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**Title**: A Systematic Scoping Review of Psychological Therapies for Psychosis within Acute

**Psychiatric Inpatient Settings** 

**Short Title:** Systematic review of acute inpatient therapies

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# A Systematic Scoping Review of Psychological Therapies for Psychosis within Acute Psychiatric Inpatient Settings

#### **Abstract**

*Background*: People with psychotic disorders account for most acute admissions to psychiatric wards. Psychological therapies are a treatment adjunct to standard medication and nursing care, but the evidence base for such therapies within inpatient settings is unclear. *Aims*: To conduct a systematic scoping review of the current evidence base for psychological therapies for psychosis delivered within acute inpatient settings (PROSPERO: CRD42015025623).

*Methods:* All study designs, and therapy models, were eligible for inclusion in the review. We searched PubMed, PsychINFO, EThOS, ProQuest, conference abstracts and trial registries.

Results: We found 65 studies that met criteria for inclusion in the review, 21 of which were randomised controlled trials (RCTs). The majority of studies evaluated cognitive-behavioural interventions. Quality was variable across all study types. The RCTs were mostly small (N<25 in treatment arm), and many had methodological limitations including poorly described randomisation methods, inadequate allocation concealment and non-blinded outcome assessments. We found studies used a wide range of different outcome measures, and relatively few studies reported affective symptoms or recovery-based outcomes. Many studies described adaptations to treatment delivery within inpatient settings, including increased frequency of sessions, briefer interventions and use of single-session formats. Conclusions: Based on these findings, there is a clear need to improve methodological rigour within inpatient research. Interpretation of the current evidence base is challenging given the wide range of different therapies, outcome measures and models of delivery described in the literature.

## **Declarations of interests**

The authors declare no competing interests.

#### Introduction

Psychiatric inpatient care is a scarce and expensive resource in healthcare systems across the world. Admission to hospital is usually a last resort for the most acutely unwell patients, and consequently the majority of inpatients have a psychosis diagnosis (1). Patient satisfaction with the care they experience during an inpatient admission is generally low (2, 3). A common source of dissatisfaction with acute inpatient care is the lack of access to psychological therapies, as an adjunct to medication (4). Good practice guidelines for inpatient wards recommend access to evidence-based psychological therapies (5). However, it is not clear what constitutes an evidence-based inpatient psychological therapy. International treatment guidelines for schizophrenia recommend Cognitive Behavioural Therapy for psychosis (CBTp) (6-8). However, these recommendations are largely based on trials conducted in community settings. At the time of writing the protocol for the current review, no systematic reviews or meta-analyses focusing solely on psychological interventions for psychosis within inpatient settings had been either published or registered on the PROSPERO database. The aim of the current paper was therefore intended mainly as a 'scoping' review. This kind of review is used to find out the potential size and scope of the available research literature, and may include ongoing or planned research (9). Scoping reviews are particularly relevant to areas of healthcare where it is not clear whether the evidence exists to answer a more precise question, such as the effectiveness of a particular therapy within a particular setting. The aim of this review was therefore to explore and map out the evidence base for psychological therapies for psychosis within acute inpatient settings.

#### Method

A review protocol was written and registered in the public domain before searching and data extraction began (PROSPERO Registration: CRD 42015025623). Five review questions were set in advance:-

- 1) What is the current state of the evidence base for psychological therapies for psychosis within acute psychiatric inpatient settings?
- 2) What study designs are used to evaluate psychological therapies for psychosis within acute inpatient settings?
- 3) How are psychological therapies for psychosis within acute psychiatric inpatient settings evaluated, and what are considered to be the key outcome measures?
- 4) What health care professionals are involved in delivering psychological therapies for psychosis, and in which roles (e.g. sole therapist, group co-facilitator, clinical supervisor)?
- 5) How are psychological therapies for psychosis adapted for use within acute psychiatric inpatient settings?

We included only studies published in English, with no date restrictions on searches. Searches were initially run in September 2015, and updated in December 2016. We planned to include a wide range of different study types to address the main review question pertaining to the current state of the evidence base. We anticipated that there would be relatively few eligible randomised controlled trials (RCTs), and the majority of studies would be small-scale, uncontrolled, non-randomised studies. Eligible studies therefore included RCTs, uncontrolled studies, observational studies, case studies, study protocols and qualitative studies. We searched for studies on psychological therapies for psychotic symptoms within acute psychiatric inpatient care (adult wards only). We defined inclusion based on the care setting, rather than solely the diagnosis of patients, on the basis that acute care is not diagnosis-specific in most countries, and not all patients receiving inpatient care may yet have an established diagnosis. We defined acute psychiatric care as including triage/acute assessment wards, general acute wards and psychiatric intensive care units (PICU). Non-acute inpatient care settings were excluded (e.g. rehabilitation wards, specialist units, residential therapy units). Non-inpatient acute services were also excluded (e.g. day

hospitals, crisis/home treatment teams). We included any psychological intervention/therapy aimed at alleviating distress or impairment to functioning arising from psychotic symptoms (e.g. voices, delusions) or aimed at emotional difficulties commonly associated with psychotic symptoms (e.g. anxiety, depression). This therefore excluded compliance therapy, and any intervention focused primarily on improving psychiatric 'insight'. We included individual, family and group therapies, delivered by any health care professional, of any length, frequency or duration, but not purely staff-based interventions, therapeutic community or milieu therapy. We included any therapies started within the acute inpatient setting, whether or not the therapies continued post-discharge. We included CBT-based psychological therapies, broadly defined as a talking therapy based on an underlying theoretical model of the relationship between thoughts, emotions and behaviours. So-called third-wave cognitive therapies including mindfulness, acceptance and commitment therapy (ACT), meta-cognitive therapy (MCT), dialectical-behavioural therapy (DBT) and compassion-focused therapy were included and classified as sub-types of CBT. Non-CBT based therapies such as psychodynamic therapy were also included. Cognitive-remediation therapy (CRT) was excluded on the basis that it is aimed primarily at remediating cognitive deficits rather than emotional difficulties associated with psychotic symptoms (likewise any intervention such as social skills training which is focussed primarily on the remediation of functioning). Arts therapies including art, drama and movement therapy were also excluded. Studies with any, or no control conditions, were included. The search strategy and search terms for each resource is available in online supplementary material.

Eligible studies were identified by the primary (PJ) and secondary (KH) reviewer. In the first stage, PJ independently screened all titles and abstracts identified from searches to determine which met the inclusion criteria. In the second stage, PJ and KH both independently screened full text articles for inclusion or exclusion, with discrepancies resolved by discussion. For included studies, we linked multiple reports from the same study, so that each study (rather than each report) was the unit of interest in the review. A standard data extraction template was used to record relevant information from each included study. Data for each study were extracted by either PJ or KH, with each reviewer cross-checking each of the other reviewer's forms to ensure consistency and accuracy of data extraction. In keeping with the range of this 'scoping' review, the quality of eligible studies was assessed using the Mixed Methods Appraisal Tool (MMAT; Pluye (10)). The MMAT is designed to assess quantitative, qualitative and mixed methods studies using a single integrated tool. The initial stage

involved assessing each study according to two standard screening questions (is there a clear research question, and do the data collected address this question). Further assessment with the MMAT was not feasible or appropriate for studies which failed the screening questions, or which did not report any outcomes (whether quantitative or qualitative). The second stage involved assessment under 1 of 5 categories, depending on the type of study, each with 4 assessment criteria. A summary score was calculated by dividing the number of criteria definitely met (i.e. scored as a 'yes') divided by 4, and expressed as a percentage. Quality scores therefore ranged from 0%, 25%, 50%, 75% to 100%. We additionally assessed the RCTs using the Cochrane Risk of Bias criteria (11).

#### **Results**

As shown in Figure 1, we identified 65 studies for inclusion in the review. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in summarising the search results (12). Fourteen of the 65 studies were linked to at least one other record (e.g. Drury et al (13) was published as 3 peer-reviewed journal articles as well as a PhD thesis). In this case, where at least one of the records was a peer-reviewed journal article, this was taken as the 'primary' reference. In the case of RCTs, which often published acute-phase and follow-up data in separate journal articles, the paper that had been published first was designated as the primary paper. However, the data extraction form was completed using all relevant information across all linked studies. Overall, 58 out of the 65 studies had a peer-reviewed journal article designated as the primary paper. Of the remaining studies, 4 were published solely as book chapters, 1 was published as a PhD thesis and we could not find any subsequent published journal articles (14) and the remaining 2 existed only as trial registry records - one of these had not yet been published in a peer-reviewed journal because the trial was still on-going (15), and the other reported results on the trial registry website but we could find no evidence of subsequent publication in a peer-reviewed journal (16).

Figure 1: PRISMA Flowchart

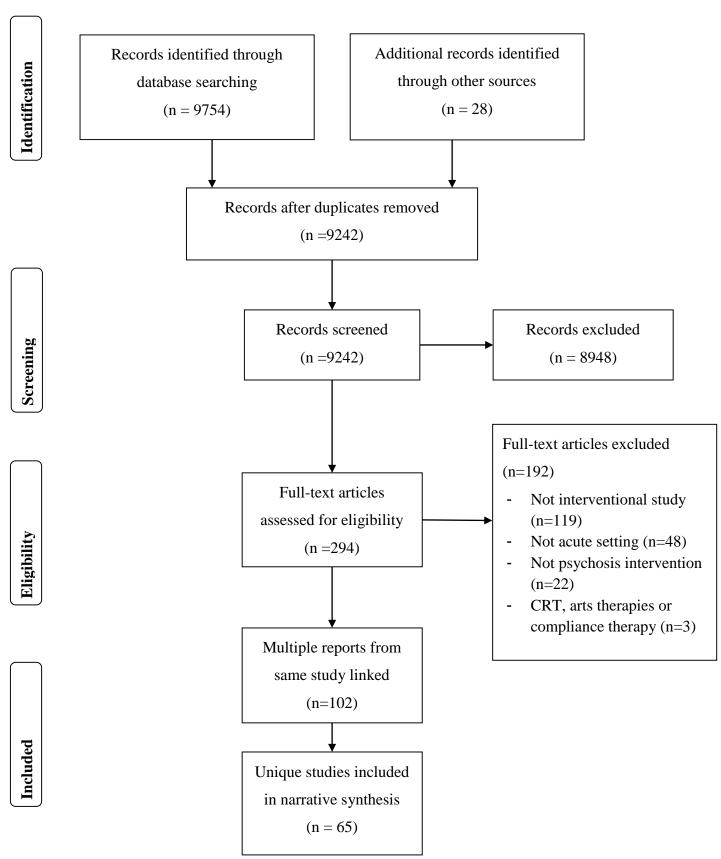


Figure 1: PRISMA Flowchart

# Review Question 1: Current state of evidence base

Sixty-five studies were included in the review (see online supplementary material). Overall, 40% of studies failed the initial MMAT screening stage (26/65). Of the remaining 60% which were assessed further, 21.5% were rated as high quality, 20% were medium quality and 18.5% were low-quality. We broadly categorised therapies into CBT, and non-CBT models, with sub-types of therapy noted where appropriate. Overall, we found there were slightly more CBT studies (N=35) than non-CBT therapies (N=28). We took a broad definition of therapy models, but even so were unable to categorise two studies into a recognisable therapy model (Dichos therapy (17) & Computer-facilitated therapy (18)). Among the CBT studies, there was a noticeable increase in so-called third wave cognitive therapies in recent years, with 12 studies categorised as either mindfulness, compassionfocused, or acceptance and commitment therapy (ACT). The majority of the non-CBT studies were psychodynamic (N=17). A clear difference emerged between countries in their dominant therapy models. For the UK studies, over 75% were CBT based (16/20). However, the reverse was true for the USA studies, with 62% of studies being non-CBT based (16/26). For other countries (which were predominantly European), CBT and non-CBT studies were more evenly balanced (11 CBT and 8 non-CBT). The first CBT studies did not emerge until the 1980s, but they represent the majority of studies included in the review published since 2000.

In order to provide a broad overview of the main findings of the studies in the review, relevant studies were identified according to four criteria. These were 1) the stated aim of the study was described as evaluating efficacy/effectiveness 2) the study reported at least one outcome measure 3) the study stated which was the primary outcome measure, where multiple outcomes were reported and 4) the study passed MMAT screening stage. Twelve studies in total met all these criteria and are summarised in Table 1, in chronological order. No exclusions were made based on study quality, therefore the findings should be interpreted with appropriate caution, and in the context of the associated MMAT quality scores (see online supplementary material).

 $Table\ 1\ Summary\ of\ main\ findings\ (efficacy\ studies\ with\ primary\ outcomes\ only)$ 

Author (year)	Treatment	Control condition(s)	Primary Outcome Measure	Main Findings
Study Design	n=no. of participants	n=no. of participants		
Country				
Bookhammer et al	Rosen's Direct	Treatment as Usual	Binary outcome of	No difference in rates
(1966)	Analysis	(TAU)	improved/unimproved as rated by treating	of improvement between the Direct
Non-randomised Controlled Trial	n=14	n=37	clinician at 5 year follow-up	Analysis and TAU groups
USA				
Serok and Zemet	Gestalt group therapy	Treatment as usual	Neuropsychological	Gestalt group showed
(1983)		(TAU)	reality perception test	evidence of improvement in
Non-randomised Controlled Trial	n=16	n=15		perception of self and others
Israel				
Beutler	1) Behavioural/task	Treatment as usual	Composite symptom	Compared to TAU
(1984)	(BT)	(TAU)	measure (including	group:-
D 1 ' 1	2) Expressive-		symptom check-list,	1) no change in BT
Randomised Controlled Trial	experiential (EE) 3) Process-oriented		nurse assessment, and group facilitator	group, 2) deterioration in EE
Controlled IIIai	(PO)		ratings)	group
USA	(10)		ratings)	3) improvement in
	Number of			PO group
	participants in each			
	group not stated			
	(Total n=176			
	including controls)			
Cholet	Humanistic-	Equivalent time as in	Behavioural	No difference
(1984)	existential (HE) psychotherapy	treatment condition spent with college	adjustment scale (staff rated)	between groups on mood, co-operation
Randomised	psycholierapy	student	(starr rateu)	or communication
Controlled Trial		student		sub-scale but
	n=20	n=20		significant
USA				improvement on
				social contact scale in
				HE group compared
				to control
Cole and Greene	Unstructured	Structured	Patient self-report of	Patients preferred the
(1988)	psychodynamic	occupational therapy	which group they	occupational therapy
Service Evaluation	group	group	preferred	group to the psychodynamic
Service Evaluation	n=20 (repeated	n=20 (repeated		group
USA	measures design –all	measures design –all		8
	patients did both	patients did both		
	groups)	groups)		
Bach and Hayes	Acceptance and	Enhanced Treatment	Re-admission to	Re-admission to
(2002)	Commitment	as Usual (ETAU)	hospital at 4-month	hospital was
Dandamias 1	Therapy (ACT)		post-discharge	significantly lower in
Randomised Controlled Trial	n=40	n=40		the ACT group (20%) compared to
Controlled IIIai	11-40	11—40		the ETAU group
USA				(40%)
Hauff et al (2002)	Specialist therapy	Standard care on	Global mental health	No difference
· · · · /	ward with individual	acute ward	status at 7 year	between outcomes
Non-randomised	psychotherapy +		follow-up	for patients treated on
Controlled Trial	psychodynamic			the specialist therapy
	milieu			ward compared to the
N	25	71		standard care ward
Norway	n=25	n=71		

Lewis et al (2002)	Cognitive-behaviour therapy (CBT)	Supportive counselling	Psychotic symptoms at 70 day follow-up	All patients improved significantly over time, with a trend to
Randomised Controlled Trial	n=101	n=106		faster improvement in the CBT group
UK		Treatment as usual (TAU)		
		n=102		
Startup et al (2004)	Cognitive-behaviour therapy (CBT)	Treatment as usual (TAU)	Psychotic symptoms at 12 month follow-	The CBT group showed significantly
Randomised Controlled Trial	n=47	n=43	up	greater improvement compared to the TAU group
UK				
Veltro et al (2006)	Cognitive-behaviour group therapy (CBT) as part of ward	Ward routine care before introduction of CBT programme	Total re-admissions up to 4 year follow-up	The re-admission rate was significantly lower in the 4 years
Non-randomised Controlled Trial	routine care  n=352	(pre-post design) n=150		following the introduction of CBT (24%) compared to
Italy				the year before its introduction (38%)
Klingberg et al (2010)	Cognitive Behaviorally Oriented Service	Individual supportive treatment – individual and group	Mean time to relapse (defined by deterioration on	Mean time to relapse was significantly longer in the CBOS
Randomised Controlled Trial	(CBOS) – individual, group and family sessions	sessions based on practical and non- directive emotional	psychotic symptom rating scale)	group (168 days) compared to the control group (157
Germany		support		days)
	n=84	n=85		
Moritz et al (2011)	Meta-Cognitive Therapy (MCT)	Cogpak (computerised cognitive remediation	Delusions severity at end of treatment	Significantly greater decline in delusion severity in the MCT
Randomised Controlled Trial	n=24	therapy)		group compared to control group
Germany	11-27	11-27		

# Review Question 2: Types of study design (including quality assessment)

As expected, a full range of study designs were included in the review, from single case studies to large-scale RCTs. RCTS were more likely to describe CBT, rather than non-CBT interventions, and the converse was true for non-randomised controlled trials. Service evaluation, case series/studies and qualitative studies were more evenly matched between CBT and non-CBT models. Quality assessment scores were variable across different categories of study designs. For the RCTs (N=21), there was evidence of an improvement in quality over time, as all studies published pre-2000 were rated as low-medium quality (0-50%), but post-2000 included at least 5 studies rated as high quality (75-100%). This probably reflects improvements in trial reporting guidelines arising from the first publication

of the CONSORT statement in the 1990s (19), and its subsequent adoption by most major journals.

In addition to the MMAT, we also assessed RCTs using the Cochrane Risk of Bias (see online supplementary material). Overall, the risk of bias was lower for attrition and reporting bias, with most RCTs reporting <20% loss to follow-up at trial end-point, and appropriately reporting pre-specified trial outcomes. However, randomisation methods, allocation concealment and blinding were causes for concern (Figure 2). Only two of the RCTs clearly stated using the 'gold standard' of an independent randomisation service with randomly varying block sizes, with a large number of studies not specifying the randomisation method at all (N=10). A minority of studies mentioned blinding of outcome assessors, and blinding of the inpatient and/or community teams potentially involved in treatment decisions. Size of trials was also a concern – out of the 19 RCTs with published results, over half (N=10) had fewer than 25 people in the treatment arm. Finally, most of the RCTs used TAU (or 'enhanced' TAU in the Gaudiano trials) as the control arm (N=11), and therefore did not control for non-specific therapy factors such as time and attention from a warm, empathic therapist. A minority of trials did use an active control arm. One of the largest trials had a strong design in this respect, and included both a supportive counselling and TAU condition, with over 100 participants in each arm (20).

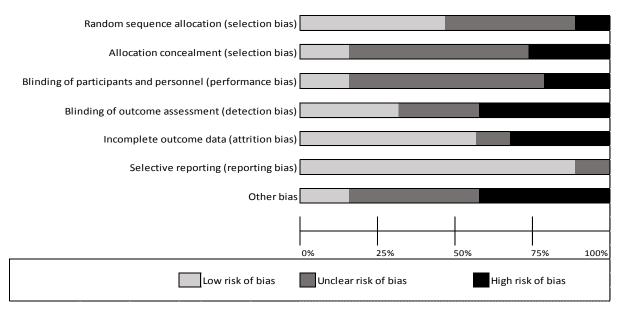


Figure 2 Risk of Bias Summary for RCTs presented as percentages across included studies (N=19)

# Review Question 3: Evaluation and Outcome measures

Most of the studies included in the review reported collecting some kind of outcome measure (N=48). We categorised the outcome measures used into four main categories (psychotic symptoms, affective symptoms, general/clinical functioning, and readmission/relapse). The results are summarised in Table 2. Where outcome measures were reported, these were usually focused on assessing psychotic symptoms and/or general functioning. There were relatively few studies that reported assessing affective symptoms, such as depression or anxiety. Only 3 of the 65 studies used self-report recovery measures. Even though they were not usually the primary outcome measure, many studies reported readmission/relapse data. The timing of outcome assessments was variable, and usually included a combination of different time points (e.g. baseline, discharge and 6-month follow-up). The assessment schedule was not specified in two studies. For the remaining studies 46 studies, 32 reported data at baseline, 12 reported outcomes session-by-session, 4 at mid-therapy and 26 at discharge/end of therapy. Twenty-one studies reported follow-up data beyond the end of therapy. The longest follow-up point was 6 months or less for 10 studies, and longer than 6 months for the remaining 11 studies.

Table 2 Summary of outcome measures for studies reporting any kind of outcome (N=48)

	INCLUDED?	
DOMAIN (No. of studies including each scale in parentheses)   N=48 studies (21 RCTs)	Yes (RCTs only)	No (RCTs only)
1) Psychotic symptoms	21 (16)	27 (5)
- UNPUBLISHED SCALES (4) - PANSS (7) - PSYRATS (5) - BPRS (5) - PAS (2) - SAPS/SANS (2) - SAHI (1)	21 (10)	21 (3)
2) Affective symptoms  - UNPUBLISHED SCALES (3)  - BAI/BDI (2)  - HADS (1)  - DASS (1)  - HDI (1)	7 (2)	41 (19)
3) General/Clinical Functioning  - GAF (3) - HSRS (1) - GAS (3) - ADL (1) - CORE (34 OR 10 ITEM) (2) - CGI-S (1) - SFS (3) - NOISE (1) - OQ-45 (1)	14 (7)	34 (14)
4) Recovery  - Self-rating of goals (1) - MHCS (2) - QPR (1)	3 (1)	45 (20)
5) Readmission  Relapse (defined other than just readmission e.g. exacerbation in symptoms)	13 (10) 6 (4)	35 (11) 42(17)

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<sup>&</sup>lt;sup>1</sup> Some studies included more than 1 scale within the same domain

Key to abbreviations: PANSS=Positive and Negative Syndrome Scale (21); PSYRATS= Psychotic Symptom Rating Scales (22); BPRS=Brief Psychiatric Rating Scale (23); PAS=Psychiatric Assessment Scale (24); SAPS=Scale for the Assessment of Positive Symptoms (25); SANS=Scale for the Assessment of Negative Symptoms (26); SAHI=Structured Auditory Hallucinations Interview (27); BDI=Beck Depression Inventory (28); BAI=Beck Anxiety Inventory (29); HADS=Hospital and Anxiety Depression Scale (30); DASS=Depression, Anxiety & Stress Scales (31); HDI=Hamilton Depression Inventory (32); GAF=Global Assessment of Functioning (33); HSRS=Health Sickness Rating Scale (34); GAS=Global Assessment Scale (35); ADL=Activities of Daily Living; CORE=Clinical Outcomes in Routine Evaluation(36); CGI-S=Clinical Global Impression Scale (37); SFS=Social Functioning Scale (38); NOISE=Nurses' Observation Scale for Inpatient Evaluation (39); OQ-45=Outcome Questionnaire-45 (40); MHCS=Mental Health Confidence Scale (41); QPR=Questionnaire about the Process of Recovery (42)

## Review Question 4: Delivery of therapies

The most common mode of delivery was group therapy (N=27), followed by individual therapy (N=19). There was a notable difference in the types of trial design between group and individual treatment modalities. The majority of the studies describing individual therapies were RCTs (12/19), compared to 3/27 of the group therapy studies. As anticipated, a variety of staff groups were involved with delivering psychological therapies within inpatient settings, including psychologists, psychiatrists, nurses, occupational therapists, social workers, family therapists, CBT therapists and clinical trainees from different disciplines. It was notable however that almost a third of the studies included in the review failed to specify the professional group delivering the intervention. This limits the interpretation and replicability of such studies. The primary, or sole, therapist was described as a Clinical Psychologist in the majority of studies where the profession was specified (N=14).

Training, supervision and checks on treatment fidelity were generally poorly described or entirely absent. Over 50% of studies included in the review gave no details about training and supervision of therapists. For the 21 RCTs in the review, only a third of studies (N=7) clearly reported that the staff delivering the intervention were both trained and supervised. An additional third reported either staff training or supervision, but not both. The final third gave no details on either. The majority of RCTs gave no details on checking treatment fidelity. Only eight studies reported fidelity checks – this was usually done by an independent rater reviewing a sample of audiotapes of therapy sessions (N=6), but the use of direct observation (N=1) and videotapes (N=1) was also reported.

# Review Question 5: Adaptations to facilitate delivery within acute settings

After an initial review of the included studies, we identified and categorised studies according to five main adaptations. These were 1) increased frequency of sessions ( $\geq 2$  sessions a week), 2) briefer interventions (≤5 sessions), 3) shorter sessions (<50 minute standard length of sessions), 4) use of single session format (i.e. each session is stand-alone, although therapy may include more than one session) and 5) continuing therapy post-discharge. The most common adaptation was an increased frequency of sessions. An increased frequency of sessions sometimes reflected an attempt to deliver a larger number of sessions within a shorter period of time to fit the typical length of an inpatient admission. Other studies aimed to deliver a smaller number of sessions, but still had an increased frequency of sessions to fit in with short lengths of admissions (43, 44). Only a quarter of studies reported briefer interventions (15/65), with 5 or fewer planned sessions. This is perhaps surprising given concerns that acute admissions are short, and so there is limited time to provide psychological therapies. However, the number of planned sessions, or the average number of sessions delivered per patient, was often not stated, and we were unable to extract this information for many studies. We found that the use of the standard therapy 'hour' (i.e. around 50 minutes) was in fact the most commonly reported length of session (41/65). Over a third of studies reported using a single-session format (24/65). This may be particularly helpful in settings when length of admission is unpredictable, and discharges may occur unexpectedly in the middle of treatment. Single-session formats may be particularly useful in groups, in meeting the needs of people who may attend only 1 session, but also in allowing people to flexibly 'drop in' over the course of an admission. In relation to group interventions, the use of single-session formats is of course closely linked to whether the group is open (people can join and leave at any session) or closed (people can join only at the beginning and are encouraged to stay for the full course). We found that open groups were the most common format reported (N=17), with only two studies explicitly reporting a closed group format (45, 46). It was not always clear whether group formats were open or closed. There was some reference to continuing therapy post-discharge in 13 studies. This was sometimes to allow people to complete a set number of sessions, for a group (47) or individual intervention (43). Some studies offered booster sessions post-discharge, but take-up of these was generally low. (20, 48)

#### **Discussion**

We conducted a systematic scoping review of psychological therapies for psychosis within acute inpatient settings. We found that there were a broad range of therapies in the published literature, delivered in many different ways, by different groups of professionals, and evaluated using a wide range of approaches. This makes a coherent synthesis of current evidence challenging. Quality was varied across different study types and over time, but we found significant methodological weaknesses in many studies, including in RCTs. Such a high degree of heterogeneity surely provides a challenge to any quantitative synthesis of findings by means of a meta-analysis. Reporting of diagnosis or symptom profile is also inconsistent in the literature – and indeed, in practice often there is no clear diagnosis for inpatients. For this reason the present review took the pragmatic step of selecting studies on the basis of setting (acute inpatient) and type of psychological therapy (e.g. CBT for psychosis). We would recommend all future inpatient research on psychological therapy for psychosis report diagnostic information on participants where available, in addition to symptom profiles using established assessment tools.

Evaluating therapies within inpatient settings is undoubtedly challenging. It is not possible, or indeed ethical, to control or keep constant all other elements of treatment each person is receiving, such as medication, nursing care or occupational therapy. Attributing change, whether it be improvement or deterioration, to any single component of treatment is therefore not normally possible. There is also the problem of accounting for 'natural' recovery after a mental health crisis. The added value of any psychological intervention should therefore always be carefully assessed.

## Outcome assessment

The present study focussed on patient outcomes – as opposed for example to change in ward milieu or in staff well-being. Direct patient outcomes can relate to well-being during admission (e.g. psychotic symptoms, length of admission), or after (e.g. subsequent relapse or readmission rates), or both. The studies reviewed included a wide range of primary and secondary outcomes and assessment tools, making it difficult to draw conclusions. The field may therefore benefit from the development of an agreed standardised set of outcomes, known as 'core outcome sets' (COS). A COS can be used as the minimum to be reported for

any study or trial, and makes it easier to combine and compare the results of studies, over time, and from different countries. The urgent need for a COS in psychosis can be no better demonstrated than by the findings of a recent review of schizophrenia intervention trials (both drug and psychological therapy trials) which found 2194 different scales were used to measure outcomes, with every fifth study introducing a new rating instrument (49). We would encourage development of COS for inpatient research that address core outcomes both during and post admission.

## *Therapy delivery*

Only 3/27 evaluations of group therapies used an RCT design, which may reflect methodological challenges in evaluating inpatient groups – in-patient group therapies are normally open to everyone on a ward, for ethical and practical reasons, and there is also increased risk of treatment "contamination" between conditions on inpatient wards where patients are in close proximity. One potential solution is to use a cluster randomised design, where individual wards are randomised to a particular intervention, rather than individual patients, although there are often important differences between wards (e.g. catchment area, therapeutic milieu) and larger sample sizes are needed, which is often a barrier to conducting this kind of study in routine clinical practice. (50)

## Adapting therapy protocols for in-patient settings.

The majority of studies reported having adapted psychological therapy for delivery within inpatient settings. Commonly this meant offering traditional numbers of sessions but more frequently, or offering fewer sessions, or developing a single-session format. We would recommend that future research describe more clearly the process of adapting therapies and protocols: for example, giving a clear rationale for the need to adapt a therapy; a clear rationale for the chosen adaptations; a clear statement about if and how the adaptations were piloted (e.g. a small case series); being clear about the degree of service user consultation and participation throughout the process. Furthermore, future research might examine, perhaps through mixed methods, the impact of the specific adaptations made.

## Strengths and limitations

As this review was planned as a scoping review, we designed the strategy accordingly, and published our search strategy and review questions in advance on the PROSPERO database. A particular strength of this review is that we searched for literature from a wide variety of sources, including those not readily available (e.g. non-digitised book chapters, unpublished PhD theses). However, work not published in academic journals has not been subject to the same degree of peer review or scrutiny, and therefore should be interpreted with caution. We also attempted to search for studies underway as well as completed, by searching trial registries for planned or ongoing research, and by contacting experts in the field. However, despite increasing calls for all trials to be pre-registered on a public registry, compliance is still variable. Therefore, we cannot exclude the possibility that there is work underway that we would not have found from registry searches. There were some challenges in defining acute care for the purposes of this review, as care settings vary from country to country, and over time within the same country. We therefore adopted a liberal definition of acute care, and erred on the side of being over-, rather than under-inclusive. In circumstances where the care setting was unclear, or did not easily fit into standard categories of inpatient care, we focused on assessing the eligibility of the intervention itself, and included interventions that seemed feasible to deliver within an average 30-day admission. However, difficulties in defining key terms in the search strategy may have led to relevant studies being excluded, or less relevant studies being included in the final review.

# Conclusions and implications for practice

As this was a scoping review rather than a formal attempt to synthesise efficacy data, we cannot draw any firm conclusions in terms of what psychological interventions are most efficacious within acute inpatient settings. However, from the efficacy studies summarised in Table 1 there appears to be some promising evidence for the role of CBT-based approaches in reducing psychotic symptoms and reducing risk of relapse over the short-term. A systematic approach is now clearly needed to develop the evidence base for inpatient psychological interventions, and to progress from promising pilot studies to larger, well-designed RCTs in line with guidelines for developing complex interventions (51). The nature of inpatient care has undoubtedly changed over the 60+ years covered by this review; for example, in UK settings, there has been a move towards shorter acute admissions and an

increasing proportion of involuntary admissions (1). This not only poses new challenges for inpatient therapies in terms of developing briefer interventions, which can be effectively integrated within a larger care pathway, including community and crisis services, but also highlights opportunities for acute care to be a time to engage patients in psychological therapies which may outlast the admission. Qualitative research (including pre-trial assessment) also has a role to play, for example in optimising use of interventions within RCTs and in informing future choice of interventions (52). Core outcome sets are required to establish common, minimum outcomes both during and post admission, and the process of adapting therapies for in-patient settings needs greater methodological rigour and clarity.

#### **Contributors**

All authors contributed to the design of the review protocol. PJ designed the literature search. PJ and KH reviewed abstracts, selected studies for inclusion, and extracted data. PJ wrote the review, and all authors read and approved the final manuscript.

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#### **Research Ethics**

Ethical approval not required.

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary  2 Provide a structured summary including, as applicable: background; objectives; data sources; study eligibilit criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusion and implications of key findings; systematic review registration number.		2	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.	N/A

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	Sk of bias across studies  15 Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).		11
Additional analyses	dditional analyses  16 Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.		N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics  18 For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up and provide the citations.		Supplementary material	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11
		For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

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# **Online Supplementary Material**

# **Search Terms**

Category	Database/resource searched	Search Terms
1. Electronic Databases  Combination of searches with 3 concepts:- Concept 1 – PSYCHOTHERAPY (includes all sub-types of therapy)  AND Concept 2 – SCHIZOPHRENIA (includes psychosis)  AND Concept 3 – ACUTE/INPATIENT psychiatric setting	PsychINFO	<ul> <li>brief psychotherapy</li> <li>hospital admission</li> <li>psychiatric hospital admission</li> <li>psychiatric hospitalization</li> <li>psychiatric hospitals</li> <li>psychiatric units</li> <li>psychotherapy</li> <li>schizophrenia</li> </ul> (.tw.) qualifier used to search following terms in title and/or abstract:- <ul> <li>acute</li> <li>hospita*</li> <li>inpatient?</li> <li>psychosis</li> <li>psychoses</li> <li>schizo*</li> <li>therap*</li> </ul>
	PubMed	((inpatient) AND psychosis) AND (psychotherapy OR therapy)
	EThOS	

2. Th	eses/Dissertations	ProQuest	(any word)=psychosis OR schizophrenia AND (acute OR inpatient)				
3. Public	Professional Body cation	Clinical Psychology Forum	Hand-searched				
4. abstra	Conference acts	Conference Proceedings Citation Index - Science (CPCI-S)	(Topic Heading=(psychosis OR psychotic OR schizo*) AND TS=(acute OR hospita* OR inpatient*) AND TS=therap*)				
5.	Trial Registries	ISRCTN registry Clinicaltrials.gov Cochrane Central Register of Controlled Trials	Condition=psychosis OR schizophrenia Inclusion criteria=inpatient OR acute Interventions=therapy OR behavioral				
6.	<b>Existing Reviews</b>	Cochrane Library	TOPIC=mental health OR schizophrenia/psychosis AND therapy				
7.	Grey Literature	Trip Database Open Gray	(Area of Clinical Practice = Medicine OR Psychology OR Psychiatry OR Mental Health) AND (Psychotherapy OR Psychological therapies) AND (Inpatient OR Hospital)				

# **Studies included in review (with quality assessment)**

For ease of interpretation, MMAT scores are colour-coded with low quality scores (0%-25%) in red, a medium score (50%) in orange and high scores (75%-100%) in green.

No.	Author	Study	Therapy Model	Mode of	Outcome	MMAT	MMAT
	(year)	Design (Record	(Sub-type)	Delivery	Data Reported?	Section assessed	score
	n=total no. of participants	type)			Reporteu:	under	
	Country						
1	Kanas et al. (1980) (1)	RCT <sup>2</sup> (JA) <sup>3</sup>	Non-CBT <sup>4</sup> (Psychodynamic)	Group	Yes	2. RCT	0%
	n=86						
	USA						
2	Beutler (1984) (2)	RCT (JA)	CBT	Group	Yes	2. RCT	25%
	n=176						
	USA						
3	Cholet (1984) (3) n=40	RCT (Thesis)	Non-CBT (Humanistic- Existential)	Individual	Yes	2. RCT	50%
	USA						
4	Glick et al (1985) (4)	RCT (JA)	CBT (Family Intervention)	Family	Yes	2. RCT	50%
	n=144						
	USA						

<sup>&</sup>lt;sup>2</sup> RCT=Randomised Controlled Trial

<sup>&</sup>lt;sup>3</sup> JA=Journal article

<sup>&</sup>lt;sup>4</sup> CBT=Cognitive-Behavioural Therapy

5	Youssef (1987) (5) n=30 USA	RCT (JA)	Non-CBT (Psychoeducation only)	Family	Yes	2. RCT	0%
6	Drury et al (1996) (6) n=62 UK	RCT (JA)	СВТ	Individual + Group + Family	Yes	2. RCT	0%
7	Wahass and Kent (1997) (7) n=6 Saudi Arabia	RCT (JA)	CBT (Culturally adapted)	Individual	Yes – but failed MMAT screening stage		
8	Haddock et al (1999) (8) n=21 UK	RCT (JA)	CBT	Individual	Yes	2. RCT	25%
9	Bach and Hayes (2002) (9) n=80 USA	RCT (JA)	CBT (Third-wave)	Individual	Yes	2. RCT	50%
10	Lewis et al (2002) (10) n=309 UK	RCT (JA)	CBT	Individual	Yes	2. RCT	100%
11	Hall and Tarrier (2003) (11) n=25	RCT (JA)	СВТ	Individual	Yes	2. RCT	100%

	UK						
12	Bechdolf et al (2004) (12)	RCT (JA)	CBT	Group	Yes	2. RCT	100%
	n=88 Germany						
13	Startup et al	RCT	CBT	Individual	Yes	2. RCT	25%
	(2004) (13)	(JA)		Individual		2.101	2070
	n=90 UK						
14	Gaudiano	RCT	CBT	Individual	Yes	2. RCT	50%
	and Herbert	(JA)	(Third-wave)				
	(2006) (14)						
	n=40						
	USA						
15	Klingberg et	RCT	CBT	Individual + Group	Yes	2. RCT	50%
	al (2010) (15) n=169	(JA)		+ Family			
	Germany						
16	Moritz et al	RCT	CBT	Individual	Yes	2. RCT	100%
	(2011) (16)	(JA)		+ Group		2.1.01	10070
	n=48						
	Germany						
17	Boden (2013)	RCT	CBT	Individual	Yes	2. RCT	0%
	(17)	(TR) <sup>5</sup>	(Third-wave)				
	n=18						
	USA						
18	Gaudiano	RCT	CBT	Individual	No (trial		
	(2015) (18)	(TR)	(Third-wave)		protocol only)		

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<sup>&</sup>lt;sup>5</sup> TR=Trial Registry

	n=60 (target) USA						
19	Habib et al (2015) (19)  n=42  Pakistan	RCT (JA)	CBT (Culturally adapted)	Individual	Yes	2. RCT	50%
20	Jacobsen et al (2016) (20)  n=60 (target)  UK	RCT (JA)	CBT (Third-wave)	Individual	No (trial protocol only)		
21	Tyrberg et al (2016) (21)  n=21  Sweden	RCT (JA)	CBT (Third-wave)	Individual	Yes	2. RCT	75%
NOI	N-KANDOM.	ISED CON	TROLLED TRI	IALS (N=J	L <b>4</b> )		
No.	Author (year)  n=total no. of participants  Country	Study Design (Record type)	Therapy Model (Sub-type)	Mode of Delivery	Outcome Data Reported?	MMAT Section assessed under	MMAT score
1	Feifel and Schwartz (1953) (22) n=68 USA	Non- randomised CT <sup>6</sup> (JA)	Non-CBT (Psychodynamic)	Group	Yes	3. QNR <sup>7</sup>	50%

<sup>&</sup>lt;sup>6</sup> CT=Controlled Trial
<sup>7</sup> QNR=Quantitative Non-Randomised

2	Walker and Kelley (1960) (23) n=82 USA	Non- randomised CT (JA)	Non-CBT (Psychodynamic)	Individual	Yes	3. QNR	25%
3	Bookhammer et al (1966) (24) n=51	Non- randomised CT (JA)	Non-CBT (Psychodynamic)	Unclear	Yes	3. QNR	0%
4	Stern et al (1972) (25) n=75 USA	Non- randomised CT (JA)	Non-CBT (Psychodynamic)	Individual	Yes	3. QNR	50%
5	Gould et al (1975) (26) n=17 USA	Non- randomised CT (JA)	Non-CBT (Psychodynamic)	Group	Yes	3. QNR	75%
6	Serok and Zemet (1983) (27) n=31 Israel	Non- randomised CT (JA)	Non-CBT (Gestalt)	Group	Yes	3. QNR	75%
7	Levene et al (1989) (28) n=10 Canada	Non- randomised CT (JA)	Non-CBT (Family Therapy)	Family	Yes	3. QNR	25%
8	Hodel et al (1998) (29) n=19	Non- randomised CT (JA)	CBT (Emotional Management Therapy)	Individual	Yes	3. QNR	75%

	Switzerland						
9	Hauff et al (2002) (30)	Non- randomised CT	Non-CBT (Psychodynamic)	Individual	Yes	3. QNR	50%
	n=96	(JA)					
	Norway						
10	Veltro et al (2006) (31)	Non- randomised CT	CBT	Group	Yes	3. QNR	0%
	n=502	(JA)					
	Italy						
11	Schmid and Wanderer (2007) (32) n=320	Non- randomised CT (JA)	Non-CBT (Phantasy therapy)	Group	Yes – but failed MMAT screening stage		
	Switzerland						
12	Mortan et al (2011) (33) n=12	Non- randomised CT (JA)	CBT	Group	Yes	3. QNR	50%
	Turkey						
13	Owen et al (2015) (34) n=112	Non- randomised CT (JA)	CBT (Third-wave)	Group	Yes	5. MM	50%
14	UK Witkowska	Non-	Non-CBT	Individual	Yes – but		
14	(2015) (35) n=60	randomised CT (JA)	(Psychoeducation only)	marviqual	failed MMAT screening stage		
	Poland						
SER	<b>VICE EVAI</b>	LUATION (	N=18)				
No.	Author (year)	Study Design	Therapy Model (Sub-type)	Mode of Delivery	Outcome Data	MMAT	MMAT score

	n=total no. of participants  Country	(Record type)			Reported?	Section assessed under
1	Coffey (1954) (36) n=not stated USA	Service Evaluation (BC) <sup>8</sup>	Non-CBT (Psychodynamic)	Group	No	
2	Goldberg et al (1955) (37) n=not stated USA	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Group	No	
3	Canter (1956) (38) n=60 USA	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Group	No	
4	Chazan (1974) (39) n=not stated	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Family (Group)	No	
5	Birckhead (1984) (40) n=not stated USA	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Group	No	
6	Cole and Greene (1988) (41) n=20	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Group	Yes	4. QD <sup>9</sup> 0%

<sup>&</sup>lt;sup>8</sup> BC= Book chapter<sup>9</sup> QD= Quantitative Descriptive

1							
	USA						
7	Kelly et al (1990) (42) n=not stated	Service Evaluation (JA)	Non-CBT (Supportive Counselling)	Group	No		
8	Aviera (1996)	Service	No clear therapy	Group	No		
0	(43)	Evaluation (JA)	model	Gloup	NO		
	USA						
9	Linszen et al (1998) (44)	Service Evaluation (JA)	CBT (Family Intervention)	Family	Yes – but failed MMAT screening		
	n=76				stage		
	Netherlands						
10	Dodd and Wellman (2000) (45) n=23	Service Evaluation (JA)	СВТ	Group	Yes – but failed MMAT screening stage		
11	Fell and Sams (2004) (46) n=91 UK	Service Evaluation (JA)	CBT	Group	Yes – but failed MMAT screening stage		
12	Durrant et al (2007) (47) n=14 UK	Service Evaluation (JA)	CBT (Third-wave)	Individual	Yes	4. QD	50%
13	Tickle et al	Service	CBT	Group	Yes – but		
13	(2009) (48)	Evaluation (JA)		Stoup	failed MMAT screening		
	n=not stated				stage		

14	UK Lynch et al (2011) (49) n=78 USA	Service Evaluation (JA)	CBT	Individual + Group	Yes	4. QD	75%
15	Raune and Daddi (2011) (50) n=137	Service Evaluation (JA)	СВТ	Group	Yes	4. QD	75%
16	Steiner and Harland (2011) (51) n=not stated UK	Service Evaluation (JA)	Non-CBT (Psychodynamic)	Group	No		
17	Heriot- Maitland et al (2014) (52) n=not stated	Service Evaluation (JA)	CBT (Third-wave)	Group	Yes	5. MM <sup>10</sup>	75%
18	Nikolitch et al (2016) (53) n=40 Canada	Service Evaluation (JA)	CBT (Third-wave)	Group	Yes	4. QD	75%
CAS	SE SERIES (1	N=5)					
No.	Author (year)	Study Design (Record type)	Therapy Model (Sub-type)	Mode of Delivery	Outcome Data Reported?	MMAT Section assessed under	MMAT score

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<sup>&</sup>lt;sup>10</sup> MM= Mixed Methods

	n=total no. of participants						
	Country						
1	Boyd (1979) (54)	Case Series (JA)	Non-CBT (Psychodynamic)	Individual + Group	No		
	n=3						
	USA						
2	Cole (1993) (55)	Case Series (BC)	CBT (Family Intervention)	Family	No		
	n=3						
	USA						
3	Ahmed et al (1997) (56)	Case Series (JA)	No clear therapy model	Individual	Yes – but failed MMAT screening		
	n=3				stage		
	USA						
4	Kerr (2001) (57)	Case Series (JA)	Non-CBT (CAT) <sup>11</sup>	Individual	No		
	n=4						
	UK						
5	Freemantle and Clarke (2009) (58)	Case Series (BC)	CBT (Third-wave)	Individual	No		
	n=2						
	UK						
SIN	GLE CASE S	STUDIES (	N=4)				
No.	Author (year)	Study Design (Record type)	Therapy Model (Sub-type)	Mode of Delivery	Outcome Data Reported?	MMAT Section assessed under	MMAT score

<sup>&</sup>lt;sup>11</sup> CAT= Cognitive-Analytical Therapy

	n=total no. of participants						
	Country						
1	Dublin (1973) (59) n=1 USA	Case Study (JA)	Non-CBT (Gestalt)	Individual	No		
2	Ginsburg (2000) (60) n=1 USA	Case Study (JA)	Non-CBT (Supportive Counselling)	Individual	No		
3	Mansell and Fadden (2009) (61) n=1 UK	Case Study (BC)	CBT (Family Intervention)	Family	No		
4	Cooper (2014) (62) n=1 UK	Case Study (JA)	Non-CBT (Psychodynamic)	Group	Yes – but failed MMAT screening stage		
OTIA		ONIT V/ (NI	2)				
	LITATIVE	· · · · · · · · · · · · · · · · · · ·					
No.	Author (year) n=total no. of participants	Study Design (Record type)	Therapy Model (Sub-type)	Mode of Delivery	Outcome Data Reported?	MMAT Section assessed under	MMAT score
	Country						
1	Holma and Aaltonen (1997) (63)	Qualitative (JA)	Non-CBT (Family Therapy)	Family	Qualitative data only	1. Qual	50%
	n=15						

2	Finland  Gonzalez de Chavez et al (2000) (64)  n=32  Spain	Qualitative (JA)	Non-CBT (Psychodynamic)	Group	Qualitative data only	1. Qual	75%
3	York (2007) (65) n=8 UK	Qualitative (JA)	CBT (Third-wave)	Group	Qualitative data only	1. Qual	75%

# Risk of bias summary for RCTs only using Cochrane Tool

		Selection Bi	as	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias
		Random sequence generation	Allocation concealment	Blinding (participants and personnel)	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	
1	Kanas et al.(21) USA	?	?		•		?	No ITT analysis
2	Beutler (22) USA	?	?				•	No ITT analysis
3	Cholet (14) USA		-	?	?	•	•	Unclear if ITT analysis Small N (N=20 in treatment arm)
4	Glick, Clarkin (23) USA	?	?			•	•	Unclear if ITT analysis
5	Youssef (24) USA	?	?	?	?		?	No ITT Analysis Small N (N=15 in treatment arm)
6	Drury, Birchwood (25)	?	?	•			•	No ITT analysis
7	Wahass and Kent (26)			?		•	•	Small N (N=3 in treatment arm)

	Saudi							1
	Arabia							
8	Haddock,							Unclear
8	Tarrier (27)							if ITT
	Tarrier (21)	$\overline{2}$	(?)	(?)	•	(?)	(+)	analysis
	UK							Small N
	OK							(N=10 in
								treatment
								arm)
9	Bach and							No ITT
	<b>Hayes (28)</b>				?			analysis
		(?)	(?)					
	USA							
10	Lewis,							None
	Tarrier (20)				•	•	(+)	
	UK							
11	Hall and							No ITT
	Tarrier (29)	•		(?)	?	•	<b>(+</b> )	Analysis
	1117							Small N
	UK							(N=12 in
								treatment arm)
12	Bechdolf,						_	None
12	Knost (30)			(?)		<b>+</b>	•	None
	Kilost (50)						•	
	Germany							
13	Startup,							None
10	Jackson Jackson		?	?				110110
	(31)							
	UK							
14	Gaudiano							Small N
	and					•	•	(N=19 in
	Herbert							treatment
	(32)							arm)
	1							
1.5	USA							TT 1
15	Klingberg,							Unclear
	Wittorf (33)			[ (?)				if ITT
	Commons							analysis
	Germany							

16	Moritz, Veckenstedt (34)	•	?	?	•	•	•	Small N (N=24 in treatment arm)
17	Boden (16) USA	?	?	?	?		•	Unclear if ITT analysis Small N (N=12 in treatment arm)
18	Gaudiano (15) USA	NOT ASSES	SSED – TRIAL	PROTOCOL O	ONLY			
19	Habib, Dawood (35) Pakistan	•	•	?	•	?	•	No ITT analysis Small N (N=21 in treatment arm)
20	Jacobsen, Peters (36) UK	NOT ASSES	SSED – TRIAL	PROTOCOL C	DNLY			
21	Tyrberg, Carlbring (37) Sweden	•	?	?		•	•	Small N (N=11 in treatment arm)

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