Combined individual and family therapy in comparison to treatment as usual for people at-risk of psychosis: A feasibility study (IF CBT): Trial rationale, methodology and baseline characteristics

Authors:

Heather Law[1, 2], Emma Izon[1, 2], Karmen Au-Yeung[1], Anthony P. Morrison[1, 2], Rory Byrne[1, 2], Caitlin Notley[3], Alison Yung[2], John Norrie[4], and Paul French[5,61],

[1] Greater Manchester Mental Health NHS Foundation Trust, Research and Development

[2]University of Manchester

[3]University of East Anglia, Norwich Medical School

[4] University of Edinburgh, Centre for Population Health Sciences

[5] Manchester Metropolitan University

[6] Pennine Care NHS Foundation Trust

ABSTRACT

Background:
Current National Institute for Health and Care Excellence (NICE) guidelines for psychosis recommend psychological therapy with or without family intervention for individuals at-risk of developing psychosis. NICE guidelines have a specific research recommendation to investigate the clinical and cost effectiveness of combined individual and family intervention. We report the rationale, design and baseline characteristics of a feasibility study investigating combined Individual and Family Cognitive Behavioural Therapy (IFCBT).

Methods:
The IFCBT study was a single blind, pilot randomised controlled trial (RCT) to compare a combined individual and family Cognitive Behavioural Therapy (CBT) intervention to treatment as usual. Participants were assessed using the Comprehensive Assessment of the At-risk Mental State (CAARMS) and randomly allocated to either therapy or enhanced treatment as usual (ETAU). All participants were followed up at six and twelve months. Primary feasibility outcomes were recruitment and retention of participants. Secondary outcomes included transition to psychosis and assessment of mood, anxiety and the relationship of the individual and nominated family member.

Results:
We report data showing entry into the study from initial enquiry to randomisation. We report the characteristics of the recruited sample of individuals (n=70) and family members (n=70) at baseline

Conclusions:
The study recruited to 92% of target demonstrating it is feasible to identify and recruit participants. Our study aimed to add to the current evidence base regarding the utility of family interventions for people at-risk of psychosis.

Trial registration:

-ISRCTN42478021

This article presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference PB-PG-1014-35075). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Data Sharing

The data that support the findings of this study are available from the corresponding author upon reasonable request.

INTRODUCTION

Over the last decade there has been increasing interest in the ability to identify and intervene early in the onset of psychosis (Fusar-Poli et al., 2013). Researchers have validated operational criteria to identify those with an 'At-risk Mental State' (ARMS) for psychosis, allowing early identification of individuals at high risk of developing Schizophrenia or related psychotic disorders. Following successful identification of people meeting criteria for ARMS, researchers and clinicians are now focusing on prevention and intervention strategies. The personal, social and economic burden associated with psychosis has been a key driver for development of effective interventions to prevent transition to psychosis.

Previous studies of transition rates and interventions for people at-risk of psychosis

A systematic review which examined 28 studies, indicated transition rates of children and adolescents from ARMS to psychosis were 40% at 6 months, between 17-20% at 1 year, and between 7-21% at 2 years (Tor et al., 2017). These rates are consistent with an earlier meta-analysis of transition outcomes, which found individuals to be at very high risk of developing psychosis within the first 3 years of clinical presentation (Fusar-Poli et al., 2012). In the long-term, the ARMS is significantly associated with increased risk of developing psychosis, but the accuracy is modest, demonstrating the Brief Limited Intermittent Psychotic Symptoms (BLIPS) subgroup at a higher risk compared to the Attenuated Psychotic Symptom (APS) subgroup ($p<0.001$) (Fusar-Poli et al., 2017).

Several randomised controlled trials (RCTs) of interventions for individuals who meet criteria for ARMS have been conducted. Interventions included non-pharmacological interventions such as CBT (Morrison et al., 2004; Morrison et al., 2012; Stain et al., 2016; Addington et al., 2011), family therapy (Miklowitz et al., 2014) and cognitive remediation (Hooker et al., 2014; Urben et al., 2012); pharmacological interventions using antipsychotics (Bechdolf et al., 2017; McGorry et al., 2013; McGlashan et al.,

2006; Woods et al., 2003) and experimental pharmacotherapies such as omega-3 fatty acids (Amminger et al., 2010).

The National Institute for Health and Care Excellence (NICE, 2014) guidelines (guideline CG178) development group, found moderate evidence for CBT, concluding that further research in complex psychological interventions is required. This was consistent with findings published in NICE guidelines (2014) for psychosis and schizophrenia that suggests antipsychotic medication should not be used as a first line treatment of ARMS but supported the use of psychological interventions. They also made a specific research recommendation for the conduct of a trial of combined individual and family therapy for this group.

A further meta-analysis supported the findings of the NICE guideline group (van der Gaag et al., 2013). A 2014 meta-analysis focusing specifically on CBT found that the relative risk of developing psychosis was reduced by more than 50% for those receiving CBT at every time point and concluded that CBT-informed treatment is associated with a reduced risk of transition to psychosis at 6, 12 and 18–24 months, and reduced symptoms at 12 months (Hutton & Taylor, 2014).

Results from previous treatment studies have been invariably mixed and often conflicting. The evidence for a specific intervention superiority in psychosis prevention remains inconclusive (Davies et al., 2018). However earlier meta-analysis that compare all trial interventions (both psychosocial and pharmacological) with needs-based interventions indicate that in group-level analysis of most ARMS individuals improve in their symptoms and functioning over time, with transition rated reduced and delayed (Nelson, Amminger & McGorry, 2018).

Study rationale and aims

To our knowledge, there have been two published studies examining the potential for family interventions with this group to reduce the rate of transition to psychosis. This is despite the evidence base for family interventions for psychosis, which show an ability to reduce relapse rates and provide better prognosis (Pharoah, Mari, Rathbone, & Wong, 2010; Pitschel-Walz, Leucht, Bäuml, Kissling, & Engel, 2001). In addition, a recent systematic review looking at the family environment in ARMS found higher criticism and hostility linked to poorer functioning and worse symptoms in families of ARMS, with similar rates of high expressed emotion compared to First Episode Psychosis (Izon et al., 2018). Miklowitz et al. (2014) found 6 of 102 participants transitioned to psychosis, with an overall risk of 6%. None of the 6 participants who converted were taking antipsychotic medications at entry. There were fewer transitions in the FI group (2% compared to 11%) with the FI

participant transitioning within 30 days of randomisation. The FI was associated with greater improvements in attenuated symptoms over 6 months relative to control. Key components included psychoeducation and development of a prevention plan with the service-user and family. Sessions focused on improving communication and focusing on enhancing problem solving skills. A further study (Landa et al, 2016) investigated different group-and-family based CBT interventions, finding statistically significant decreases in attenuated psychotic symptoms, negative symptoms, depression and improvements in functioning. Family members showed significant improvements in use of CBT skills, enhanced communication with their offspring, and greater confidence in their ability to help. However, this was a small (N=6), open, uncontrolled study and methodological shortcomings from the poor design limit its interpretation.

Additional family studies found integrated treatment of social skills training and multi-family group psychoeducation significantly reduced risk of transition compared to standard care in ARMS individuals with schizotypal disorder (Nordentoft et al, 2006). One pilot study separated individuals at the highest risk of psychosis transition to a family-aided assertive community treatment, whilst those with lower risk were assigned to community care (McFarlane et al, 2015). Although there were no differences in transition, the family treatment had some benefits over community care. There is limited literature of family RCTs with suggestions for treatment strategies combining family and individual CBT (Stafford et al., 2013; Miklowitz et al., 2014; NICE, 2014).

The current study aimed to investigate the feasibility of a combined Individual and Family Cognitive Behavioural Therapy (IFCBT) for people considered to be at-risk of developing psychosis. Our primary outcome was to recruit and consent to participate in a randomised trial, adhere to the intervention, retain participants across both arms through assessment at follow-ups and gather data to inform outcome

parameter estimates. From this, we will be able to assess the acceptability of the intervention to service users and their key family member/carer. Furthermore, the trial will provide initial indications of the impact of a combined approach of individual CBT and family intervention on transition rates to inform the primary outcomes for a future definitive randomised controlled Trial (RCT).

METHODS

The main study was a single (rater) blind randomised feasibility study with two conditions; Individual and Family CBT (IFCBT) plus enhanced treatment as usual (ETAU) vs. ETAU alone in people considered to be at high-risk of developing psychosis. The trial randomly allocated participants who met criteria to a 6-month package of either condition, using a secure telephone randomisation service.

Assessments were conducted by research assistants, who were blind and independent to treatment group. Participants were made aware to conceal their allocation from the research assistants when they were in correspondence and during follow-up assessment. All allocation data was inaccessible to research assistants, with separate offices utilised to retain the blind. Assessments were conducted at baseline, post treatment (6 months) and follow-up (12 months) with both the individual and their nominated family member/carer. There was also a nested qualitative study to identify key themes associated with the acceptability of IFCBT in individuals at high risk of psychosis and experiences of being involved in the trial. Additionally, family members/carers of participants were interviewed to explore their unique experiences to inform these outcomes.

The study was approved by the North West - Greater Manchester East Ethics Committee (REC reference: 16/NW/0278).

Participants

A sample size of 60 is considered adequate for obtaining reliable sample size estimates, which will facilitate the main aims of a feasibility study (Sim & Lewis, 2012). Based on requiring 60 participants across conditions, a target recruitment of 76 (38 per condition) over the recruitment period would allow a dropout rate of 20%.

Formal sample size calculations were not appropriate for a pilot study aimed at establishing feasibility and statistical significance of any findings will not be the primary focus of the analysis. The sample will also include a family member, carer or loved one as nominated by each participant (we will use the term family/carer for this throughout this paper).

Recruitment took place across 2 mental health trusts in North West England (Greater Manchester Mental Health NHS foundation Trust and Pennine Care NHS Trust) primarily via Early Intervention in Psychosis teams. Participants were also able to self-refer via posters or leaflets. Participants were required to meet the following criteria:

Inclusion Criteria

a) Aged 16-35.

b) Screen positive on the CAARMS for an At-risk Mental State.

c) Be living (or in regular contact) with a family member, carer or loved one.

d) Help seeking.

Exclusion Criteria

a) Receipt of anantipsychotic medication to treat symptoms of psychosis.

b) Moderate to severe learning disability.

c) Organic impairment.

d) Insufficient fluency in English.

e) Significant risk to self or others.

Assessment of eligibility and outcome measures

Trial eligibility was assessed using the Comprehensive Assessment of At-risk Mental States (CAARMS) with participants meeting criteria for one of the three ARMS subgroups

i) trait vulnerability risk factors, defined by the presence of either a first degree relative with a history of psychosis or a pre-existing schizotypal personality disorder;

ii) state risk factors, defined by the presence of transient psychotic symptoms, called Brief Limited Intermittent Psychotic Symptoms (BLIPS);

iii) state risk factors, defined by Attenuated Psychotic Symptoms (APS).

According to the CAARMS criteria (Yung et al., 2006), individuals within each subgroup also need to display reduced or chronic low functioning and need to be help seeking.

Full assessments were conducted by assessors blind and independent to treatment group on three occasions: initial baseline, 6 months post randomisation (post-treatment for the therapy group) and 12 months post randomisation. Individual participants were reimbursed £20 for their time at each assessment, family member/carers £10 and both received £10 for any additional qualitative interviews. All eligibility decisions were confirmed by a qualified clinician and all assessors were fully trained in the measures used. Table 1 summarises the measures used at each assessment time point.

[Insert Table 1 Assessment schedule]

The main objective was to evaluate the feasibility of the trial. Primary feasibility outcomes were therefore: recruitment and retention of participants in both arms of the study and adherence to therapy. The primary clinical outcome is transition to psychosis as defined by the Comprehensive Assessment of At-risk Mental States (CAARMS).

Secondary outcome measures for both participant and family member/carer will include the Time Use Survey, Beck Depression Inventory (BDI) and the Social Interaction Anxiety Scale (SIAS).

Data on health status will be collected by the EQ-5D and used to estimate the health-related utility scores of participants. Furthermore, we assessed the relationship and individual's perceptions of their relationship between themselves and the carer using the Family Questionnaire, Five Minute Speech Sample, Relationship Structure Questionnaire (ECR-RS) and the Perceived Criticism and Warmth Questionnaire. Additionally, we assessed carer burden and

additional measures on their carer health (GHQ), and carer needs (BDI, SIAS, EPQ)

Randomisation

Following written consent, eligible participants were randomised using Christie's secure telephone randomisation service. Randomisation (at the individual level) was independent and concealed, using randomised-permuted blocks of 6-8 and stratified by age and gender. Allocation was communicated to trial manager (to monitor adherence to the randomisation algorithm), trial therapist and made known to the participant by letter from the administrator. Blinding of allocation was maintained for research assistants, until all outcome measures for all subjects were collected. Blindness was maintained using a range of measures (e.g. separate offices for therapist and researchers, protocols for answering phones, message taking and secretarial support, separate diaries and security for electronic randomisation information). A dual-purpose independent Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC) was set up to oversee the study.

Interventions

The intervention was a combination of Individual and Family Cognitive Behavioural Therapy (IFCBT). The individual CBT treatment was based on that used in several previous treatment studies (French & Morrison, 2004; Morrison et al., 2012; Morrison et al., 2004). The family component was an additional 4 - 6 sessions of CBT with key family members such as parents or carers, to compliment the individual work. Sessions focused on assessment, formulation, problems and goal setting, communication styles and problem solving. The family intervention followed NICE guidelines by including the client and taking account of the relationship between the parent and or carer and the young person. The family/carer component was delivered in tandem with the individual CBT and delivered by the same therapist to maintain engagement and consistency of approach. Participants received the intervention as well as enhanced treatment as usual (ETAU).

Participants who were not allocated to the intervention arm received (ETAU) alone. Irrespective of their group allocation, all Participants were able to access or continue with their treatment as usual (which may include care from an

Early Intervention Service). Early Intervention Services offer treatment to prevent psychosis in accordance with current NICE guidelines which state they should "offer individual cognitive behavioural therapy (CBT) with or without family intervention" and "offer interventions recommended in NICE guidance for people with any of the anxiety disorders, depression, emerging personality disorder or substance misuse" (NICE, 2014).

Enhancements to TAU involved monitoring of symptoms via structured interview, which is associated with the perceived benefits including having a chance to talk at length about concerns. Participants were also given a crisis card providing contact details for appropriate local sources of help in psychiatric emergency and offered a full assessment summary letter. ETAU included liaison with the clinical team, especially around risk issues with a clear safety protocol to alert clinicians, should suicidal or dangerous ideation emerge. The use of ETAU as a control has the advantage of ensuring all trial participants derive some benefit from the trial, ensuring that it conforms to the highest ethical standards.

Analysis

The main aims of the feasibility study will be delivered both via the continued monitoring of descriptive data and the analysis of data at the end of the last follow-up assessment. This will include reporting data in line with the Consolidated Standards of Reporting Trials (CONSORT) 2010 Statement, showing attrition rates and loss to follow-up. Analyses of outcomes will not be focused on statistical significance, but will concentrate on descriptive statistics and confidence intervals for treatment effects. The primary clinical outcome, conversion to psychosis, will be examined using a discrete-time survival model. A detailed statistical analysis plan will be produced prior to the examination of any of the outcome data.

Results

Recruitment to the trial finished in August 2018 with a final sample of 70, with 34 individuals allocated to ETAU and 36 allocated to the Individual and Family Cognitive Behavioural Therapy (IF CBT). The final sample of 70 represented 92% of the original target sample size of 76. Each individual participant nominated a family member/carer to take part, leading to an overall final sample of 140. Initially, participants were able to nominate multiple family/carers (some nominating up to 3). However, it became

apparent that this number of family/carer participants would not be feasible to follow up within the study. Therefore, participants were required to choose just one family/carer for the remainder of the study.

Demographic characteristics of the sample can be seen in table 2. Baseline variable scores including CAARMS subscale scores for participants can be found in table 3. Table 4 includes baseline variable scores for family member/carer. The initial CONSORT diagram for entry into the trial is shown in figure 1. The CONSORT highlights a high proportion of initial enquiries, with only a third referred. This may reflect Early Intervention of Psychosis services that aim to meet the needs of those at-risk of developing psychosis, those who have already experienced a first episode of psychosis, as well as service-users reporting high levels of risk and disengagement.

[insert Table 2: Demographics and referral sources of participants in the IFCBT Trial]

[insert Table 3: Baseline variable scores (main participant)]

[insert Table 4: Family member/carer baseline variable scores]

[insert Figure 1 CONSORT diagram for entry into the study]

Discussion

The IF CBT study was a single rater, blind randomised feasibility study comparing individual and Family CBT (IFCBT) plus enhanced treatment as usual (ETAU), to ETAU alone in people considered to be at high risk of developing psychosis. This pilot feasibility study was in line with the research recommendation in the NICE guidelines for psychosis and schizophrenia in children and young people (NICE., 2014), which states a need to establish the clinical and cost effectiveness of a combined family intervention with individual CBT for those considered to be at-risk of developing psychosis. Previous meta-analysis (Davies et a., 2018) suggests conflicting results regarding the efficacy of many trials and their tested treatments. As discussed, two studies examined the potential for family interventions for ARMS with reduced rates of transition to psychosis in comparison to usual care, fewer transitions and greater improvements in attenuated symptoms in the FI group relative to control (Miklowitz et al., 2014), albeit, despite methodological shortcomings of one study (Landa et al., 2014). In line with treatment recommendations from NICE guidelines (2014), the current trial is the first of its kind that compares a combined approach of individual and family intervention to usual care. This study provides a significant first step in establishing the evidence base for such a combined intervention.

Our sample was mostly male, young and predominantly White British. This is a similar sample profile to other ARMS studies (McGorry, 2014; Morrison et al., 2012), although the lack of ethnic diversity in the sample may limit generalisability of findings to

other ethnic groups. The majority of participants were eligible for the trial due to experiencing attenuated psychotic symptoms and having moderately to severely impaired functioning. Again, this is consistent with other trials of the ARMS population.

The study enabled referrals from voluntary sectors, self-referrals as well as NHS sector organisations, enabling multiple entrances into the trial. Unlike other trials of interventions for people at-risk of developing psychosis, referrals to the study were predominantly from Early Detection and Intervention in Psychosis Services. The high number of referrals received in the trial and those ineligible is likely to reflect the evolving role of Early Intervention Services to meet the needs of those at-risk of developing psychosis, as well as those who have already experienced a first episode of psychosis. In terms of feasibility of future studies for young people with an at-risk mental state and indeed a definitive trial of combined family and individual interventions, this evolution of Early Intervention Services allows researchers to have a direct referral pathway for ARMS populations from clinical services into research trials, allowing an efficient and effective way to identify eligible participants and offer them the option of taking part in research.

Interestingly, despite the increased availability of support and intervention from these clinical services, many young people still opted to take part in the research trial. Only 13% declined to take part after being referred, with reasons varying from not help seeking, not being interested in the research or personal reasons for not wanting to be involved. An additional 9% decided not to take part due to not wanting family member/carer involved in their care or not having anyone they could nominate to be involved. The majority of young people chose to nominate their parent as the family/carer in the study, although interestingly, a quarter of participants chose to nominate a partner to take part in the intervention, which may suggest a need for a partner/spouse specific intervention. In comparison to previous family studies, other relatives and friends could be involved, who were deemed to have a particular importance to the individual. This may complicate the specific family intervention and be difficult to compare between individuals and groups, however it may be more reflective of clinical need of individuals who wish significant others to be involved in their care and treatment but not a parent.

There were no refusals to be randomised following assessment of eligibility. This low rate of declines/refusals suggests the study and the intervention are highly acceptable to this group, and therefore recruitment to a definitive trial would be feasible.

The sample presented with high levels of comorbid emotional disorders such as moderate to severe depression and high levels of social anxiety. This is highly consistent with the existing literature and sample characteristics from other trials with the ARMS population (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014) . CAARMS scores highlighted high levels of distress in relation to symptoms, particularly on the non-bizarre ideas subscale. In addition to high levels of comorbidity and distress for the individuals taking part in the study, some nominated family members/carers also presented with moderate depression (BDI score 20-28), anxiety and physical health problems.

Data collection was complete in June 2019 and we will report feasibility and acceptability via retention rates, completion of the intervention, safety and qualitative feedback as outlined in this paper and our statistical analysis plan following completion of the trial.

References

Addington, J., Epstein, I., Liu, L., French, P., Boydell, K. M., & Zipursky, R. B. (2011). A randomized controlled trial of cognitive behavioral therapy for individuals at clinical high risk of psychosis. *Schizophrenia Research, 125*(1), 54-61. doi:http://dx.doi.org/10.1016/j.schres.2010.10.015

Amminger, G. P., Schafer, M. R., Papageorgiou, K., Klier, C. M., Cotton, S. M., Harrigan, M. S. M., . . . Berger, G. E. (2010). Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: A randomized, placebo-controlled trial. *Archives of General Psychiatry, 67*(2), 146-154. doi:http://dx.doi.org/10.1001/archgenpsychiatry.2009.192

Bechdolf, A., Müller, H., Stützer, H., Lambert, M., Karow, A., Zink, M., . . . Klösterkotter, J. (2017). 108. PREVENT: A randomized controlled trial for the prevention of first-episode psychosis comparing cognitive–behavior therapy (CBT), clinical management, and aripiprazole combined and clinical management and placebo combined. *Schizophr Bull, 43, S56-57*.

Davies, C., Cipriani, A., Ioannidis, J., Radua, J., Stahl, D., Provenzani, U., … Fusar-Poli, P. (2018). Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, *17*(2), 196–209. doi:10.1002/wps.20526

French, P., & Morrison, A. (2004). *Early Detection and Cognitive Therapy for People at High Risk of Developing Psychosis*. Wiley: London. doi:10.1002/9780470713259.ch14.

Fusar-Poli, P., Bonoldi, I., Yung, A. R., Borgwardt, S., Kempton, M. J., Valmaggia, L., . . . McGuire, P. (2012). Predicting Psychosis Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk. *Arch Gen Psychiatry, 69*(3), 220-229. doi:10.1001/archgenpsychiatry.2011.1472

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rossler, A., Schultze-Lutter, F., . . . Yung, A. (2013). The Psychosis High-Risk State. *JAMA Psychiatry, 70*, 107–120.

Fusar-Poli, P., Nelson, B., Valmaggia, L., Yung, A. R., & McGuire, P. K. (2014). Comorbid Depressive and Anxiety Disorders in 509 Individuals With an At-Risk Mental State:

Impact on Psychopathology and Transition to Psychosis. *Schizophrenia Bulletin, 40*(1), 120-131. doi:10.1093/schbul/sbs136

Fusar-Poli, P., Rutigliano, G., Stahl, D., Davies, C., De Micheli, A., Ramella-Cravaro, V., . . . McGuire, P. (2017). Long-term validity of the At Risk Mental State (ARMS) for predicting psychotic and non-psychotic mental disorders. *European Psychiatry, 42*, 49-54. doi:https://doi.org/10.1016/j.eurpsy.2016.11.010

Hooker, C. I., Carol, E. E., Eisenstein, T. J., Yin, H., Lincoln, S. H., Tully, L. M., . . . Seidman, L.J. (2014). A pilot study of cognitive training in clinical high risk for psychosis: Initial evidence of cognitive benefit. *Schizophr Res, 157*, 314–316.

Hutton, P., & Taylor, P. J. (2014). Cognitive behavioural therapy for psychosis prevention: a systematic review and meta-analysis. *Psychological Medicine, 44*(3), 449-468.

Izon, E., Berry, K., Law, H., & French, P. (2018). Expressed emotion (EE) in families of individuals at-risk of developing psychosis: A systematic review. *Psychiatry research*, *270*, 661-672.

Landa, Y., Mueser, K. T., Wyka, K. E., Shreck, E., Jespersen, R., Jacobs, M. A., . . . Walkup, J. T. (2016). Development of a group and family-based cognitive behavioural therapy program for youth at risk for psychosis. *Early Interv Psychiatry, 10*, 511–521.

Mari, J. D. J., & Streiner, D. L. (1994). An overview of family interventions and relapse on schizophrenia: meta-analysis of research findings. *Psychological Medicine, 24*(3), 565-578.

McFarlane, W. R., Levin, B., Travis, L., Lucas, F. L., Lynch, S., Verdi, M., . . . Spring, E. (2015). Clinical and functional outcomes after 2 years in the early detection and intervention for the prevention of psychosis multisite effectiveness trial. *Schizophr Bull, 41*, 30–43.

McGlashan, T. H., Zipursky, R. B., Perkins, D., Addington, J., Miller, T., Woods, S. W., . . . Breier, A. (2006). Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. *Am J Psychiatry, 163,* 790–799.

McGorry, P. (2014). Preventive strategies in emerging mental disorders in young people: Clinical staging and translational research. *International Journal of Neuropsychopharmacology, 17*, 2.

Miklowitz, D. J., O'Brien, M. P., Schlosser, D. A., Addington, J., Candan, K. A., Marshall, C., . . . Cannon, T. D. (2014). Family-focused treatment for adolescents and young adults at high risk for psychosis: results of a randomized trial. *Journal of the*

American Academy of Child & Adolescent Psychiatry, 53(8), 848-858. doi:https://dx.doi.org/10.1016/j.jaac.2014.04.020

Morrison, A. P., French, P., Stewart, S. L. K., Birchwood, M., Fowler, D., Gumley, A. I., . . . Dunn, G. (2012). Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *British Medical Journal, 344*. doi:10.1136/bmj.e2233

Morrison, A. P., French, P., Walford, L., Lewis, S. W., Kilcommons, A., Green, J., . . . Bentall, R. P. (2004). Cognitive therapy for the prevention of psychosis in people at ultra-high risk: randomised controlled trial. *Br J Psychiatry, 185*, 291-297. doi:10.1192/bjp.185.4.291

Nelson, B., Amminger, G. P., & McGorry, P. D. (2018). Recent meta-analyses in the clinical high risk for psychosis population: clinical interpretation of findings and suggestions for future research. *Frontiers in psychiatry*, *9*, 502. doi:10.3389/fpsyt.2018.00502

NICE. (2014). *Psychosis and schizophrenia in adults: Preventing Psychosis*. Retrieved from NICE clinical guidelines, London:

Nordentoft, M., Thorup, A., Petersen, L., Ohlenschlager, J., Melau, M., Christensen, T. O., . . . Jeppesen, P. (2006). Transition rates from schizotypal disorder to psychotic disorder for first-contact patients included in the OPUS trial. A randomized clinical trial of integrated treatment and standard treatment. *Schizophr Res, 83*, 29–40.

Pharoah, F., Mari, J. J., Rathbone, J., & Wong, W. (2010). Family intervention for schizophrenia. *The Cochrane Library*.

Pitschel-Walz, G., Leucht, S., Bäuml, J., Kissling, W., & Engel, R. R. (2001). The effect of family interventions on relapse and rehospitalization in schizophrenia—a meta-analysis. *Schizophrenia Bulletin, 27*(1), 73-92.

Sim, J,, & Lewis, M. (2012). The size of a pilot study for a clinical trial should be calculated in relation to considerations of precision and efficiency. *J Clin Epidemiol, 65*, 301-308.

Stafford, M. R., Jackson, H., Mayo-Wilson, E., Morrison, A. P., & Kendall, T. (2013). Errata: Early interventions to prevent psychosis: systematic review and meta-analysis. *BMJ 346*, f762–f762.

Stain, H. J., Bucci, S., Baker, A. L., Carr, V., Emsley, R., Halpin, S., . . . Startup, M. (2016). A randomised controlled trial of cognitive behaviour therapy versus non-directive reflective listening for young people at ultra high risk of developing psychosis: The detection and evaluation of psychological therapy (DEPTh) trial. *Schizophr Res, 176*, 212–219.

Tor, J., Dolz, M., Sintes, A., Muñoz, D., Pardo, M., de la Serna, E., . . . Baeza, I. (2017). Clinical high risk for psychosis in children and adolescents: a systematic review. *European Child & Adolescent Psychiatry*. doi:10.1007/s00787-017-1046-3

Urben, S., Pihet, S., Jaugey, L., Halfon, O., & Holzer, L. (2012). Computer-assisted cognitive remediation in adolescents with psychosis or at risk for psychosis: A 6-month follow-up. *Acta Neuropsychiatr, 24,* 328–335.

van der Gaag, M., Smit, F., Bechdolf, A., French, P., Linszen, D. H., Yung, A. R., . . . Cuijpers, P. (2013). Preventing a first episode of psychosis: meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups. *Schizophr Res, 149*(1-3), 56-62. doi:10.1016/j.schres.2013.07.004

Woods, S. W., Breier, A., Zipursky, R. B., Perkins, D. O., Addington, J., Miller, T. J., . . . Tohen, M. (2003). Randomized trial of olanzapine versus placebo in the symptomatic acute treatment of the schizophrenic prodrome. *Biological Psychiatry, 54*(4), 453-464.

Yung, A. R., Stanford, C., Cosgrave, E., Killackey, E., Phillips, L., Nelson, B., & McGorry, P. D. (2006). Testing the ultra high risk (prodromal) criteria for the prediction of psychosis in a clinical sample of young people. *Schizophrenia Research, 84*(1), 57-66.

Table 1 Assessment schedule

Measure	**Baseline**		**6 months**		**12 month**	
	Individual	Family	Individual	Family	Individual	Family
CAARMS	✓		✓		✓	
SOFAS	✓		✓		✓	
EQ-5D	✓	✓	✓	✓	✓	✓
GHQ	✓	✓			✓	✓
Time Use Interview	✓		✓		✓	
BDI	✓	✓	✓	✓	✓	✓
SIAS	✓	✓	✓	✓	✓	✓
PSWQ	✓	✓	✓	✓	✓	✓
FMSS		✓		✓		✓
FQ	✓	✓	✓	✓	✓	✓
ECR-RS	✓	✓	✓	✓	✓	✓
PCPW	✓	✓	✓	✓	✓	✓

Abbreviations: CAARMS (Comprehensive Assessment of At Risk Mental States); SOFAS (Social and Occupational Functioning Assessment Scale); EQ-5D (Health Questionnaire); GHQ (General Health Questionnaire); BDI (Beck Depression Inventory); SIAS (Social Interaction Anxiety Scale); PSWQ (Penn State Worry Questionnaire); FMSS (Five Minute Speech Sample); FQ (Family Questionnaire); ECR-RS (Relationship Structures); PCPW (Perceived Criticism and Warmth Questionnaire).

Table 2: Demographics and referral sources of participants in the IFCBT Trial

Variables of Interest	**N (%) or M (SD)** ***N* = 70**
Age at entry Range (years)	22.2 (4.9) (16-35)
Male:Female ratio	42:28
Ethnicity	
White	61 (87.14%)
Mixed	4 (5.71%)
Asian	3 (4.29%)
Other	2 (2.86%)
Highest Education	
Primary (school)	9 (12.9%)
Secondary (GCSEs)	30 (42.9%)
Further (A levels)	22 (31.4%)
Higher (University)	9 (12.9%)
Relationship with Other	
Parent	43 (61.4%)
Other relative	3 (2.9%)
Partner	18 (25.7%)
Friend or Other (E.g. neighbour)	6 (5.7%)
Living Arrangements	
Parents	20 (28.6%)
Partner	13 (18.6%)
Alone	5 (7.1%)
Parents and Siblings	20 (28.6%)
Other (e.g. friends)	12 (15.7%)
Previous Receipt of CBT	
Yes	23 (32.9%)
No	46 (65.7%)
Referral Source	
Early Detection / Intervention in Psychosis Service	51 (72.9%)
Substance Misuse	5 (7.1%)
CAMHS	1 (1.4%)
College	1 (1.4%)
Self-referral	4 (5.7%)
IAPT Plus	1 (1.4%)
Employment Support	2 (2.9%)
Primary Care	2 (2.9%)
Other e.g. previous engagement in research	3 (4.3%)

Table 3: Baseline variable scores (main participant)

Variable		***n***	**Percentage or M (SD)**		
CAARMS subgroup at entry to trial					
	Attenuated Psychosis	*56*	80%		
	ARMS Vulnerability	*3*	4.3%		
	ARMS BLIPS	*0*	-		
	More than one ARMS group	*11*	15.7%		
SOFAS total		*70*	43.09 (9.75)		
BDI total		*69*	28.1 (13.3)		
SIAS total		*69*	42.9 (15.9)		
EQ5D health state mean		*69*	56.4 (23.18)		
CAARMS subscale scores		***N***	**Whole sample M (SD)**	***N***	**Only participants experiencing the phenomenon M (SD)**
	Unusual thought content severity	*70*	2.5 (1.82)	*52*	3.37 (1.22)
	Unusual thought content frequency	*70*	2.59 (1.92)	*52*	3.48 (1.35)
	Unusual thought content distress	*67*	39.40 (38.20)	*49*	53.88 (34.78)
	Non-bizarre ideas severity	*70*	3.07 (1.47)	*63*	3.41 (1.10)
	Non-bizarre ideas frequency	*70*	3.50 (1.54)	*63*	3.89 (1.05)
	Non-bizarre ideas distress	*69*	61.12 (36.31)	*62*	68.02 (31.51)
	Perceptual abnormalities severity	*70*	3.50 (1.48)	*63*	3.89 (0.95)
	Perceptual abnormalities frequency	*70*	2.89 (1.37)	*63*	3.21 (1.02)

	Perceptual abnormalities distress	*68*	53.13 (37.96)	*61*	59.23 (35.24)
	Disorganised speech severity	*70*	1.57 (1.10)	*52*	2.12 (0.68)
	Disorganised speech frequency	*67*	2.67 (1.93)	*49*	3.65 (1.20)
	Disorganised speech distress	*67*	33.94 (38.40)	*49*	46.41 (37.90)
	Aggression severity	*70*	2.86 (1.51)	*63*	3.17 (1.23)
	Aggression frequency	*69*	3.17 (1.61)	*62*	3.53 (1.26)
	Suicidality severity	*70*	2.37 (1.53)	*54*	3.07 (0.93)
	Suicidality frequency	*67*	2.27 (1.85)	*51*	2.98 (1.53)

Table 4: Family member/carer baseline variable scores

Variables	*n*	M (SD) or N (%)
BDI total	*69*	11.97 (13.09),
SIAS total	*69*	22.83 (15.36)
EQ-5D Dimension		
Mobility No problems Problems	*69*	 54 (78.3%) 15 (21.7%)
Self-care No problems Problems (*N*, %)	*69*	 65 (94.2%) 4 (5.8%)
Usual Activity No problems Problems	*69*	 53 (76.8%) 16 (23.2%)
Pain / discomfort No problems Problems	*69*	 43 (62.3%) 26 (37.7%)
Anxiety / depression No problems Problems	*69*	 40 (58.0%) 29 (42.0%)
Health State Mean	*69*	71.99 (18.87)
ECR-RS **Attachment related avoidance** **Attachment related anxiety**	*69*	 20.94 (8.15) 7.48 (5.45)

Figure 1 CONSORT diagram for entry into the study