging whether positive RCT findings are likely to generalise to all acute inpatients with schizophrenia. Whilst some of the studied psychoeducation interventions were developed specifically for acute inpatient settings (e.g., Chan et al., 2007; Vickar et al., 2009), others were adapted from interventions developed for outpatient settings (e.g., Bechdolf et al., 2004) and ACT and MCT were also developed in outpatient settings (Hayes, Strosahl, & Wilson, 1999; Moritz & Woodward, 2007), where patients might be assumed to be suffering from less acute manifestations of psychosis. Whilst the interventions were adapted in frequency and length for acute inpatient settings (e.g., holding sessions twice a week over a 5-week period), it is unclear if and how they were adapted in content. Thus arguably inpatients were introduced to quite complex and abstract ideas – such as considering the pros and cons of different kinds of attributional styles, rating the plausibility of different interpretations of situations, and conducting behavioural experiments to test beliefs – without any adaptations to cater for the increased

cognitive and attentional deficits exhibited by inpatients with acute schizophrenia (Park et al., 2002). This is in direct contrast to the views of front-line nursing staff and other clinicians involved in delivering interventions in acute inpatient settings, who have expressed doubt about the capacity of acutely unwell inpatients to concentrate on and process even minimally complex and abstract content and have emphasised the importance of adapting standard interventions to make them simpler (Sharp et al., 2018). However, comparison of participant characteristics suggests that patients' symptom level may have been surprisingly similar across outpatient trials and the included acute inpatient trials. For instance, positive symptom severity (as rated on the Positive and Negative Symptom Scale) ranged between 14 and 25 in the analysed inpatient MCT trials; our informal literature search identified a range between 14 and 24 in outpatient MCT/CBT trials using this measure (Briki et al., 2014; Lewis et al., 2002; Moritz & Woodward, 2007; Peters et al., 2010). This casts doubt on whether the patients participating in the included trials were truly at the most acute end of the schizophrenic spectrum and raises the issue of potential selection bias. Indeed, several of the included trials specify that individuals demonstrating high levels of disturbed behaviour, distress, hostility, suspiciousness or thought disorder were excluded (Aghotor et al., 2010; Habib et al., 2015; Hall & Tarrier, 2003). Beyond this, clinicians may have preferentially recommended patients with less severe symptoms to participate, or patients with more severe symptoms may have refused to participate or may have lacked capacity to consent. Thus, it is unclear whether the meta-analysis' findings are generalisable to inpatients experiencing the most severe manifestations of acute psychosis.

All of the reviewed interventions require further testing in well-designed RCTs. In particular, our positive findings on the effectiveness of ACT, MCT and psychoeducation in acute inpatient settings require replication and further evidence is also needed to confirm or disconfirm our negative findings on CBT and CRT and to investigate the effect of

intervention subtypes and of active versus non-active/usual treatment control conditions. Future trials should be more rigorously designed, in particular using concealed allocation and blinded outcome assessments. They should also pre-publish their planned outcome measures, should publish clear data on attrition, and should publish meta-analysable data on positive symptoms, general psychopathology, relapse and re-hospitalisation in addition to considering wider outcomes such as social functioning, insight, and quality of life. Furthermore, future trials should be explicit about the extent to which their samples are representative of the typical acute inpatient schizophrenia population and should discuss the potential for selection bias and the implications of any decisions to exclude more disturbed patients.

Conclusion

Overall, our meta-analyses suggested that psychological interventions can be effective for improving several key outcomes for patients with schizophrenia-spectrum disorders who are treated in acute inpatient settings, with strongest evidence so far for the effectiveness of psychoeducation and preliminary evidence for beneficial effects of ACT and MCT. Study methodology often posed a high or unclear risk of bias and further research should use more rigorous RCT designs and publish meta-analysable data on positive symptoms, general psychopathology, social functioning, relapse/ re-hospitalisation and treatment compliance, in addition to considering wider outcomes.

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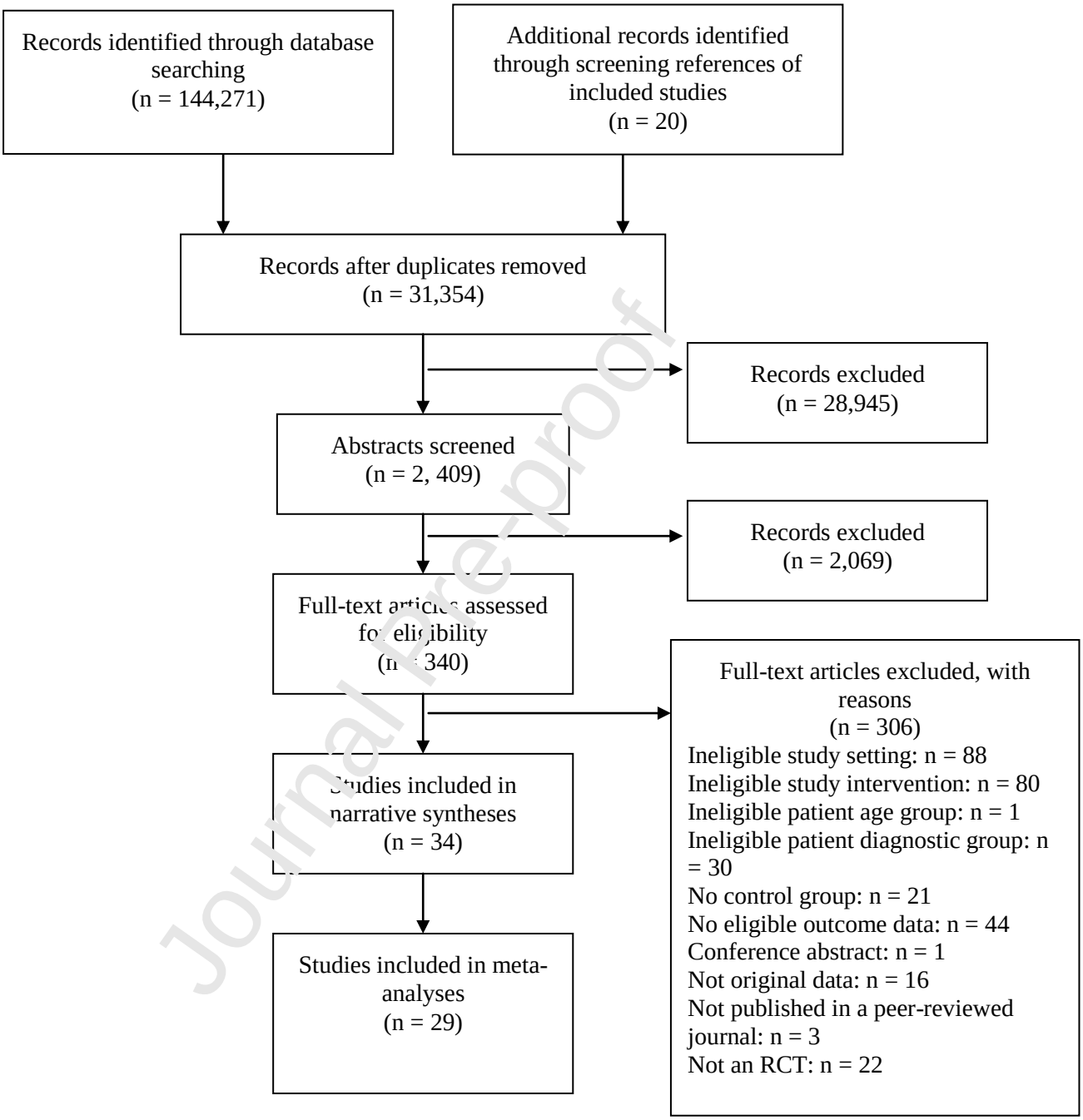

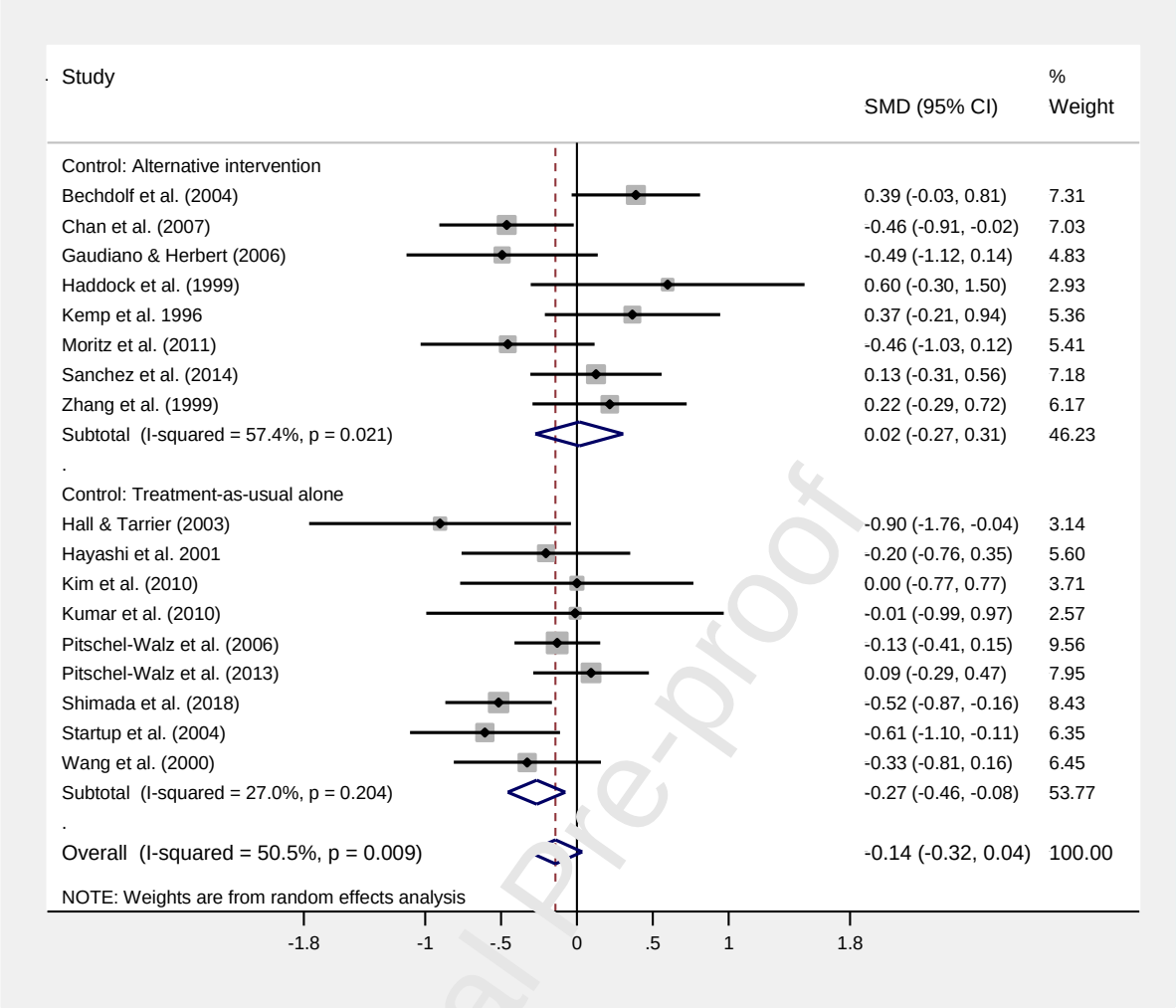

Figure 2. Meta-analysis of psychological interventions versus control treatment for post-intervention general psychopathology

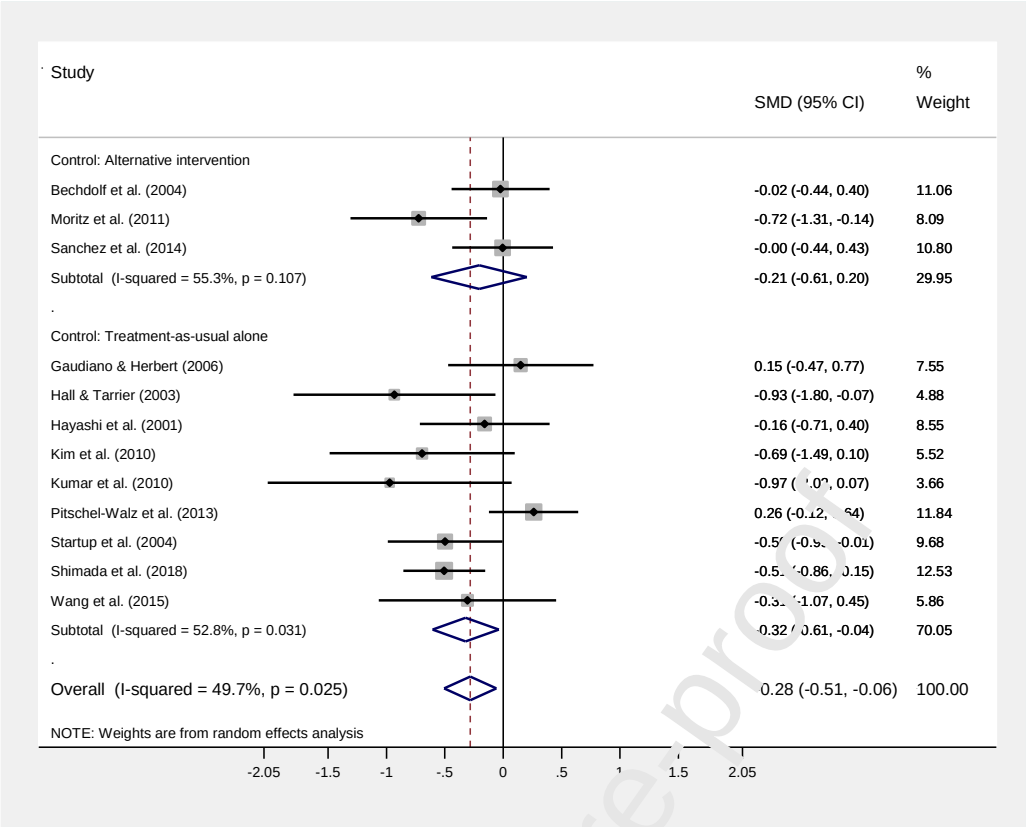

Figure 3. Meta-analysis of psychological interventions versus control treatment for post-intervention positive symptoms

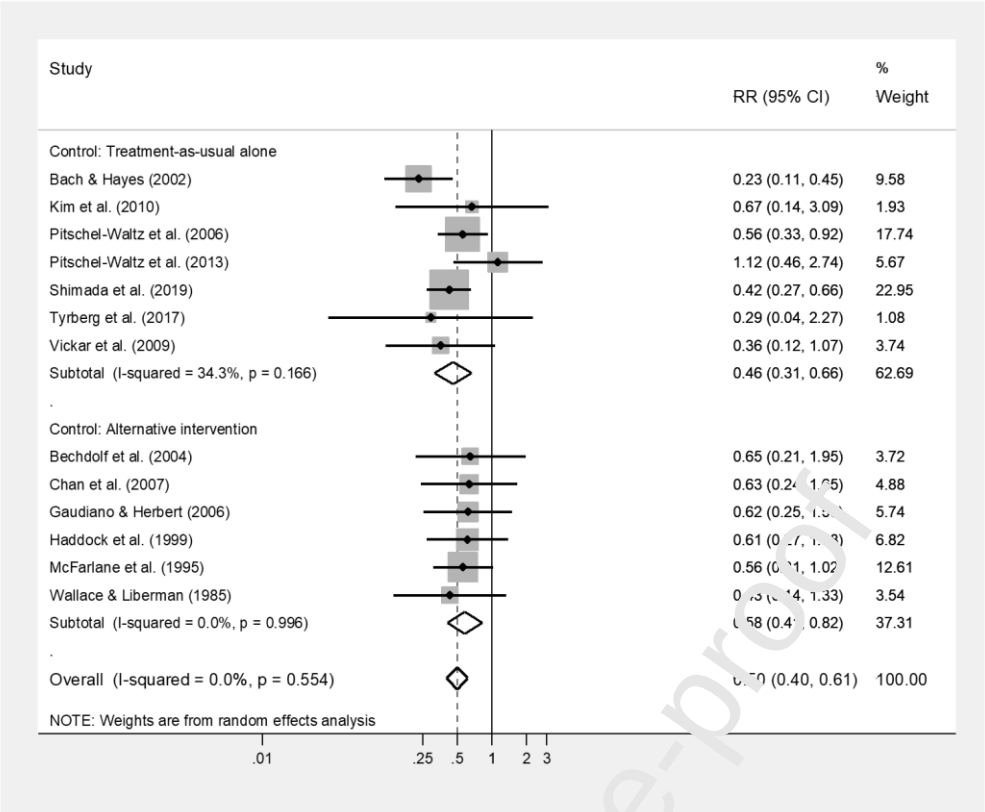

Figure 4. Meta-analysis of psychological interventions versus control treatment for relapse/ re-hospitalisation by follow-up

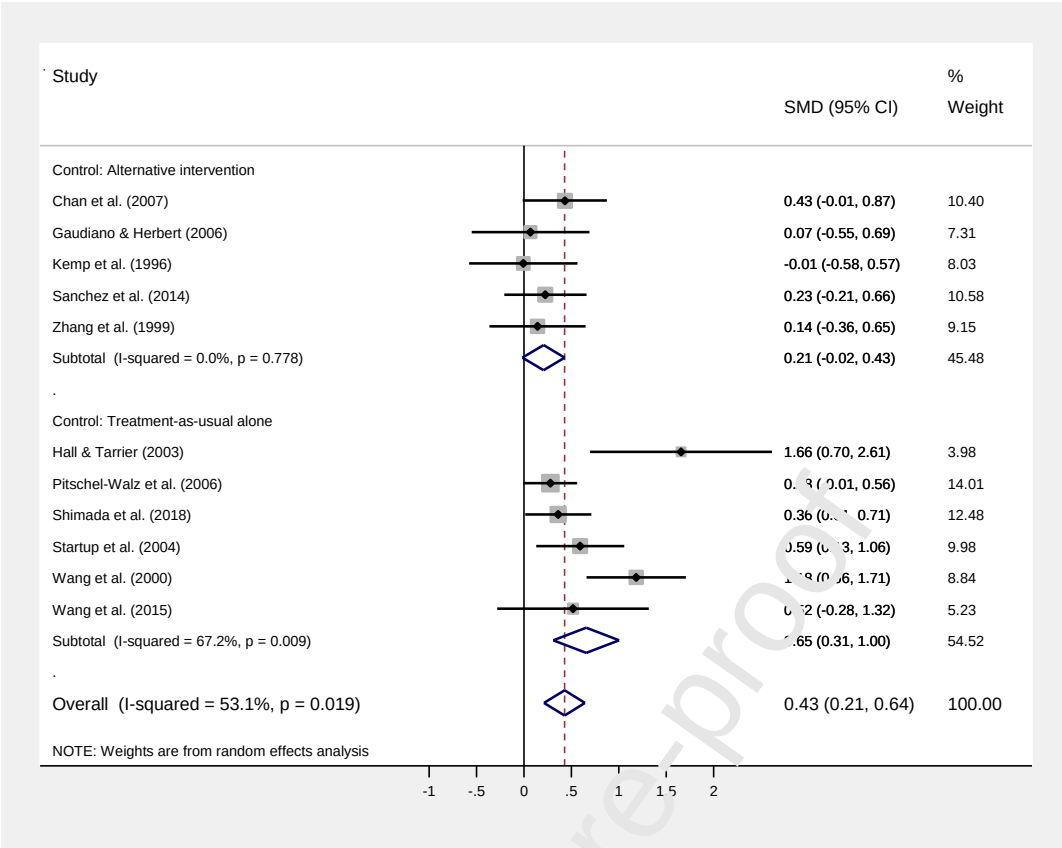

Figure 5. Meta-analysis of psychological interventions versus control treatment for post-intervention social functioning

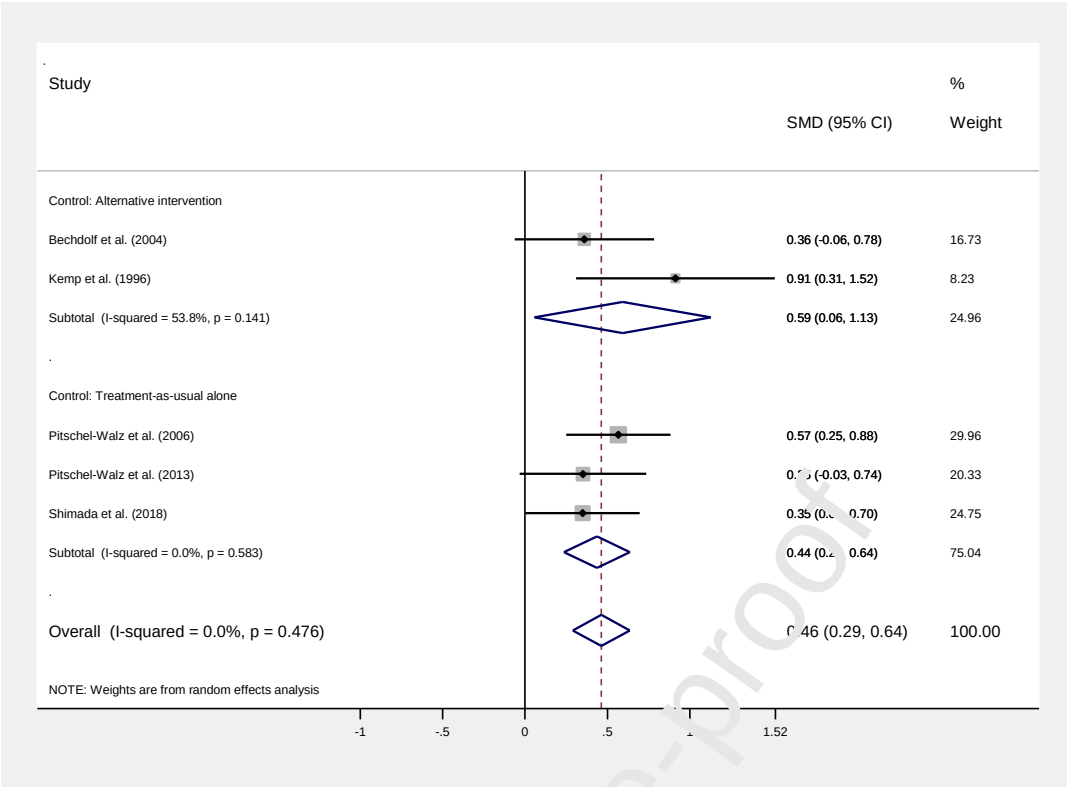

Figure 6. Meta-analysis of psychological interventions versus control treatment for post-intervention treatment compliance

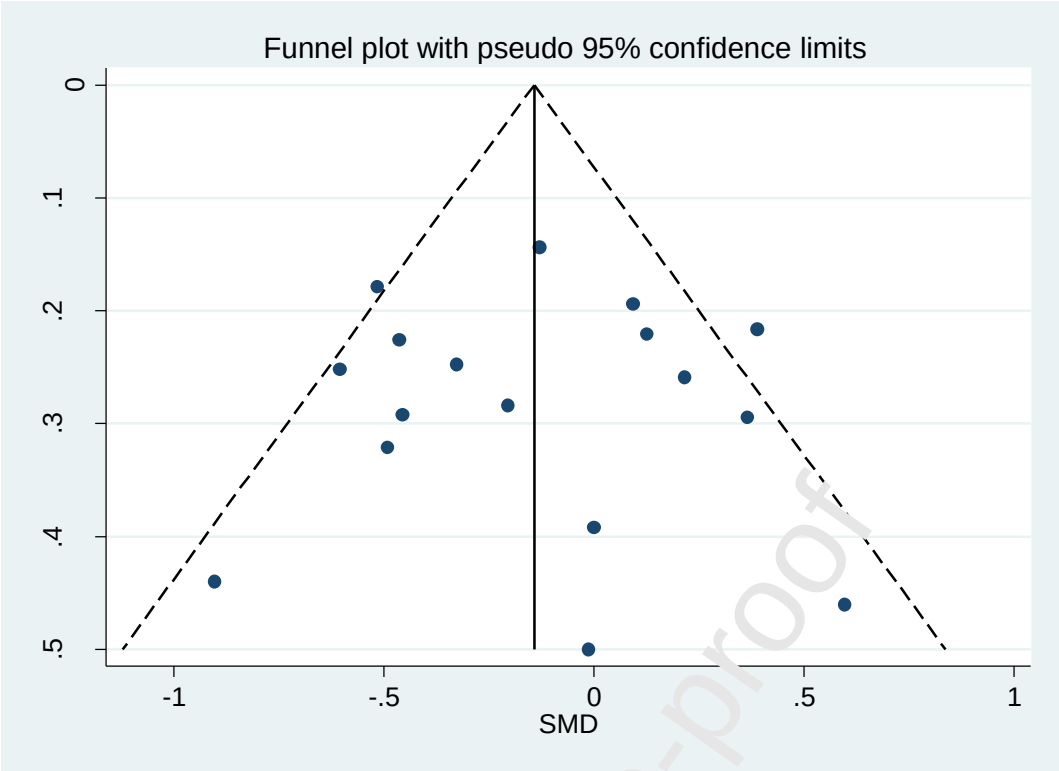

Figure 7. Funnel plot of SMD against standard error for general psychopathology outcomes (17 RCTs).

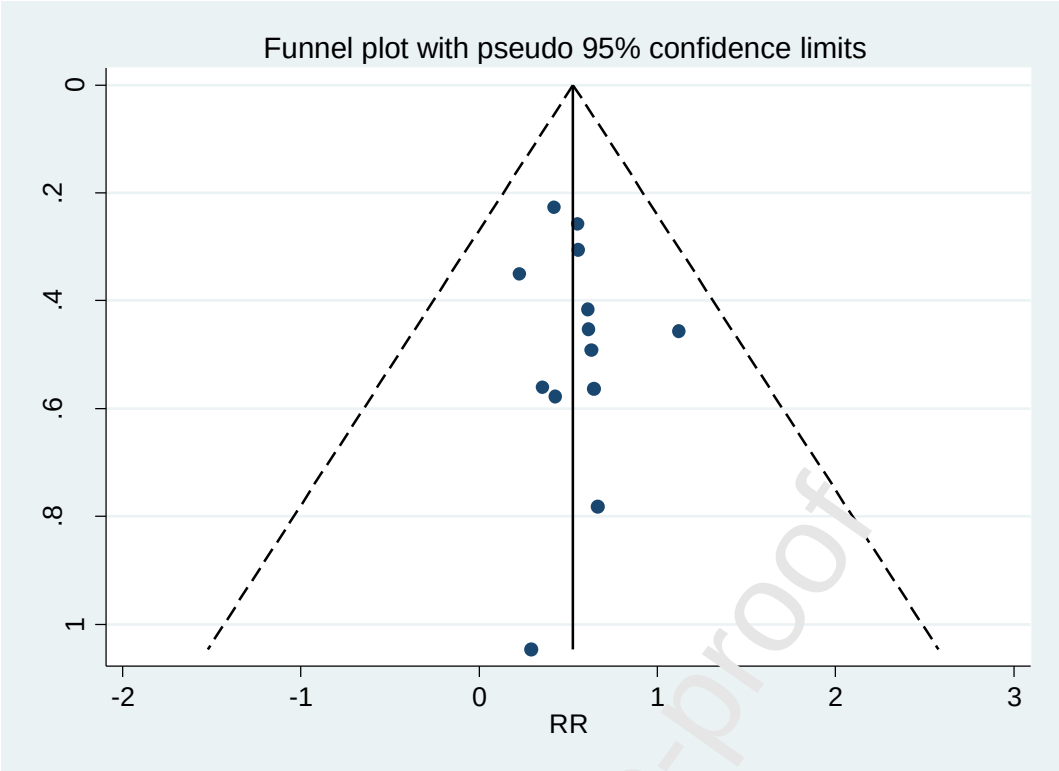

Figure 8. Funnel plot of risk ratio (RR) against standard error of log RR for relapse/ re-hospitalisation (13 RCTs).

Intervention	Intervention sub-type	Study	Sample size	Contro
ACT	ACT	Bach and Hayes (2002)	I = 40, C = 40	TAU alone
ACT	ACT	Gaudiano and Herbert (2006)	I = 19, C = 21	Non-directive
ACT	ACT	Tyrberg, Calrbring, and Lundgren (2017)	I = 12, C = 10	TAU alone
ACT	Morita therapy	Wang et al. (2000)	I = 33, C = 33	TAU alone
CBT	Cognitive therapy	Zhang, Yao, and Fang (1999)	I = 30, C = 30	Non-directive
CBT	CBT for internalised stigma	Wood, Byrne, Enache, and Morrison (2018)	I = 15, C = 15	Psycho-educat
CBT	CBT for low self-esteem	Hall and Tarrier (2003)	I = 12, C = 13	TAU alone
CBT	CBT for psychosis	Bechdolf et al. (2004)	I = 40, C = 48	Psycho-educat
CBT	CBT for psychosis	Haddock et al. (1999)	I = 10, C = 11	Non-directive Psycho-educat
CBT	CBT for psychosis	Habib, Dawood, Kingdon, and Naeem (2015)	I = 21, C = 21	TAU alone
CBT	CBT for psychosis	Startup, Jackson, and Bendix (2004)	I = 47, C = 43	TAU alone
CRT	Cognitive remediation therapy	Pitschel-Walz et al. (2013)	I = 59, C = 57	TAU alone
CRT	Cognitive remediation therapy	Sanchez et al. (2014)	I = 38, C = 54	Leisure group
CRT	Cognitive remediation therapy	Van der Gaag, Kern, van den Bosch, and Liberman (2002)	I = 21, C = 21	TAU alone
EMDR	EMDR	Kim et al. (2010)	I = 15, C = 15	TAU alone

Intervention	Intervention sub-type	Study	Sample size	Contro
Interpersonal	Interpersonal therapy	Kanas, Rogers, Kreth, Patterson, and Campbell (1980)	I = 40, C = 46	Activity group
MCT	Metacognitive training	Aghotor, Pfueller, Moritz, Weisbrod, and Roesch-Ely (2010)	I = 16, C = 14	Discussion gro (NP)
MCT	Metacognitive training	Kumar et al. (2010)	I = 8, C = 8	TAU alone
MCT	Metacognitive training	Moritz, Veckenstedt, Randjbar, Vitzthum, and Woodward (2011)	I = 24, C = 24	CRT
Motivational	Compliance therapy	Kemp, Hayward, Applewhaite, Everitt, and David (1996)	I = 25, C = 22	Non-directive
Motivational	Motivational interviewing	Hayashi, Yamashina, Igarashi, and	I = 25, I = 25	TAU alone

		Kazamatsuri (2001)		
Psycho-education	Patient-based psycho-education	Bechdolf et al. (2004)*	I = 40, C = 48	CBT for psych
Psycho-education	Patient-based psycho-education	Chan, Lee, and Chan (2007)	I = 44, C = 37	Occupational t (NP)
Psycho-education	Patient-based psycho-education with video self-observation	Davidoff, Forester, Ghaemi, and Bodkin (1998)	I = 9, C = 9	Patient-based psychoeducatio comedy video
Psycho-education	Patient-based psycho-education	Klingberg, Wiedemann, and Buchkremer (2001)	I = 63, C = 61	TAU alone
Psycho-education	Patient-based psychoeducation	Pitschel-Walz et al. (2006)	I = 125, C = 111	TAU alone

Intervention	**Intervention sub-type**	**Study**	**Sample size**	**Contro**
Psycho-education	Patient-based psycho-education	Wallace and Liberman (1985)	I = 14, C = 14	Social skills tra
Psycho-education	Patient-based psycho-education	Wang et al. (2015)	I = 14, C = 13	TAU alone
Psycho-education	Patient-based psycho-education	Wood, Byrne, Enache, and Morrison (2018)*	I = 15, C = 15	CBT for intern stigma
Psycho-education	Multiple family psycho education	McFarlane et al. (1995)	I = 83, C = 89	Single family p education
Psycho-education	Single family psycho-education	Haas, Glick, Clarkin, Spencer, and Lewis (1988)	I = 37, C = 55	TAU alone
Psycho-education	Single family psycho-education	Vickar, North, Downs, and Marshall (2009)	I = 26, I = 31	TAU alone
Psycho-education	Individualised occupational therapy	Shimada et al. (2018, 2019)	I = 68, C = 68	TAU alone
Social Skills	Social skills training	Wallace and Liberman (1985)*	I = 14, C = 14	Psychoeducati

Key. ACT = Acceptance and commitment therapy; C = Control condition; CBT = Cognitive behavioural therapy; CRT = Cognitive remediation therapy; EMDR = Eye movement desensitisation and reprocessing; Family = Family therapy; I = Intervention condition; MCT = metacognitive training; Non-directive SC or Nd-SC = Non-directive supportive counselling; NP = Non-psychological; TAU = Treatment as usual. * Study has been double-entered as control condition comprised a psychological intervention of interest. Risk of bias key a = randomisation method; b= allocation concealment; c= blinding of participants and personnel (omitted); d = blinding of outcome assessments; e = attrition bias; f = selective outcome reporting; H = high risk; L = low risk; U = unclear risk.

Table 1. Summary of included studies

- We reviewed trials of psychological interventions for acute inpatient schizophrenia
- Psychological interventions improve positive symptoms, functioning and compliance
- Psychological interventions reduce risk of relapse or re-hospitalisation
- Psychoeducation improves psychopathology and functioning and reduces relapse
- Specific evidence for other psychological interventions is preliminary or absent