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Invited essay

Positive memory training for the treatment of depression in schizophrenia: A randomised controlled trial

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ABSTRACT

Background: Around half of people diagnosed with schizophrenia suffer from co-morbid depression, yet there are no evidence-based psychological treatments to target this presentation.
Method: Participants were aged 18–65 years old, had a clinical diagnosis of schizophrenia or schizoaffective disorder and at least a mild level of depression. Participants were randomly assigned (1:1) to receive PoMeT or treatment as usual. PoMeT was delivered in up to 12 individual sessions within 3 months. We stratified randomisation by site and by severity of depression using randomised-permuted blocks. Assessments were carried out at baseline, 3-month, 6-month and 9-month by assessors who were blind to treatment allocation. The primary outcome was reduction in the symptoms of depression at 3-month, 6-month and 9-month as measured by the BDI-II. Analysis was by intention-to-treat with linear mixed-effects models. The trial was registered with the ISRCTN registry number 99485756.
Results: One hundred participants were randomly assigned to either PoMeT (n = 49) or treatment as usual (n = 51). The reduction in BDI-II total score at 3 months was significantly greater for PoMeT than for treatment as usual (mean difference = 4.33, SE = 2.00, 95% CI 0.38 to 8.23; p = 0.03).
Discussion: To our knowledge this is, to date, the largest powered randomised controlled trial focused on the psychological treatment of depression in people diagnosed with schizophrenia. Results indicate that a brief targeted intervention can reduce the symptoms of depression in the group. The main limitation of the study is the lack of an active control group which may contribute to an inflated treatment effect.

1. Introduction

Schizophrenia incurs an estimated treatment cost of £2 billion per annum within the UK alone (Mangalore & Knapp, 2007). The development of cost-effective interventions is therefore a priority. Previous research has culminated in the current UK government guidelines recommending 16 individual sessions of cognitive-behaviour therapy (CBT) over a period of 6 months (NICE, 2009). The protocols used within CBT for schizophrenia have typically been generic and flexible, so that clinicians can treat the wide range of presenting problems associated with a psychotic disorder. CBT for schizophrenia, therefore, currently requires a prolonged period of training for clinicians, which has contributed to a low level of availability (Haddock et al., 2014). Consequently, recent efforts have been focussed on the development of

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brief manualised psychological interventions for psychosis which require less training and delivery time. Typically, these interventions target a specific psychotic symptom, such as paranoia (Freeman et al., 2015) or a specific co-morbid presentation, such as post-traumatic stress disorder (Steel et al., 2017; van den Berg et al., 2015).

Low mood is highly prevalent within people diagnosed with schizophrenia, with an estimated 50% suffering from a diagnostic level of depression (Buckley, Miller, Lehrer, & Castle, 2009). This co-morbid condition is associated with particularly high levels of health care use, and a suicide rate of 5% (Palmer, Pankratz, & Bostwick, 2005). The effectiveness of anti-depressants is small for this group (Helfer, Samara, Huhm, Klupp, Leucht, Zhu et al., 2016).

The evidence base for the psychological treatment of depression originates from clinical trials which have excluded people who present with a psychotic disorder. To date, most reports of a psychological approach to treating depression in schizophrenia have been small pilot and feasibility studies (e.g. Gaudiano et al., 2015; Gumley et al., 2017; Singer, Addington, Bobson, & Wright, 2014). Opoka and Lincoln's (2017) review of the area includes five trials, and concludes that cognitive behavioural interventions can successfully treat co-morbid depression in this group. However, only one study (Freeman et al., 2014) included both a control group and follow-up. The intervention was brief (6-sessions), targeted, and associated with a significant decrease in the secondary outcomes of depression and self-esteem which were not maintained during the follow-up phase. A more recent study evaluated 6-months of generic CBT targeting depression and self-esteem in a sample of 63 participants from an early psychosis population (Sonmez, Romm, Ostefjells, Grande, Jensen, Hummelen et al., 2020) and did not show a significant effect of the intervention.

Psychological models of psychosis suggest that negative affect has a central role in the development and maintenance of positive symptoms (Garety et al., 2001). It is therefore likely that a significant change in mood will result in a subsequent change in psychotic symptoms severity within people diagnosed with schizophrenia. This latter point is supported by a recent review specifically with respect to delusions (Opoka, Ludwig, & Lincoln, 2018). Low mood, therefore, represents an important but relatively neglected treatment target in this group. Further, low mood is likely to be maintained through negative self-concepts, and low levels of self-esteem, which have also been found to be prevalent within people diagnosed with a psychotic disorder (Smith, Fowler, Freeman, Bebbington, Bashforth, Garety., et al., 2006). Change in mood is therefore likely to be mediated through a change in self-esteem.

The current study aimed to evaluate the effect of a short-term psychological intervention, which specifically targets the cognitive processes associated with mood disorder, for people diagnosed with schizophrenia.

1.1. Development of the current intervention

A recently developed evidence based treatment for depression and self-esteem is termed 'competitive memory training' (CoMeT) (Ekkers, Korrelboom, Huijbrects, Smits, Cuijpefrs & van der Gaag, 2011; Korrelboom, de Jong, Huirbrechts, & Daansen, 2009; Korrelboom, Marissen, & van Assendelft, 2011; Korrelboom, Marrisen & Huijbrechts, 2012; Korrelboom, van der Weele, Gjaltema, & Hoogstraten, 2009). The name is based on the theory that we all have access to a number of different self-representations, each of which is associated with personally relevant memories (Brewin, 2006). Any of these representations may be activated within a certain situation, thus, the element of 'competition'. It is argued that individuals with depression suffer from negative self-representations which are easily triggered by a wide range of stimuli, along with the associated experience of negative memories and low mood. During the CoMeT intervention, patients are trained to enhance the activation of a positive self-representation using a variety of experiential techniques. Latter stages of the protocol involve activating their positive self-representation during the kind of stressful experiences which had previously triggered negative self-representations. Hence, the positive representations are given a competitive 'edge'.

The training element of the intervention is comparable to the approach taken within cognitive remediation programmes for schizophrenia, which has been shown to be effective (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). The use of a training-based method which employs imagery and experiential techniques means that the intervention does not require the patient to have high levels of 'executive' skills (e.g. planning, memory and attention), which are often reduced within the patient group (Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005). The advantages of using CoMeT over standard CBT for schizophrenia therefore include (i) it specifically targets a key psychological process in the maintenance of depression and (ii) the manualised protocol requires a lower level of therapist training in order to achieve adherence. CoMeT is also shorter in duration (3 months) than other evidence-based treatments for depression, such as Beckian CBT (Butler, Chapman, Forman, & Beck, 2006), behavioural activation (Jacobsen, Martell & Dimidjan, 2001) and mindfulness (Kuyken et al., 2008). Clinical trials indicate that CoMeT is effective for the treatment of mood problems within a range mental health conditions, including eating disorders and personality disorders (Ekkers et al., 2011; Korrelboom et al., 2009a, 2009b, 2011, 2012). Also, an adapted form of CoMeT has been used in a study which targeted the treatment of depression within people who experienced distressing auditory hallucinations and were diagnosed with schizophrenia (van der Gaag, van Oosterhout, Daalman, Somer, & Korrelboom, 2012). The outcomes, included in the Opoka and Lincoln (2017) review, were a small effect on depression and no effect on auditory hallucinations.

Prior to conducting the current study, we worked with service users diagnosed with schizophrenia to adapt the original CoMeT protocol. Modifications included the potential to deliver the protocol through an increased number of sessions, and editing some of the written materials. The resultant protocol was termed 'positive memory training' (PoMeT) to reflect the predominant focus on a positive self-image within the treatment.

1.2. The present investigation

As detailed in our protocol (Steel et al., 2015), the primary hypothesis to be tested was whether within patients who are diagnosed with schizophrenia and exhibit at least a mild level of depression, those who receive positive memory training will demonstrate a higher level of reduction in depressive symptoms than those who receive treatment as usual. The secondary hypotheses was that positive memory training will reduce the level of distressing psychotic symptoms. Further analyses will be conducted so as to assess for the role of self-esteem mediating any observed change in levels of depression within the treatment group. Also, self-esteem and depression will be assessed as potential mediators of change within the severity of psychotic symptoms within the treatment group. Health economic outcomes will be published separately from the main clinical outcomes.

2. Method

2.1. Trial design

This was a randomised, controlled, single-blind trial conducted in two UK centres: the Berkshire National Health Service (NHS) Foundation Trust and the Southern Health NHS Foundation Trust. The sites covered populations of about 0.8 and 1.2 million people respectively. We sought referrals of patients aged 18–65 with a current DSM-V diagnosis of schizophrenia or schizo-affective disorder from both centres. The inclusion criteria were: exhibiting at least a mild level of depression, defined as a score of 14 or over on the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996), no organic

impairment which was considered the primary diagnosis, able and willing to provide consent, do not exhibit a learning disability, and a sufficient understanding of spoken English to engage with assessments and the clinical intervention.

The study was approved by the NHS Research Ethics Committee (reference 13/SC/0634) and the trial protocol has been published (Steel et al., 2015) and registered prospectively (ISRCTN99485756). No changes were made to the published trial protocol after the first randomisation.

2.2. Randomisation and masking

Following eligibility and baseline assessment we randomly assigned (1:1) participants to either an intervention (PoMeT) or control (TAU) group using an online service (sealedenvelope). We stratified randomisation by site and by severity of depression (above and below a BDI-II score of 29, i.e. a severe level of depression) using randomised-permuted blocks of 4–6. Group allocation was revealed to the participant, trial manager and trial therapists whilst assessors were masked. The trial adhered to procedures to maintain separation between research staff who measured outcomes and clinical staff who delivered the intervention. This included the use of separate offices, separate booking systems when seeing participants and separate agendas within team meetings. Where an allocation was revealed to an assessor during an assessment, masking was maintained through outcome data being obtained via the recording of the assessment being rated by another assessor. This occurred on 11 occasions (approximately 3% of the total number of assessments).

2.3. Procedures

The trial intervention (PoMeT) was delivered in up to 12 sessions over a period of 3-months, with 8 sessions or more being considered a full 'dose' of therapy. Sessions were delivered individually, lasted approximately 1 h and took place within an NHS clinic or in the participant's home.

PoMeT is designed to enhance access to positive self-representations resulting in reduced levels of depression and increased self-esteem. It is based on a theoretical account of mood disorder (Brewin, 2006) which suggests that positive self-representations are relatively dormant within individuals suffering from depression, at least in part due to infrequent activation. The first stage of therapy involved the patient identifying their core negative self-representation, such as being "worthless". Within the first session the therapist moved towards the identification of personality characteristics which were inconsistent with being "worthless". Homework involved writing as many specific examples as possible within which the patient has demonstrated these characteristics, e.g. being thanked for being a good friend. Subsequent sessions moved towards working with as many of these specific 'positive memories' as possible, through the use of imagery, posture and self-statements whilst 'reliving' these past positive events. Repeated rehearsal was aimed at maximising the extent to which the positive self-representations would be more easily activated in the 'retrieval competition' with the negative self-representations. It was important that the meaning of the positive events provided a direct challenge to the originally identified negative self-representation. A major component of the intervention protocol was daily practice of positive self-representation recall in between weekly sessions. The final stages of the intervention involved the patient being trained to activate a positive self-representation at a time when an external environmental cue triggered a negative self-representation. The intervention is manualised and highly structured. Whilst the original protocol adopted 8 sessions of 1 h (Korrelboom, de Jong, et al., 2009), on the advice of a service-user focus group our study protocol allowed up to 12 sessions to enable some flexibility in the delivery.

The intervention was delivered by three clinicians; a mental health nurse who was an accredited cognitive behavioural therapist, a counselling psychologist and a clinical psychologist. Supervision was provided by team members (KK and MvdG) with relevant expertise both in the intervention and patient group. Sessions were recorded where the patient gave consent. Adherence to treatment protocol was monitored through the use of a measure specifically designed for the current trial and aimed to differentiate between the delivery of PoMeT and standard CBT or counselling.

TAU was delivered by mental health professionals from within the NHS Trusts and was based on local protocols. All treatment was recorded as part of the amended Client Service Receipt Inventory (Beecham & Knapp, 2001) used for the collection of health and social care data and typically included medication and contact with psychiatrists and community psychiatric nurses, while information on the PoMeT intervention was recorded as part of specific therapist diaries.

2.4. Measures

Assessments were conducted by graduate psychologists at baseline (prior to randomisation) at 3 months (end of treatment for those who received it) and 6 months and 9 months after baseline (i.e. follow-up assessments).

The primary outcome was current level of depressed mood as measured by the BDI-II (Beck et al., 1996) at 3-month, 6-month and 9-months. Secondary outcome measures were self-esteem as measured by the Rosenberg Self- Esteem Scale (Rosenberg, 1965), psychotic symptoms measured by the Positive and Negative Syndrome Scale (PANSS; Kay, Opler, & Lindenmayer, 1987) and the Psychotic Symptom Rating Scale (PSYRATS; Haddock, McCarron, Tarrier, & Faragher, 1999), anxiety measured using the Generalised Anxiety Disorder Assessment (GAD7; Spitzer, Kroenke, Williams, & Lowe, 2006) and functioning measured using the Work and Social Adjustment Scale (WASAS; Mundt, Marks, Shear, & Gresit, 2002). Patient wellbeing was assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMBS, Tennant, Hiller, Fishwick, Platyt, Jospeh, Weich et al., 2007).

Patients' health-related quality of life was measured by the EuroQol EQ-5D (EuroQol Group, 1990), while broader wellbeing was measured by the ICECAP-A (Al-Janabi, Flynn, & Coast, 2012) and OxCAP-MH (Simon et al., 2013) instruments.

All measures were completed at baseline, 3-month and 9-month assessments. The 6-month assessment included only measures of depression and health-related quality of life.

All serious adverse events were documented throughout the trial and reported to the Data Monitoring and Ethics Committee, where the independent chair determined whether the event was attributed to the delivery of the intervention.

2.5. Statistical analysis

All analyses were carried out on an intention to treat principle. Sample size was estimated on the basis of 50 participants per group having 80% power to detect the PoMeT + TAU group presenting with a BDI-II score of 7 or more lower than the TAU group (SD = 10) at the 2.5% level of significance (two-tailed). Outcome measures for the intervention and treatment as usual (control) groups were compared using linear mixed-effects models. The dependent variables were the outcome measures at post-intervention and follow-up. Outcome measures at baseline, group membership and time were included as fixed explanatory variables. The models also included random effects for patients to allow for the correlation between post-intervention and follow-up outcome measures. Additionally, the models contained interaction between time and group to test whether the effects of the intervention and usual treatment varied between post-intervention and follow-up time points. Standard diagnostic evaluations of model assumptions were conducted to ensure valid inference. Uncertainty in the base case results was assessed using non-parametric methods and

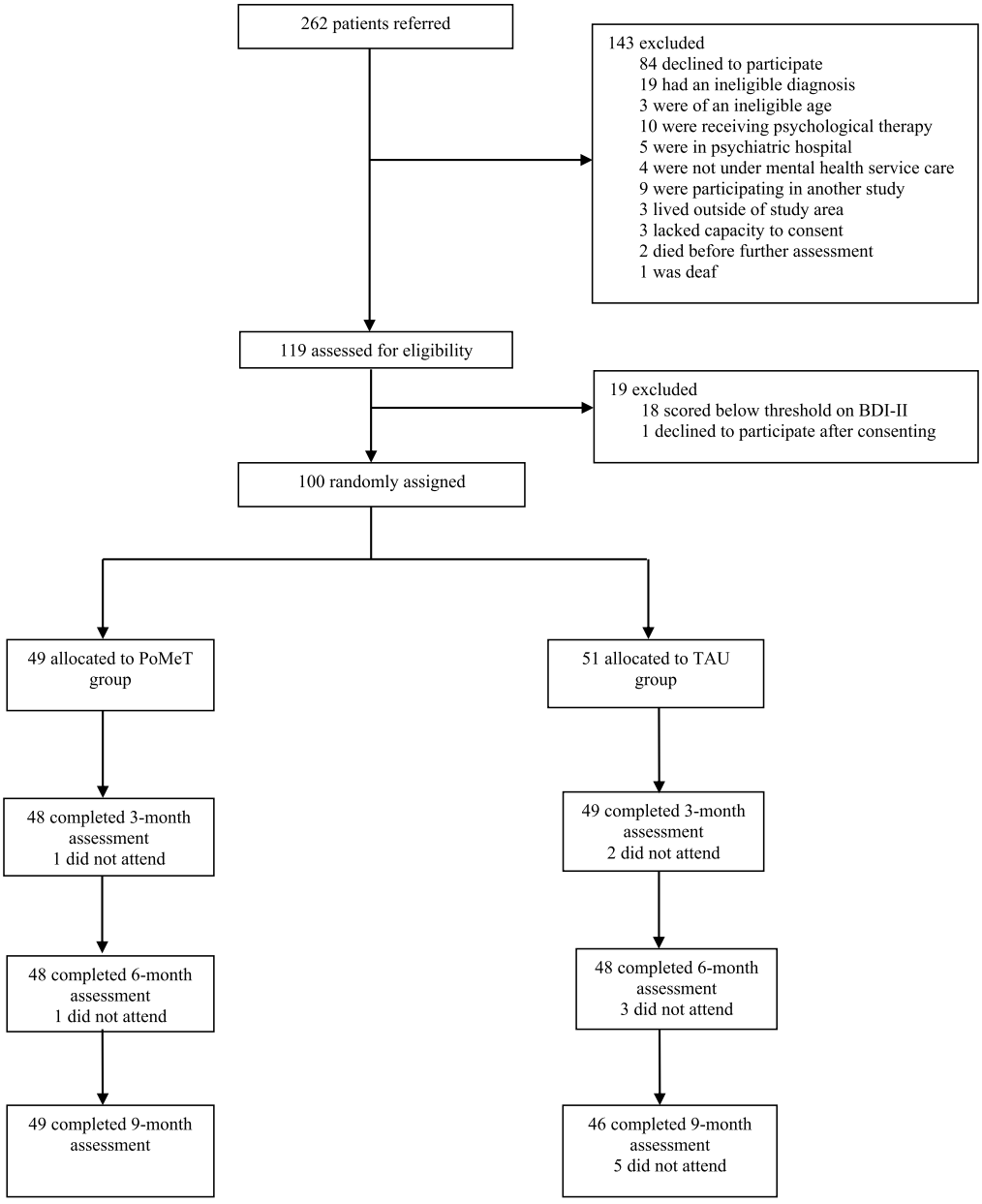

Fig. 1. Consort diagram.

extensive sensitivity analyses (Thanbane, Mbuagbaw, Zhang, Samaan, Marcucci, Ye et al., 2013).

2.6. Mediation analysis

Analyses were conducted so as to assess for the role of self-esteem mediating any observed change in levels of depression within the treatment group. Also, self-esteem and depression were assessed as potential mediators of change within the severity of psychotic symptoms within the treatment group.

3. Results

3.1. Sample characteristics

In total 262 referrals were provided for the study of whom 119 gave consent and were assessed for eligibility using the BDI-II (see Fig. 1), and 100 were eligible and randomly assigned to either the PoMeT group (n = 49) or treatment as usual (n = 51). Fifty-three of the 100 participants were recruited from SHFT whilst 47 were recruited from BHFT.

As seen in Table 1, the majority of the sample were male, of white British ethic origin and unemployed. The most common psychiatric diagnosis was schizophrenia, with the majority having received at least one psychiatric admission to hospital during their lifetime. All but 5 participants (all from the TAU group) were taking antipsychotic medication, whereas 44 participants (19 from the POMET group, and 25 from the TAU group) were not taking antidepressant medication (see Table 1).

Of the 49 who were allocated to receive PoMeT, 40 (82%) received a full dose of between 8 and 12 sessions, whilst 5 (10%) attended between 4 and 7 sessions and 4 (8%) disengaged from the intervention within the first two sessions. There was one trial therapist based at SHFT who delivered PoMeT to all those allocated to receive it within that site (n = 26), as well as to 5 of the 23 allocated to received PoMeT within the BHFT site. The remaining 18 cases within the BHFT site were allocated to two trial therapists seeing 16 and 2 participants. A random recorded session from 20% of the treatment cases were assessed by an

Table 1
Baseline characteristics of the sample.

	PoMeT (n = 49)	TAU (n = 51)	Total (n = 100)
Demographics			
Mean age in years (SD)	42.5 (9.9)	43.4 (11.2)	43.0 (10.6)
Male (%)	69.4	80.4	75.0
White (%)	91.8	88.2	90.0
Age left formal education	16.4 (1.3)	16.5 (1.6)	16.4 (1.5)
Currently Employed (%)	12.2	5.9	9.0
Primary Diagnosis			
Schizophrenia	69.4	70.6	70.0
Schizoaffective disorder	30.6	29.4	30.0
Psychiatric history			
Prior psychiatric Hospitalization (%)	83.7	82.4	83.0
Mean number of prior Admissions	5.1 (7.1)	4.0 (5.3)	4.5 (6.2)
Mean age at first contact with mental healthservicesChlorpromazine-equivalent dose of antipsychotic drug (mg/day)	25.1 (8.3) 591.7 (545.8)	25.6 (9.1) 489.3 (395.5)	25.4 (8.7) 539.5 (475.5)
Fluoxetine-equivalent dose of antidepressant drug (mg/day)	29.5 (29.2)	29.4 (40.1)	29.4 (35.0)

independent expert in the intervention and all were rated as adherent to the treatment protocol.

3.2. Outcome measures

Compared with the TAU group, those who received the PoMeT intervention showed a significant moderate effect of treatment on the primary outcome (depression) at 3 months (adjusted mean difference = 4.33; 95% CI = 0.38–8.23; p = 0.03; Cohen's d = 0.43). Although the gains were preserved in the experimental group, the effect reduced over time and was non-significant both at 6-months and 9-months (see Table 2). There were no other significant treatment effects on any of the secondary outcome measures (see Table 3). Whilst the outcome effect at 3 months for PSYRATS hallucinations was in the moderate range, the large confidence intervals indicate a non-significant result. This outcome will be a product of the smaller sample size when only those who reported experiencing auditory hallucinations as baseline were considered, i.e. n = 63.

Overall, we recorded 22 serious adverse events (11 from the PoMeT group and 11 from the TAU group) with one death (TAU group) and no suicide attempts. None were associated with the delivery of the trial intervention. These events consisted of brief periods in medical hospital due to a variety of conditions (5 for PoMeT group and 6 for TAU group) and time spent in psychiatric hospital due to a period of symptom exacerbation (7 for PoMeT group and 5 for TAU group).

3.3. Mediation analysis

Inference about mediation was based on the unstandardised indirect effect of treatment on outcome through the mediator (Hayes and Rockwood, 2017). Elucidating the role of self-esteem in mediating the treatment effect on depression at 3 months involved fitting two separate models each containing baseline measures of depression and self-esteem as covariates. The indirect effect of PoMeT on depression through self-esteem was not significantly different from zero (0.98; 95% CI -0.90-3.10).

We also evaluated whether changes in depression and self-esteem mediated change within psychotic symptom (hallucination and delusion) outcome scores at 3 months by estimating each mediator effect on outcome, adjusted for the other mediator. Indirect effects of PoMeT on hallucinations through depression (2.38; 95% CI -0.67-6.90) and through self-esteem (−0.40; 95% CI -3.07-1.91) were not significant. Also, the indirect effects of PoMeT on delusions through depression (1.14; 95% CI -0.54-2.90) and through self-esteem (−0.24; 95% CI -1.63-0.47) were not significant.

4. Discussion

Results partially support our primary hypothesis in that individuals who received positive memory training demonstrated a greater reduction in the symptoms of depression, at the end of treatment, than those who received treatment as usual. However, the level of change in depression scores was below the seven-point difference that the study was designed to detect. Also, during the follow-up period, the control group also exhibit a symptom reduction and group differences are not maintained. The current moderate end of treatment effect size of 0.43 is comparable to that of 0.36 reported within the only meta-analysis of CBT for psychosis outcomes on mood (Wykes, Steel, Everitt, & Tarrier, 2008). However, given the current trial was conducted with a high level of methodological rigor, the more meaningful comparison would be with the effect size of 0.08 which was reported for the equivalent high-quality trials within the same meta-analysis. Further, our outcomes were obtained within a 3-month treatment period. This is considerably shorter than the majority of trials reported within the meta-analysis and those trials which have contributed to the current UK government guidelines (NICE, 2009). It is of interest that the recent Sonmez et al. (2020) study adopted a generic CBT approach and did not report significant effects at the end of treatment. Whereas, the current approach, along with that adopted by Freeman et al. (2014), are brief interventions targeting specific mechanisms associated with the maintenance of depression. Both approaches also put an emphasis on developing positive thoughts and emotions, rather than negating a negative. However, positive memory training places more emphasis on training the activation of specific positive self-representations that Freeman et al. (2014), which worked with a wider range of positive thoughts and emotions. Both approaches produced a significant effect at the end of treatment which was not maintained at follow-up. Evidence would therefore suggest future interventions focus on targeting specific mechanisms associated with depression, generate positive thought and emotion, and are modified to maximise the potential for gains to be maintained.

Our secondary hypothesis of a reduction in psychotic symptoms was not supported, and there were no significant effects on any other outcome measures. The outcomes on psychotic symptoms are at odds with the Opoka et al. (2018) review. However, it is of note that the change in auditory hallucination scores indicated an end of treatment effect size of 0.46, which is in line with the outcome of the most recent meta-

Table 2
Primary outcome at baseline, 3-months, 6-months and 9-months.

	Unadjusted mean (SD) BDI-II		Adjusted mean difference (SE)	95% CI	Cohen's d	p value
	PoMeT	TAU				
Month 0	0.6 (10.3)	30.3 (9.8)	4.33 (2.00)	(0.38, 8.23)	0.43	0.03
Month 3	21.1 (11.8)	24.9 (11.6)				
Month 6	21.2 (13.6)	22.9 (13.2)	2.27 (1.66)	(-1.03, 5.58)	0.23	0.17
Month 9	21.5 (14.0)	21.0 (12.6)	0.22 (2.01)	(-3.76, 4.20)	0.02	0.91

Table 3
Secondary outcomes at baseline, 3-months and 9-months.

	Unadjusted mean (SD)		Adjusted mean difference (95% CI)	Cohen's d	p value
	PoMeT	TAU			
Self-Esteem (RSES)					
Month 0	28.4 (5.7)	28.6 (5.4)	0.90 (−0.83, 2.64)	0.16	0.30
Month 3	26.5 (5.0)	28.0 (6.3)			
Month 9	26.1 (7.1)	26.6 (6.1)	−0.07 (−2.07, 1.94)	−0.01	0.94
PANSS Total					
Month 0	74.5 (15.8)	77.4 (15.2)	−0.31 (−5.78, 5.16)	−0.02	0.91
Month 3	72.8 (17.0)	75.0 (15.0)			
Month 9	71.3 (18.3)	73.0 (18.6)	0.94 (−6.78, 4.76)	0.06	0.74
PANSS General					
Month 0	39.3 (8.3)	41.0 (8.5)	−0.09 (−3.27, 3.19)	−0.01	0.96
Month 3	38.8 (9.1)	40.0 (7.9)			
Month 9	37.3 (10.0)	37.9 (10.3)	0.97 (4.21, 2.27)	0.12	0.56
Positive Symptoms (PANSS pos)					
Month 0	18.5 (5.9)	18.4 (6.0)	−0.52 (−2.28, 1.24)	−0.09	0.56
Month 3	17.6 (6.1)	16.8 (6.4)			
Month 9	17.6 (6.9)	17.1 (6.4)	−0.32 (−2.36, 1.72)	−0.05	0.75
Negative Symptoms (PANSS neg)					
Month 0	16.7 (4.9)	17.9 (5.4)	1.15 (−0.30, 2.59)	0.22	0.12
Month 3	16.4 (4.3)	18.2 (4.3)			
Month 9	16.4 (5.0)	18.0 (4.7)	0.85 (−0.88, 2.58)	0.16	0.33
Hallucinations (PSYRATS) <					
Month 0	24.4 (12.4)	24.6 (11.8)	5.51 (−1.07, 12.09)	0.46	0.10
Month 3	16.8 (15.7)	21.9 (13.4)			
Month 9	18.9 (15.8)	18.7 (15.9)	−0.04 (−7.64, 7.56)	0.00	0.99
Delusions (PSYRATS)					
Month 0	12.7 (6.9)	12.4 (7.6)	−0.79 (−3.79, 2.21)	−0.11	0.60
Month 3	12.4 (7.2)	11.6 (7.6)			
Month 9	10.7 (8.1)	11.5 (7.9)	0.84 (−2.35, 4.02)	0.11	0.60
Anxiety (GAD7)					
Month 0	10.7 (6.2)	11.6 (5.1)	1.49 (−0.34, 3.32)	0.26	0.11
Month 3	9.6 (6.0)	11.6 (5.5)			
Month 9	9.6 (7.1)	10.0 (6.3)	−0.03 (−2.36, 2.31)	0.00	0.98
Functioning (WASAS)					
Month 0	27.3 (7.6)	26.7 (8.8)	−2.06 (−5.36, 1.23)	−0.25	0.22
Month 3	26.5 (8.5)	23.9 (10.6)			
Month 9	26.1 (8.5)	23.8 (10.5)	−1.61 (−4.98, 1.76)	−0.20	0.35
Wellbeing (WEMWBS)					
Month 0	34.7 (11.2)	33.8 (9.9)	−1.40 (−4.33, 1.52)	−0.13	0.34
Month 3	37.6 (9.5)	35.5 (11.3)			
Month 9	37.0 (11.1)	37.4 (11.8)	0.67 (−2.52, 3.87)	0.06	0.68

RSES = Rosenberg Self-Esteem Scale. PANSS = Positive and Negative Symptom Scale. PSYRATS = Psychotic Symptom Rating Scales. GAD7 = Generalised Anxiety Disorder 7. WASAS = Work and Social Adjustment Scale. WEMWBS = Warwick-Edinburgh Mental Well-being Scale.

analysis of CBT for hallucinations (van der Gaag, Valmaggia, & Smit, 2014). Although not all of our sample reported experiencing hearing voices and therefore were not included in this section, resulting in reduced power for this analysis. Cost-effectiveness outcomes will be reported separately. Further analyses did not reveal any mediation effects of self-esteem on change in depression, or on either of these variables mediating any change in psychotic symptoms.

The increased mood levels obtained during the delivery of positive memory training were maintained at 6 and 9-month follow-ups. The 9-month assessment represents a no treatment follow-up duration of twice the length of the actual treatment itself, which is unusually extensive for a psychological treatment trial. However, the follow-up outcomes for PoMeT are non-significant, due to the symptom recovery exhibited within the treatment as usual group. The reduced levels of depression in our control group is at odds with the epidemiological data for co-morbid depression (Buckley et al., 2009), but is a common occurrence within clinical trials of psychological therapies. Participants were not recruited at a time of crisis, so regression to the mean would seem an unlikely explanation. One possibility is that participants randomised to a treatment as usual condition receive an enhanced level of care, both during the trial intervention period and beyond, compared to that which would have occurred had the trial not existed. This may be through those involved in the participant's care becoming more alert to their psychological needs and providing, or facilitating access to, increased clinical input.

The most significant limitation of our study is that the comparison group did not control for therapist contact time or provide an active treatment. Therefore, we are limited in the confidence with which we can conclude that the significant treatment effect was due to the specific content of the positive memory training protocol. Our conclusions are based on what can be determined about the likely outcomes of the interventions that could have been chosen as an active control from the available literature. An ideal active control would have been generic CBT for psychosis. As has been discussed, a meta-analysis of outcomes on mood for high quality CBT for psychosis trials indicated an effect size of 0.08, considerably lower than that obtained in the current trial. Another limitation is that the study was only conducted in two NHS Trusts in the South of England, and by only three clinicians. Further work is required to confirm generalisability.

The current study is the largest randomised controlled trial of a psychological therapy specifically targeting the treatment of depression in people diagnosed with schizophrenia. Positive memory training was feasible to deliver, demonstrated high levels of acceptability and there were no serious adverse effects associated with the intervention. Within our sample, patients exhibited a degree of natural recovery from depression over time. However, the recovery was quicker for those who

received positive memory training. This outcome is likely to be of value to service-users and may have an impact on relapse rate reduction, although larger studies are required to address this question. Overall, our results suggest that if low mood is the primary target within a psychological approach to this disorder, then positive memory training provides a briefer alternative to generic CBT for psychosis, and is likely to have a larger impact. The impact of PoMeT on quality of life and the cost-effectiveness of the intervention has been subject to a specific health economic analysis and will be reported separately.

CRediT authorship contribution statement

Craig Steel: Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Kees Korrelboom:** Conceptualization, Writing - review & editing, Supervision, Funding acquisition. **M. Fazil Baksh:** Conceptualization, Methodology, Formal analysis, Writing - review & editing. **David Kingdon:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition. **Judit Simon:** Conceptualization, Methodology, Writing - review & editing, Supervision, Funding acquisition. **Til Wykes:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition. **Peter Phiri:** Conceptualization, Methodology, Investigation, Writing - review & editing, Project administration, Funding acquisition. **Mark van der Gaag:** Conceptualization, Methodology, Writing - review & editing, Supervision, Funding acquisition.

Declaration of competing interest

None.

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