A parallel group randomised open blinded evaluation of Acceptance and Commitment Therapy for depression after psychosis: Pilot trial outcomes (ADAPT)

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ABSTRACT

Background: Depression is one of the major contributors to poorer quality of life amongst individuals with psychosis and schizophrenia. The study was designed as a Pilot Trial to determine the parameters of a larger, definitive pragmatic multi-centre randomised controlled trial of Acceptance and Commitment Therapy for depression after psychosis (ACTdp) for individuals with a diagnosis of schizophrenia who also meet diagnostic criteria for major depression.
Methods: Participants were required to meet criteria for schizophrenia and major depression. Blinded follow-ups were undertaken at 5-months (end of treatment) and at 10-months (5-months posttreatment). Primary outcomes were depression as measured by the Calgary Depression Scale for Schizophrenia (CDSS) and the Beck Depression Inventory (BDI).
Results: A total of 29 participants were randomised to ACTdp + Standard Care (SC) (n = 15) or SC alone (n = 14). We did not observe significant differences between groups on the CDSS total score at 5-months (Coeff = −1.43, 95%CI −5.17, 2.32, p = 0.45) or at 10-months (Coeff = 1.8, 95%CI −2.10, 5.69, p = 0.36). In terms of BDI, we noted a statistically significant effect in favour of ACTdp + SC at 5-months (Coeff = −8.38, 95%CI −15.49, −1.27, p = 0.02) but not at 10-months (Coeff = −4.85, 95%CI −12.10, 2.39, p = 0.18). We also observed significant effects on psychological flexibility at 5-months (Coeff = −8.83, 95%CI −14.94, −2.71, p < 0.01) but not 10-months (Coeff = −4.92, 95%CI −11.09, 1.25, p = 0.11).
Implications: In this first RCT of a psychological therapy with depression as the primary outcome, ACT is a promising intervention for depression in the context of psychosis. A further large-scale definitive randomised controlled trial is required to determine effectiveness.
Trial registration: ISRCTN: 33306437

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1. Background

Depression contributes to poorer quality of life amongst individuals with psychosis and schizophrenia (Saarni et al., 2010). Prevalence rates suggest between 33% and 50% of individuals meet criteria for major depression (Whitehead et al., 2002; Birchwood et al., 2000). Depression is associated with greater risk of suicide (Drake et al., 1985), poorer adherence to treatment (Conley, 2009), greater interpersonal problems (Rocca et al., 2005) and greater insight (Mintz et al., 2003). Shame is key feature in the emergence of depression (Gumley et al., 2010), where individuals' envisage a bleak future status, through stigma and the loss of social, interpersonal and vocational roles (Birchwood et al., 2000).

There is a lack of robust evidence supporting the use of antidepressant (Whitehead et al., 2002) and psychological (Wykes et al., 2008) interventions for depression in context of schizophrenia. Although there

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is preliminary evidence that depression symptoms improve in people receiving CBT for psychosis (CBTp) (Wykes et al., 2008) this important outcome domain is not typically assessed in CBTp trials (Jauhar et al., 2014) so there is a need to build the treatment evidence base. Acceptance and Commitment Therapy (ACT) could offer a promising psychological intervention that helps reduce unhelpful coping strategies including rumination and avoidance, and enables commitment to behavioural changes consistent with personal values. Randomised controlled trials show that ACT reduces depression in non-psychotic populations (Hacker et al., 2016).

Previous non-blind randomised controlled trials investigating ACT for psychosis with rehospitalisation as the primary outcome have shown therapeutic promise in US acute inpatient settings (Bach and Hayes, 2002; Gaudiano and Herbert, 2006). Gaudiano and Herbert (2006) found a small effect of ACT on negative emotion in people with psychosis. White et al. (2011) investigated ACT for psychosis with the primary outcome focused on emotional distress. They found a significant difference between the ACT and Treatment as Usual (TAU) groups for negative symptoms. There was also a trend on the limit of significance for differences between the groups in depression ($p = 0.051$) and improvement in depression was associated with self-reported increases in mindfulness. In a later analysis, White et al. (2015) found that ACT was associated with significantly greater likelihood of achieving a clinically significant improvement in depression.

To summarise, feasibility research informed the present study that (a) ACT could be delivered to outpatients with psychosis and was highly acceptable, (b) that ACT appeared to improve symptoms of depression and negative symptoms and (c) that improvements in depression were associated with ACT relevant mechanisms of change (increased mindfulness skills). Therefore this study was designed as a Pilot Trial (Craig et al., 2008) to determine the parameters of a larger, definitive pragmatic multi-centre (UK wide) randomised controlled trial of Acceptance and Commitment Therapy for depression after psychosis (ACTdp) for individuals with a diagnosis of schizophrenia who also meet diagnostic criteria for major depression. In this manuscript we address the following questions:

a) What are the potential numbers of participants who fulfil eligibility criteria?
b) What proportion of potential participants provides fully informed consent to participate in the Trial?
c) What is the overall rate of follow-up in the first 5-months and at 10-months?
d) What proportion of participants engages with ACTdp?
e) What rates of improvement in primary (depression) and secondary outcomes (Positive and Negative Syndrome Scale and Questionnaire for Personal Recovery) are observed at 5-month (end of treatment) follow-up and 10-month follow-up?
f) What are the associations with ACT specific mechanisms (mindfulness skills, psychological flexibility) and outcome in terms of depression?

2. Methods/design

2.1. Design

The study was a Parallel group Randomised Open Blinded Evaluation (PROBE) of Acceptance and Commitment Therapy for depression after psychosis (ACTdp). The study protocol was registered before initiating recruitment (ISRCTN: 33306437). The protocol was published before treatment codes were broken and data were analysed (Gumley et al., 2015). Ethical approval was provided by West of Scotland Research Ethics Committee (12/WS/0311). Managerial approval was provided by NHS Greater Glasgow & Clyde (GN11CP470).

2.2. Participants

Participants were consecutively recruited, assessed and randomised. Inpatients or outpatients, aged 16 or over and receiving (a) anti-psychotic medication (b) psychiatric follow-up and (c) follow-up from a secondary mental health care community based services. Participants met DSM-IV-TR criteria for schizophrenia and major depression (confirmed by Structured Clinical Interview for DSM/SCID-I & Calgary Depression Scale/CDSS for Schizophrenia; score > 7; Kim et al., 2006). Individuals with substance use problems were eligible for inclusion but those with significant learning disability, or who were unable to speak English were not included.

2.3. Entry

Potential participants were identified by their clinical team or by self-referral. Following signed informed consent a Research Assistant (RA) conducted baseline assessments. The Psychosis and Mood Episodes section of the SCID-I was used to assess diagnostic eligibility. Inter-rater reliability for the SCID-I was 90% (range 82–100%).

2.4. Randomisation

Eligible participants were randomised following completion of the baseline assessments. Randomisation (at the individual level) was organised at the Robertson Centre for Biostatistics, a fully registered and NIHR approved UK Clinical Trials Unit. Randomisation was stratified for early (<2 years duration) versus established psychosis (>2 years duration).

2.5. Follow-up

Participants were assessed at entry pre-randomisation, 5 months and 10-months by a blinded RA. All assessments were audio-recorded with consent by the participant. Management of blind breaks, inter-rater reliability and safety reporting were governed by specifically designed Standard Operating Procedures.

2.6. Protecting the blind

RAs entered participant details via a secure web based portal. Following allocation, another member of the research group received the outcome of randomisation and informed the participant and their treatment team. Blinding was maintained using a wide range of measures (e.g. separate offices for therapists and researchers, protocols for answering phones, message taking and secretarial support, forbidding any discussions of participants between RAs and therapists following randomisation, separate diaries and security for electronic randomisation information).

2.7. Blind breaks

When a blind break occurred, the RA affected informed the Chief Investigator (CI) within two working days. In this event a second assessor (blind, where possible, to the participant's allocation) undertook an independent rating of the assessment. Following independent rating, assessors met to discuss and resolve any discrepancies. The original assessor entered agreed ratings into the Case Record Form (CRF). Where possible, another team member, who remained blind to randomisation status, completed the remaining assessments for that participant.

2.8. Inter-rater reliability

Inter-rater reliability meetings were held on a monthly basis. RAs were trained in all of the study measures before commencing data

collection. This included observation of a live assessment of psychopathology ratings (PANSS, CDSS, SCID) with an experienced research assessor. Audio recordings were used for ongoing RA training, secondary assessment when blind breaks occurred, and fidelity checking to detect and correct rater drift.

2.9. Serious adverse events

In accordance with NIHR trial management standards (Trial Managers Network, 2014), a Serious Adverse Event (SAE) was defined as any occurrence that (a) resulted in death, (b) was life threatening, (c) required hospitalisation or prolongation of existing hospitalisation, (d) resulted in persistent or significant disability or incapacity, or (e) was considered otherwise medically significant by the Chief Investigator.

2.10. Primary outcomes

The Calgary Depression Scale for Schizophrenia (CDSS, Addington et al., 1990) assessed severity of depression. The CDSS was better the BDI, PANSS – Depression subscale, and HAM-D for both sensitivity (94%) and specificity (89%) of SCID Depression diagnosis (Kim et al., 2006). Inter-rater reliability for the CDSS was 92% (range 67–100%). In this study the Intraclass Correlation Coefficient was ICC = 0.68 (95%CI, 0.46–0.82). CDSS was also associated with PANSS Emotional Distress (r_s = 0.78, 95%CI, 0.67–0.85)

The Beck Depression Scale (BDI-II; Beck et al., 1996) was used as a well-established self-report measure of depression with excellent reliability and validity. In this study Cronbach's Alpha was α = 0.91 (95%CI, 0.88–0.94). The CDSS and BDI-II were correlated r_s = 0.70 (95%CI, 0.56–0.80). This is consistent with Addington et al. (1993) who found a correlation of r_s = 0.69 amongst outpatients with a diagnosis of Schizophrenia.

2.11. Therapy mechanisms

The Kentucky Inventory of Mindfulness Skills (KIMS; Baer et al., 2004) was used to assess four mindfulness skills: observing, describing, acting with awareness, and accepting without judgement. The KIMS has good internal consistency, test retest reliability and construct validity. In this study Cronbach's Alpha was α = 0.82 (95%CI, 0.76–0.88).

Psychological flexibility was assessed with the 7 item version of the Acceptance and Action Questionnaire (AAQ-II; Bond et al., 2011). This measure has satisfactory structure, reliability, and validity. In this study Cronbach's Alpha was α = 0.88 (95%CI, 0.84–0.92).

2.12. Secondary outcomes

The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was used to measure psychiatric symptoms. We adopted the 5-factor model that yields scores for positive, negative, disorganisation, excitement and emotional distress symptoms (van der Gaag et al., 2006). Inter-rater reliability for the PANSS in this trial was 83% (range 63–97%), and the Intraclass Correlation Coefficient was ICC = 0.88 (95%CI, 0.83–0.91).

The Process of Recovery Questionnaire (QPR; Neil et al., 2009) was used to measure service user rated recovery. The QPR has two subscales measuring intrapersonal tasks and interpersonal factors relevant to personal recovery and has excellent reliability and validity. In this study Cronbach's Alpha was α = 0.93 (95%CI, 0.91–0.95).

2.13. Treatments

2.13.1. Acceptance and Commitment Therapy for depression after psychosis (ACTdp)

Individuals received up to 5 months of individual ACTdp. ACTdp is based on the rationale that the experience of psychosis can threaten progress in valued life domains. The ACTdp intervention protocol was used to enhance engagement with valued life activities through values clarification, increasing mindfulness and psychological flexibility and reducing experiential avoidance and fusion with experiences. An individual formulation based on the six ACT core processes was developed for each participant in the treatment arm. Fidelity of treatment strategy use and consistency with the ACT model were determined via weekly supervision by a senior clinician. The details of intervention have been described in greater detail elsewhere (Gumley et al., 2015; White, 2015).

2.13.2. Standard Care (SC)

Treatment received by all participants in the trial was examined in order to establish the parameters of Standard Care. For inclusion, all participants had to be in receipt of antipsychotic medication and follow-up from a secondary specialist mental health service.

2.14. Statistical analyses

As a pilot study we aimed to assess the variability in the outcome data and look for suggestive trends in order to estimate parameters for a definitive multi-site RCT. To this end, we planned exploratory repeated measures regression models, adjusting for baseline measures including the stratification variable to be fitted to assess treatment effects on the main outcome measures and the evolution of these treatment effects over time and to estimate residual variability. We aimed to explore outcome measures for strong treatment signals. Therefore we report both ITT and Per Protocol Sample (PPS).

3. Results

3.1. Population

The flow of participants into the study is described in Fig. 1. We identified 92 potential participants of whom 55 were referred to the study. Of this group, 38 gave their informed consent to enter the study and 7 were not eligible. Two participants, who initially gave their informed consent subsequently changed their mind before randomization. This left 29 participants who were fully assessed before being randomised to ACTdp + SC (n = 15) or SC alone (n = 14). In terms of follow-up of ACTdp + SC, two participants declined follow-up at 5-months and we were unable to follow-up 1 further participant at 10-months. In SC, 1 participant declined follow-up at 10-months.

The characteristics of the final sample are described in Table 1 below. The sample were on average 46.5 years old, male (n = 19, 65.5%), white Scottish (n = 27, 93.1%) with on average 13.2 years of education.

During the trial we observed 7 Serious Adverse Events (SAEs). All SAEs were related to Hospitalisation, 2 (28.6%) were in the ACTdp + SC group and 5 (71.4%) in the SC group. There were 14 unblindings during the trial. Of these 11 (78.6%) were in the ACTdp + SC group and 3 (21.4%) were in SC. All unblindings were rated by another Researcher masked to treatment allocation and subsequent follow-ups were blind rated.

3.2. Intervention

On average 17.4 (s.d. = 5.9) ACTdp sessions were scheduled, and 15.4 (s.d. = 6.2) were attended by participants. Of the remaining sessions, 0.7 (s.d. = 1.4) were cancelled and 1.2 (s.d. = 1.5) not attended.
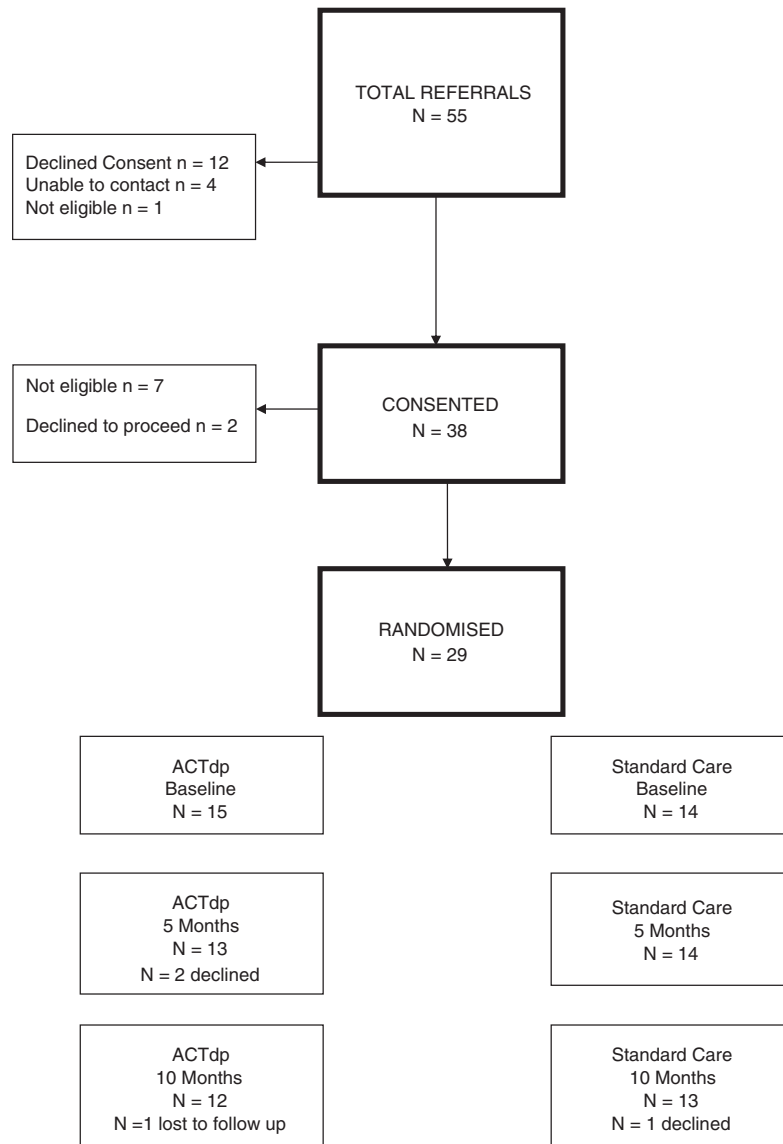
Fig. 1. Adapt consort diagram.

Table 1
Demographic characteristics of sample.

Variable	Statistic	Full ITT (N = 29)	Standard Care (N = 14)	ACTdp + SC (N = 15)
Age (Years)	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
	Mean (SD)	46.5 (9.0)	46.2 (8.9)	46.8 (9.3)
Gender	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
Male	N (%)	19 (65.5%)	9 (64.3%)	10 (66.7%)
Ethnicity	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
White	N (%)	27 (93.1%)	12 (85.7%)	15 (100.0%)
Black minority ethnic	N (%)	2 (6.9%)	2 (14.3%)	0 (0.0%)
Years of education	N_{obs} (N_{miss})	28 (1)	13 (1)	15 (0)
	Mean (SD)	13.2 (4.2)	14.0 (4.9)	12.5 (3.4)
Highest education	N_{obs} (N_{miss})	27 (2)	13 (1)	14 (1)
Primary or less	N (%)	4 (14.8%)	2 (15.4%)	2 (14.3%)
Secondary	N (%)	9 (33.3%)	3 (23.1%)	6 (42.9%)
Tertiary/further	N (%)	13 (48.1%)	7 (53.8%)	6 (42.9%)
Other general	N (%)	1 (3.7%)	1 (7.7%)	0 (0.0%)
Not known	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2
Primary outcomes at baseline, 5-months and 10-months.

Variable	Statistic	ITT (N = 29)	SC (N = 14)	ACTdp + SC (N = 15)
Calgary Depression Scale - Baseline	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
	Mean (SD)	14.0 (4.9)	15.0 (5.8)	13.1 (4.0)
Calgary Depression Scale - 5-months	N_{obs} (N_{miss})	27 (2)	14 (0)	13 (2)
	Mean (SD)	10.2 (6.1)	12.0 (6.6)	8.3 (5.0)
Calgary Depression Scale - 10-months	N_{obs} (N_{miss})	25 (4)	13 (1)	12 (3)
	Mean (SD)	9.5 (5.9)	10.0 (6.5)	9.0 (5.3)
Beck Depression Inventory - baseline	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
	Mean (SD)	31.7 (12.6)	29.9 (14.3)	33.3 (11.1)
Beck Depression Inventory - 5-months	N_{obs} (N_{miss})	27 (2)	14 (0)	13 (2)
	Mean (SD)	21.9 (10.5)	25.2 (11.3)	18.4 (8.7)
Beck Depression Inventory - 10-months	N_{obs} (N_{miss})	25 (4)	13 (1)	12 (3)
	Mean (SD)	23.5 (14.3)	25.7 (14.3)	21.2 (14.6)

The number of participants attending 10 or more sessions (our a priori definition of an adequate number of sessions) was 10 (71.4%).

3.3. Outcomes

The outcomes of depression measured by CDSS and BDI are described in Table 2 below. We did not observe significant differences between groups on the CDSS total score at 5-months (Coeff = −1.43, 95%CI −5.17, 2.32, p = 0.45) or at 10-months (Coeff = 1.8, 95%CI −2.10, 5.69, p = 0.36). Outcomes Per Protocol Sample (PPS) did not differ from ITT analysis. In terms of BDI, we noted a statistically significant effect in favour of ACTdp + SC at 5-months (Coeff = −8.38, 95%CI −15.49, −1.27, p = 0.02) but not at 10-months (Coeff = −4.85, 95%CI −12.10, 2.39, p = 0.18). In the PPS analyses we noted sustained outcomes in favour of ACTdp + SC at both 5-months (Coeff = −10.18, 95%CI −17.69, −2.68, p = 0.01) and 10-months (Coeff = −8.11, 95%CI −15.62, −0.60, p = 0.04).

The outcomes for AAQ and KIMS are described in Table 3. We observed a significant effect in favour of ACTdp + SC in terms of improved psychological flexibility (reduced AAQ score) at 5-months follow-up (Coeff = −0.883, 95%CI −14.94, −2.71, p < 0.01) but not at 10-months (Coeff = −4.92, 95%CI −11.09, 1.25, p = 0.11). In the PPS analysis outcomes at 5-months (Coeff = −10.71, 95%CI −16.16, −5.26, p < 0.01) and 10-months (Coeff = −6.27, 95%CI −11.72, −0.82, p = 0.03).

In terms of KIMS subscales we observed the following outcome signals. At 10-months significant outcomes in favour of ACTdp + SC were noted for KIMS Observing (Coeff = 4.94, 95%CI 0.47, 9.41, p = 0.03) and KIMS Total (Coeff = 10.91, 95%CI 0.22, 21.60, p = 0.05). In the PPS analysis significant effects in favour of ACTdp + SC were noted for KIMS Accepting at 5-months (Coeff = 4.78, 95%CI 0.68, 8.88, p = 0.02) and 10-months (Coeff = 5.39, 95%CI 1.29, 9.40, p = 0.01) and KIMS Total at 5-months (Coeff = 9.44, 95%CI 0.07, 18.82, p = 0.05) and 10-months (Coeff = 12.63, 95%CI 3.25, 22.00, p = 0.01).

3.4. Secondary outcomes

We did not observe any other effects on outcomes using the Questionnaire for Personal Recovery and the Positive and Negative Syndrome Scale with one exception which was that there was a significant effect in favour of ACTdp + SC on PANSS Cognitive Disorganisation (Coeff = −4.92, 95%CI −8.50, −1.35, p = 0.01) and PANSS Excitement at 5-months (Coeff = 1.98, 95%CI −3.60, −0.35, p = 0.019). In the PPS analyses we noted significant effects in favour of ACTdp + SC for PANSS Negative (Coeff = −4.03, 95%CI −7.77, −0.28 p = 0.04), PANSS Cognitive Disorganisation (Coeff = −6.16, 95%CI −10.01, −2.30, p = 0.003), PANSS Emotional Distress (Coeff = −2.46, 95%CI −4.74, −0.18, p = 0.04) and PANSS Total (Coeff = −12.45, 95%CI −23.11, −1.80, p = 0.02) at 5-months.

Table 3
Therapy specific measures at baseline, 5-months and 10-months.

Variable	Statistic	ITT (N = 29)	SC (N = 14)	ACTdp + SC (N = 15)
AAQ - baseline	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
	Mean (SD)	34.8 (7.4)	34.4 (9.5)	35.2 (5.1)
AAQ - 5-months	N_{obs} (N_{miss})	27 (2)	14 (0)	13 (2)
	Mean (SD)	32.5 (10.6)	36.4 (10.2)	28.3 (9.7)
AAQ - 10-months	N_{obs} (N_{miss})	25 (4)	13 (1)	12 (3)
	Mean (SD)	32.1 (10.3)	33.8 (9.4)	30.2 (11.3)
KIMS Observing Baseline	N_{obs} (N_{miss})	29 (0)	14 (0)	15 (0)
	Mean (SD)	36.0 (8.2)	39.4 (7.7)	32.8 (7.5)
KIMS Observing 5-months	N_{obs} (N_{miss})	27 (2)	14 (0)	13 (2)
	Mean (SD)	36.7 (8.1)	37.1 (8.8)	36.4 (7.8)
KIMS Observing 10-months	N_{obs} (N_{miss})	25 (4)	13 (1)	12 (3)
	Mean (SD)	39.9 (7.3)	39.3 (8.4)	40.6 (6.3)
KIMS Describing Baseline	Mean (SD)	21.6 (6.0)	22.8 (7.3)	20.5 (4.6)
KIMS Describing 5-months	Mean (SD)	22.9 (5.7)	22.8 (6.4)	23.0 (5.1)
KIMS Describing 10-months	Mean (SD)	24.6 (5.7)	24.1 (7.0)	25.2 (4.0)
KIMS Awareness Baseline	Mean (SD)	26.1 (6.0)	27.2 (6.0)	25.0 (5.9)
KIMS Awareness 5-months	Mean (SD)	27.1 (6.3)	27.9 (7.1)	26.4 (5.5)
KIMS Awareness 10-months	Mean (SD)	26.6 (6.1)	26.5 (5.8)	26.7 (6.7)
KIMS Accepting Baseline	Mean (SD)	23.8 (7.1)	23.6 (8.4)	24.0 (6.0)
KIMS Accepting 5-months	Mean (SD)	25.0 (6.9)	23.8 (7.3)	26.3 (6.4)
KIMS Accepting 10-months	Mean (SD)	24.7 (7.2)	22.6 (7.1)	27.0 (6.8)

3.5. Mechanisms of change

In order to investigate hypothesized mechanisms of change we calculated change scores at 5-months and 10-months for the CDSS, BDI, KIMS and AAQ. We then investigated associations between changes in depression and changes in mindfulness and psychological flexibility. Table 4 below summarizes the observed correlations at 5-months and 10-months. Consistent with the lack of observed effects on CDSS we observed no significant associations between depression and hypothesized mechanisms of change at either 5 or 10-months. With respect to changes in BDI we observed significant correlations with changes in psychological flexibility at 5-months ($r = 0.54$, $p < 0.01$) and 10-months ($r = 0.41$, $p = 0.04$). Furthermore, we observed significant associations between KIMS Observing ($r = -0.58$, $p < 0.01$), KIMS Describing ($r = -0.63$, $p < 0.01$), KIMS Awareness ($r = -0.41$, $p = 0.03$) and change in BDI at 5-months. Finally we observed as significant association between KIMS Describing ($r = -0.49$, $p = 0.01$), KIMS Awareness ($r = -0.53$, $p < 0.01$), KIMS Acceptance ($r = -0.49$, $p = 0.01$) and change in BDI at 10-months.

4. Discussion

This is the first randomised controlled trial of any psychological therapy in psychosis that specified depression as a primary outcome. We sought to map the parameters for a larger scale definitive trial of ACT for depression after psychosis. Our primary concern was the identification of outcome signals in relation to depression (CDSS, BDI-II), and established therapy mechanisms (KIMS and AAQ) as a basis to estimate the power and sample size requirements for a future trial. Over a period of 12-months recruitment, we received 92 potential enquiries, converting to 55 participant referrals (referrals 4.6 per month) leading to 29 (2.4 per month) randomisations. Over 10-months we retained 25 (86.3%) of participants in follow-up.

One of the key challenges for the study was the identification and recruitment of potential participants. Depression co-occurring with psychosis was not routinely identified by mental health staff. Positive symptoms tended to be prioritised for monitoring and assessment, there was poor discrimination between negative symptoms and depression, potential participants rarely reported depressed mood (despite severe symptoms on the BDI-II), and conversations about depressed mood and hopelessness were frequently avoided. In a future large-scale trial, supporting mental health staff with knowledge and skills to detect and respond to depression in this group would increase recruitment. Our results also point to the need to develop pathways to enhance self-referral for the assessment and treatment of depression. This is particularly important given the role of depression in reduced quality of life and serious adverse outcomes such as death by suicide (Foster, 2015; Pompili et al., 2008).

The ACTdp intervention was well tolerated. On average participants received 15 sessions over 5-months, rates of cancellation and non-attendance were low and 70% received at least 10-sessions of therapy.

Although the study was not powered or designed as an efficacy or effectiveness trial we did wish to explore treatment signals and we had established a priori primary outcomes, therapy specific outcomes, and secondary outcomes. We did not observe any change signals on the CDSS. We noted a statistically significant improvement in BDI-II for the ACTdp + SC group at 5-months but not at 10-months. We noted a between group Cohen's Effect Size of $r = 0.67$ at 5-months end of treatment and $r = 0.31$ at 10-months. These effects compare well with those identified in a recent meta-analysis (Hacker et al., 2016) who found that studies investigating ACT for depression as a primary treatment target ($n = 12$ studies comprising $n = 674$ participants) suggested also large significant between group effect size ($d = 0.73$, $p < 0.001$). For ACT versus active control conditions ($n = 15$ studies comprising $n = 755$ participants) findings suggested a small non-significant between groups effect size ($d = 0.26$, n.s.).

The different patterns of depression change scores on the observer-rated versus self-report measures have potential implications for future trials. First, the effect size for depression reduction on the CDSS for the ACT + SC care group was $d = 0.30$ at the 5 month end of treatment time-point and $d = -0.15$ at the 10 month post treatment follow-up suggesting that the CDSS detected smaller effects. Second, we noted a lower than expected ICC = 0.68 for the CDSS and this may have contributed to some inconsistency of outcomes. Given, the pilot nature of this study, it is difficult to draw firm conclusions regarding the inconsistency of these outcomes and therefore the CDSS should be retained in a future main trial. However, since service users with psychosis express a preference for self-report measures as primary trial outcomes (Crawford et al., 2011), any future RCT following from this pilot could justify being powered to detect an effect on the BDI-II.

Consistent with the model of therapeutic change in ACT and with earlier observations (White et al., 2011, 2013) we observed statistically significant changes in psychological flexibility and mindfulness. We noted significant associations between psychological flexibility at both 5 and 10-month follow-up using the BDI and associations between changes in mindfulness and depression at 5 and 10-month follow-up. Given this replication of earlier findings we propose that the strongest signals in relation to ACTdp relate to measures of self reported depression, psychological flexibility and mindfulness. Although lack of change in objective measures of symptom severity have been reported in previous trials of ACTp (e.g. Bach and Hayes, 2002) lack of any signal on any observer based measures in our study is an important consideration.

We would also argue for the additional inclusion of behaviourally based measures of functioning. This would be in keeping with the goals of ACTdp to increase behavioural activation through engagement in valued activities. A future large-scale trial could include the measurement of daily activities as a key outcome. In their trial of Social Recovery CBT (CBTsr) in first episode psychosis, Fowler et al. (2009) used the Time Use Survey (Short, 2006) as an interview based measure of hours spent in 'Constructive Economic Activity' and in 'Structured Activity'. The pilot study data showed signals suggesting that compared to TAU CBTsr was associated with improved economic activity (increase of 4.4 h versus 3.2 h) and improved structured activity (12.0 h versus 4.1 h). These measures can also be supplemented by use of objective measures of physical activity such as ActiGraphy. For example, using actigraphic measurement of daytime routines Wichniak et al. (2011) found that in people with schizophrenia, higher rates of depression were associated with lower rates of physical activity and longer time spent in bed. This is a highly relevant outcome as a lack of physical and leisure time activity is linked to poorer quality of life in schizophrenia (Vancampfort et al., 2011).

Our study had some noteworthy limitations. First, the sample size of 29 was small. But, the 11 randomised controlled trials included in the Whitehead et al. (2002) Cochrane Review of antidepressants in schizophrenia all randomised $n < 30$ participants. Of the 5 RCTs of ACTp (Bach and Hayes, 2002; Gaudiano and Herbert, 2006; White et al., 2011; Shawyer et al., 2007; Gaudiano et al., 2015) the mean sample size is

Table 4
Associations between primary outcomes (change scores CDSS and BDI) and therapy mechanisms (and respective change scores KIMS and AAQ).

Variable	KIMS Observing	KIMS Describing	KIMS Awareness	KIMS Acceptance	AAQ total
CDSS 5-months	−0.11	−0.34	−0.14	−0.31	0.30
CDSS 10-months	0.06	−0.33	−0.26	−0.33	0.28
BDI 5-months	−0.58**	−0.63**	−0.41**	−0.21	0.55**
BDI 10-months	−0.17	−0.49**	−0.53**	−0.49**	0.41*

* $p < 0.05$.
** $p < 0.01$.

40.6 (range 13–80). Gaudiano et al. (2015) conducted a randomised controlled trial of an ACT based treatment package for people with affective psychoses (mostly major depression with psychotic features) and found medium to large effects for of ACT on depression and psychosocial functioning. The study sample size was n = 13, randomization was not independent of trial team and assessment of outcome was unblinded. Taken together these findings indicate a need for large scale, well-designed methodologically rigorous trials targeting depression in the context of psychosis. A second limitation is that although our trial was blinded, our rates of unblinding were high in the ACTdp + SC group. Our RAs were instructed to remind both staff and participants about the importance of blinding. In addition, separate office facilities, an independent randomization procedure that protected the blind, banning discussions regarding participants between RAs and Trial Therapists were instituted throughout the trial. Despite these efforts, the main source of unblindings was participants and less frequently health service staff. Where an unblinding occurred we were able to allocate an alternative blinded researcher to undertake subsequent follow-up assessments. In addition, since all assessments were audio recorded (with consent) we were able to subject unblinded assessments to independent verification of symptoms severity. Finally, our approach to recruitment was informed by an earlier feasibility trial of ACT for emotional distress in psychosis (White et al., 2011). A clear signal emerging from the trial was a change in depression amongst those participants receiving ACT (White et al., 2013, 2015). All of these steps suggest that the observed treatment effect on the self-report BDI-II cannot be easily dismissed as a spurious consequence of unblinding. Similarly, the probability that the insignificant effect on the CDSS was due to inadvertent contamination of observer ratings is reduced by the steps taken to deal with unblindings. The main conclusion to draw about this relates to the importance of future trials having a very robust a priori plan for minimizing the likelihood of penetration of blind treatment allocation. This is a particular challenge in psychological treatment studies where therapy content may "leak" through in the accounts given by patients to research assessors. For example, ACTdp treated patients may inadvertently report values consistent behavior that has arisen as a consequence of receiving treatment.

Depression is a major contributor to loss of quality of life in schizophrenia and other psychotic disorders (Saarni et al., 2010) and is a clear risk factor for suicide (Drake et al., 1985). Depression has been associated with poorer adherence to treatment (Conley, 2009), longer duration of untreated psychosis (Drake et al., 2003), greater problems in family relationships (Rocca et al., 2005), poorer interpersonal functioning (Rocca et al., 2005), and greater experiences of stigma (Angermeyer et al., 2004). The development of future large scale generalizable randomised controlled trials to improve depression and functioning in people with schizophrenia and other psychoses is clearly merited. ACT is one clear candidate treatment that has the potential to improve engagement with valued life goals and activities alongside feelings of depression and demoralization.

Contributors

AG was Chief Investigator, RW supervised the therapists, RW, AB, IF and HMcL were Principal Investigators, CS, SB, JMcT, and CC recruited participants and undertook assessments, RMacL & EL delivered the experimental interventions, SB, BSR and RY undertook statistical analyses of the data. All authors contributed to the writing of the manuscript.

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Conflict of interests

None.

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