The effect on relapse of Culturally-adapted Family Intervention (CaFI) compared to usual care among Black African & Caribbean people diagnosed with psychosis in the UK: A Randomised Controlled Trial: Protocol (Phases 1 & 2)

Appendix 1: Research Protocol (Phase 1)

Phase 1 Protocol, Version 1

IRAS: 254857

Date: 12.11.2019

Full title of project

The effect on relapse of Culturally-adapted Family Intervention (CaFI) compared to usual care among Black African & Caribbean people diagnosed with psychosis in the UK: A Randomised Controlled Trial.

Plain English Summary

Schizophrenia and other forms of psychosis are serious mental illnesses that cost the UK around 9 billion pounds per year. Treatment is expensive, and many people with these illnesses cannot work. Moreover, families and friends often give 'informal care', so the actual cost of treatment is probably much higher than we think. In addition, there are significant emotional and social costs; supporting people with schizophrenia and psychosis is stressful. There is often conflict in families, and they can easily get 'burnt out'.

Black people in the UK are diagnosed with psychoses, including schizophrenia, at much higher rates than any other ethnic group. Moreover, Black people tend to get into services later than others, and they tend to have longer periods at home without receiving any treatment. This can increase family conflict. Oftentimes, families end up calling the police to help the individual get the treatment they need.

For the individual with schizophrenia, police involvement and being 'sectioned' under the Mental Health Act is part of a 'negative care pathway' that many Black people experience. Once in psychiatric services Black people receive higher doses of medication and are more often treated in seclusion. They also stay longer in hospital than White British people and get more Community Treatment Orders (compulsory treatment in the community). This makes their treatment both more expensive and less satisfactory.

Getting families to understand service users' experiences and supporting service users in understanding the impact of their behaviour on their families can reduce stress and conflict. Family Intervention (FI) is a form of 'talking treatment' that helps with this. It is a form of therapy for service users and their families and carers that can help them to talk about their feelings and to listen to each other. Service users who receive FI are more likely to take their medication and look after themselves better. This stops them from becoming unwell again and going back into hospital as often.

However, many people with schizophrenia and psychoses are not in contact with their families. For them to still benefit from FI, we realised that we needed to do things differently. We have worked with Black Caribbean service users and their families and developed Culturally-adapted FI (CaFI). CaFI is similar to FI, although its content is 'less White' and more culturally acceptable. For example, it takes into consideration things like racism and spirituality and how they affect Black people's experiences of mental illness. It also makes it possible for service users who are not in regular contact with their

families to benefit from the treatment. We did this by asking service users to choose 'trusted individuals' such as their Care Coordinators to work with them. If service users were unable to think of anyone who could do this, we invited community members to 'come alongside'

them as 'Family Support Members' (FSMs)to support them through the therapy. Half the people who received CaFI did so with FSMs, showing a clear need for them.

People who tried CaFI really liked it: 24 out of 26 families completed all ten sessions. CaFI therapists and other health workers also liked it. Everyone who took part thought that it should be available to other ethnic groups as well. We now plan to test CaFI with Black Africans, Caribbeans and people of 'Mixed' African/Caribbean heritage. Although there are differences between these groups, we think that being Black or of Mixed heritage means that some of their experiences are similar and that developing a therapy around these similarities makes sense. As Black people are more likely to be in forensic care (compulsory treatment after committing a crime), we also plan to test CaFI in these settings. FSMs may be especially needed here because people in forensic care are especially likely to lose contact with their families.

Our study has three main aims:

1. See if CaFI works at least as well as usual care and is good value for money
2. Understand what will make it easier/harder for CaFI to be taken up by services
3. Find out what can be done to make it more likely CaFI will be taken up and how best to overcome barriers

The study will run for 54 months in Manchester, Merseyside, London, Midlands, and Southampton. Sites in Bristol and Nottingham may be included later if required. This enables us to look at different services in different parts of the country. We will also talk to people about their experiences and views of CaFI.

Research questions (RCT)

1. Compared with usual care, will Culturally-adapted Family Intervention (CaFI) prove more cost and clinically-effective for African and Caribbean populations in the UK?
2. What are the main barriers and facilitators to CaFI becoming part of routine care?
3. How can facilitators be maximised and barriers overcome?

Background and Rationale

Brief literature review

The incidence of psychotic disorders was once believed to be similar across all populations, but Kirkbride et al[1] confirmed previous findings[2-7] of higher rates among Black populations. The Aetiology and Epidemiology of Schizophrenia and Other Psychoses (AESOP) study[8] reported that, compared with White British people, rates of schizophrenia are around 6 and 9 times greater in Black African and Caribbean groups, respectively.

Although there has been a rapid rise in the number of psychological interventions aimed at meeting the culturally-specific needs of ethnic minorities, they have been mostly among South Asian[9], Latina[10], and Chinese[11 12] people. Studies in Black populations have been predominantly conducted in the United States[13]. We undertook a systematic review[59] and found no trials of culturally-specific psychological therapies, such as FI, for Black populations.

Implications for current NHS policy and practice

Schizophrenia and related psychoses are serious mental illnesses (SMI) that are associated with considerable economic, societal, and personal burden[14 15]. In the UK, the estimated yearly cost of schizophrenia is £8.8bn[1]. Forty percent of this cost (£3.5bn) is attributable to service provision. Lost employment accounts for an additional 47% (£4.1bn), and informal care provided by family and friends accounts for 13% (£1.2bn). The burden of caring for someone with schizophrenia can adversely affect carers' physical and mental health[15], resulting in family conflict. This conflict can, in turn, increase rates of relapse and hospital readmission[16].

Over the past 50 years, UK research has consistently reported that people of Black African and Caribbean origin are more likely to be diagnosed with schizophrenia than other ethnic group[8 17-19]. Despite initiatives to tackle race-based inequalities in mental health[20 21], Black people continue to experience worse care and outcomes. They have longer inpatient stays and receive higher doses of psychotropic medication. They are also more likely to be discharged on Community Treatment Orders, whereby they receive continued supervised treatment, making their care more coercive and costly[22].

People with SMI become more isolated as their social networks shrink over time, which is detrimental to their mental health[23]. Conversely, social support improves mental health and wellbeing and access to care [24]. Black people diagnosed with SMI are more likely to lose contact with their families and communities[25], reducing their access to FI. Our study will enable such service users to receive CaFI by working with FSMs.

Previous research has highlighted the barriers to implementing FI as part of routine care[26 27]. Implementation science in mental health has been described as 'embryonic'[28]. The intersections of cultural adaptation and implementation science might be particularly helpful for bridging the 'translational gap' and facilitating uptake of interventions[29]. The proposed study includes process evaluation to identify and address the facilitators and barriers to implementation to improve the likelihood of CaFI becoming part of routine practice.

Why this research is needed now

Service users from Black African and Caribbean backgrounds (including those who regard themselves as 'Black British' and 'Mixed) are more likely than other ethnic groups to be diagnosed with schizophrenia[30]. Explanations for this include migration[31], living in cities ('urbanicity')[32 33], and socio-economic disadvantage[34]. Lower rates of diagnosis in Africa and the Caribbean[35 36], as opposed to in

the UK, suggest that personal and institutional discrimination are also important contributory factors[37] [38].

Alongside higher rates of diagnosis, Black people also have poorer access to mental healthcare, more negative experiences of services, and worse outcomes[20] [21]. They are more likely than other groups to be admitted to hospital with police involvement under the Mental Health Act[30] [39]. Once hospitalised, they experience higher rates of seclusion and other forms of coercive care[40] [41]. These experiences make Black people fear and mistrust mental health services[42]. Together with high rates of shame and stigma in these communities[43], it is not surprising that Black people tend to avoid contact with mental health services. Research also shows that even when they try to get help, it is not forthcoming[44] [45]. The net result is that African and Caribbean people tend to enter into services later in the illness process[45] and are sicker by the time they do so[44]. Long periods with untreated psychosis place great strain on family relationships and may partly explain why people diagnosed with SMI from these communities are especially likely to lose contact with their families[46]. This reduces their access to evidence based therapies such as Family Intervention (FI).

NICE recommend FI for schizophrenia[47]. Although there are different models of FI, they share common core components such as psycho-education, problem solving, and stress and crisis management[48] [49]. There is strong evidence that FI is both cost- and clinically-effective[48] [49]. For example, FI has been shown to improve medication compliance, self-care and problem-solving, and to reduce the risk and frequency of relapse[48]. As well as improving service users' social functioning and quality of life, FI has been found to reduce carer burden and associated ill-health[50]. However, the viewpoint that FI is time intensive and costly means that it is greatly underused in the NHS[51]. As Black service users are less likely to be in contact with their families (NICE recommends FI is offered only to people in regular contact with their families), they are even less likely to receive FI[47]. This is important, as FI offers advantages over individual therapies, such as Cognitive Behavioural Therapy (CBT), due to family member involvement[52]. We therefore propose the opportunity to offer FI to people without family contact via Family Support Members (FSMs). This might be an important step in helping them to reengage with families and communities members.

In summary, although FI is recommended by NICE for the treatment of schizophrenia, it remains currently underused in the NHS[26]. NICE have recommended developing culturally-appropriate psychological therapies to improve Black people's access to evidence-based care. Without alternative measures of delivering FI, such as involving FSMs, NICE recommendations could inadvertently worsen the inequalities in accessing psychological therapy currently experienced by Black service users and their families. This is especially pertinent for the forensic population, among whom Black service users without family contact are over-represented[20].

Previous Related Research

Given the lack of research into FI among minority ethnic groups[53], we undertook an NIHR-funded feasibility pilot[54] to determine if it was possible to culturally-adapt, implement, and evaluate FI for African-Caribbeans. Our findings demonstrated the feasibility of successfully:

1) recruiting service users and families from this 'hard-to-reach' population
2) recruiting Family Support Members (FSMs) to enable service users not in contact with their families to receive the CaFI intervention
3) delivering CaFI in the NHS in acute, rehabilitation and community settings
4) retaining family units in therapy: 24 of 26 (92%) of those who commenced our Culturally-adapted Family Intervention (CaFI) completed all 10 sessions

CaFI also received high acceptability ratings (above 80%) from service users, family members and health professionals. All groups reported positive benefits, including improved symptoms (as evidenced by better mood and less paranoia) and improvement in social functioning (as evidenced by engaging in volunteering and active planning to return to work and full-time education). Therapeutic alliance was positively rated by all groups. Improved communication between service users, families and health professionals was also reported. Service users' health utility index improved, especially among individuals who were not in contact with their families and who participated with FSMs.

The HTA-funded systematic review[55] highlighted the importance of therapeutic communication and alliance between Black and minority ethnic groups and mental health professionals. Our feasibility pilot achieved therapeutic alliance scores (WAI[56]) comparable or higher to findings from a systematic review of therapeutic alliance in psychological therapies for psychosis[57], underscoring CaFI's acceptability.

In light of the long history of negative relationships between Black people and mainstream mental health services, these are important findings. Although the study was not powered to test hypotheses, the results suggest that engaging Black families in psychological therapy has the potential to a) reduce inequalities in accessing evidence-based, NICE-recommended care and b) deliver significant cost savings. Demonstrating the effectiveness of the intervention might also have implications beyond African and Caribbean people. For example, the role of FSMs might be an important means of enabling access to psychological care for others without families in the UK such as refugees.

Concise statement of the research

The HS&DR-funded study on which this application is based was a feasibility pilot to develop and evaluate the implementation of Culturally-adapted Family Intervention (CaFI) for African-Caribbean people diagnosed with schizophrenia and psychoses, and their families [54]. The proposed study differs in important ways – specifically, it will:

1. Be randomised: In the feasibility pilot this was not the case, and results are therefore not generalizable: we cannot be certain that the findings were not due merely to chance.
2. Be fully powered: This will enable assessment of clinical effectiveness of the intervention compared with usual care.
3. Determine cost-effectiveness: Although in the pilot we proved the feasibility of collecting health utility data as the basis for health economic evaluation, the feasibility study was not designed to determine cost-effectiveness.
4. Include Black Africans: The study population of the feasibility pilot was limited to people from the Caribbean of African descent (including those who self-identified as Black British or 'Mixed', but who had parents/grandparents who migrated from the Caribbean).

5. Include the forensic population among whom Black Africans and Caribbeans are disproportionately represented[58]

Study Aims

Our study has three main aims:

i) Test CaFI's clinical and cost-effectiveness in African and Caribbeans compared with usual care
ii) Identify barriers and facilitators to successful implementation
iii) Determine how to maximise facilitators and overcome barriers

Research Plan & Methods

Phase 1: Qualitative Study

Qualitative data via one-to-one semi-structured interviews, focus groups and consensus methods will be collected and analysed to ensure the intervention is suitable for a Black population comprising Caribbeans and Sub-Saharan Africans. Semi-structured interview schedules and supporting materials (e.g. PowerPoint presentation) used in the feasibility study will be adapted for this proposal based on PPI input and emergent research evidence. Interviews and focus groups will be audio-recorded, transcribed verbatim, and analysed using Framework Analysis[81]. This approach is well-suited to our study as it allows both a priori and emergent themes to be identified. A priori themes will include: perceptions of the intervention's cultural relevance, content and structure of the intervention, and the training needs of therapists and Family Support Members. Consensus health service research methods are usually used where there is complexity and little previous work providing a mechanism for improving group decisions[80]. There are a number of approaches to building consensus. The most common being: i) Delphi studies[77,79]; ii) Nominal group technique (NGT)[78] and iii) Consensus development conferences or panels[80]. In this study, we shall use NGT to arrive at consensus on findings from interviews and focus groups via discussion and voting with experts by experience (service users and carers) and by profession (experts in the fields of transcultural mental health, psychosis, development and/or delivery of psychological interventions). In this context, 'consensus' will equate to 'near-unanimous agreement' achieved by, for example, 80% rating of items as 'high priority'[79].

Interview and focus group samples

We shall conduct separate focus groups with the following stakeholders: i) service users of Sub-Saharan African and Caribbean origin diagnosed with schizophrenia or related diagnoses; ii) relatives/carers/advocates of service users of Sub-Saharan African and Caribbean origin; and iii) healthcare professionals with experience of working with service users of Sub-Saharan African and Caribbean origin and/or their families. Each focus group will have 8-10 participants, based on literature[81] and our previous experiences of conducting focus groups with these stakeholder groups as part of the feasibility study. The minimum age for service users and relatives/carers/advocates taking part in focus groups is 16. The minimum age for healthcare professionals is 18. There is no upper age limit.

We shall conduct separate focus groups with young participants (aged 16-25) to lower potential age-related barriers to participation. However, respecting participants' right to choose, we will not exclude any participants in this age bracket from taking part in the other focus groups, if they wish to do so. We shall also conduct a fourth 'mixed' focus group with a sub-set of participants from the previous three groups to explore consensus on topics and issues discussed in the separate focus groups. These

'mixed' groups will be open to anyone from the previous focus groups if they are comfortable to participate in a group comprising people of mixed ages.

Data collection will be facilitated by Chief Investigator or local Site Principal Investigators, with support from Site Research Assistants.

Each of the following localities shall conduct all four focus groups, totalling up to (30 x 4 =) 120 unique participants:

North West: Greater Manchester Mental Health NHS Foundation Trust (research site)
Pennine Care NHS Foundation Trust (research site)
The University of Manchester (research site)
Mersey Care NHS Foundation Trust (Participant Identification Centre)

Midlands: Coventry & Warwickshire Partnership NHS Trust (research site)
Birmingham & Solihull Mental Health NHS Trust (research site)
The University of Warwick (research site)

London: King's College London (research site)
South London & Maudsley NHS Foundation Trust (research site)

Southampton: Southern Health NHS Foundation Trust (research site)

Focus group findings will inform the cultural-adaptation for Sub-Saharan African service users and their families, and further refinement of the intervention content, delivery and therapist training.

Phases 2 & 3: Internal Pilot and RCT

Study design

This is a mixed-method study comprising a qualitative intervention development phase, multi-site Randomised Controlled Trial (RCT) with an internal pilot, and a process evaluation. The main trial will involve testing Culturally-adapted Family Intervention (CaFI) in four geographical locations (6 NHS Trusts + 2 contingency Trusts) across England. This will be done with a Caribbean sample, among whom feasibility and acceptability have been established (HS&DR Feasibility Pilot)[59] and people of Sub-Saharan African origin.

Internal pilot

As CaFI was not established with African people, neither its acceptability nor the feasibility of recruitment and retention have been tested in this population. In preparing this application, we consulted with members of the Sub-Saharan African community and relevant agencies, such as African & Caribbean Mental Health Services (ACMHS), Manchester. These consultations suggested that CaFI is desired by this population and that there are sufficient similarities between African and Caribbean populations to justify further refinement of the intervention to ensure that it meets the needs of both African and Caribbean people. Specifically, the individuals we consulted felt that it was not the intervention itself that would require adaptation. Rather, the therapy manual and supporting resources would need to include African-specific material and that this would need to be reflected in therapists' cultural competence training. We shall therefore undertake work alongside setting up the main trial to culturally-adapt the intervention with a Sub-Saharan African sample, using the processes and procedures used to develop CaFI[59]. We shall then test the feasibility of recruitment, retention, and data collection in this population by running an internal pilot. Depending on the outcome, we

shall either continue with a Caribbean only sample at this stage or incorporate Sub-Saharan Africans into the main study.

Health service setting and context

Rehabilitation, community and forensic setting in eight NHS Mental Health Trusts:

Table 1: Number of potentially eligible service users across sites

Sites	N
Northwest	
Greater Manchester Mental Health (GMMH) NHS Foundation Trust (host Trust)	1,520
Pennine Care NHS Foundation Trust	375
Mersey Care NHS Foundation Trust	690
Midlands	
Birmingham & Solihull NHS Foundation Trust	3100
Nottinghamshire Health NHS Foundation Trust	1045
London	
South London & Maudsley (SLAM) NHS Foundation Trust	4140
South	
Avon and Wiltshire Mental Health Partnership NHS Trust (Bristol)	325
Southern Healthcare NH	250
Total	**11,425**

Summary Plan of Investigation (Internal pilot & RCT)

Population
The target population will be African- and Caribbean-origin service users (including people who regard themselves as 'Black British' and of 'Mixed' heritage) in rehabilitation, community and forensic settings, and their families. Where biological family members are not available, service users will be able to participate by involving Family Support Members (FSMs). FSMs will can be trusted individuals (such as friends or care coordinators/key workers) nominated by service users. Alternatively, they may be community volunteers, 'befrienders' or former service users (peer support) specifically recruited into this role.

The intervention
10x1-hour sessions of Culturally-adapted Family Intervention (CaFI) will be delivered within a 20-week 'therapy window'. The control group will receive usual care, which typically consists of medication and support from nurses. Given previous reports of lack of availability of FI and our experience of CaFI, we do not anticipate that this 'usual care' will involve forms of FI or similar psychological interventions. To ensure this, this will be one of our exclusion criteria.

Primary outcome
The primary outcome is reduction in relapse, as rated from service user records (case-notes) using a well-established definition of a two-week exacerbation of symptoms leading to a change in

management [60]. Past studies[60] have demonstrated the ability to predict rating of relapse via case-notes in 98% of participants.

Secondary outcomes

The secondary outcome is the Positive and Negative Syndrome Scale (PANSS)[61], Personal and Social Performance Scale (PSP)[62], Perceived Criticism Scale (PCS)[63], Brief Illness Perception Questionnaire (Brief-IPQ)[64], Knowledge about Psychosis Interview (KAPI)[65], General Health Questionnaire (GHQ-12)[66], EQ-5D-5L[67], Working Alliance Inventory (WAI)[68] and Service Engagement Scale (SES)[69].

Sample Size

An existing meta-analysis indicates a relative risk of 0.55 for relapse after family intervention without cultural adaptation[48]; 40% of controls relapsed. Our feasibility study to develop and evaluate CaFI's implementation in Manchester provided outcome data to confirm these findings. A reduction in risk of relapse from 40% during follow-up to 24% (i.e. a risk ratio of 0.6) would equate to a clinically-significant difference sufficiently convincing to inform commissioning and facilitate change in practice. In the control arm, we assume 70% of participants will relapse by 6 months based on previous meta-analyses[48].

Using Stata's 'power logrank' command and assuming a hazard ratio of 0.60 (i.e. the intervention is expected to lower the hazard of relapse over time), 260 participants recruited across four locations (130 in each arm) will provide 80% power, allowing for 20% withdrawal (using Schoenfeld's formula).

Based on our feasibility pilot and recruitment into a previous multi-site study, we are confident that we can recruit the numbers required. In our study, we recruited to target. The Aetiology and Ethnicity in Schizophrenia and Other Psychoses (AESOP) study[8] recruited n=447 eligible Black African and Caribbean participants and n=207 controls from three of our proposed sites - South-east London, Nottingham and Bristol over 18 months in total (Bristol last 9 months only).

Table 1 shows that, nationally, there are approximately 11,500 mental health service users who meet the ethnicity criteria. From our feasibility pilot, we anticipate that there will be missing data and errors in ethnic labelling. Whereas incorrectly labelling Africans as Caribbeans was problematic in the feasibility study, it should have limited impact on recruitment into the proposed trial, as both Africans AND Caribbeans will be recruited. Furthermore, even if half the data were either missing or flawed, that would still leave a pool of 5,750 potential participants.

Randomisation will be stratified by location (NW; Midlands; South; London) and ethnic background (AC; BA). Within each stratum, participants will be randomly allocated (1:1) to either the intervention or control arms in blocks of size 4, 6 or 8: block size will also be chosen at random.

Inclusion criteria

Service users

- African and Caribbean descent (including those who self-identified as 'Black-British', 'Black Caribbean', 'Black African', 'African-Caribbean' or 'mixed' African/Caribbean, but who had at least one parent or grandparent who was born in Sub-Saharan Africa or the Caribbean).
- Diagnosis of schizophrenia or related diagnoses (ICD F20-29/ DSM-IV) [70 71]

- Receiving treatment through psychiatric (acute or rehabilitation) inpatient services or community services within the eight participating NHS Trusts.
- 14 years or older
- Assessed by key workers as having the capacity to consent and participate
- Sufficient understanding of the English language to complete measures.
- No significant cognitive impairment implicated in aetiology (e.g. organic disorder)
- No high risk to self or others as assessed by care teams.

Family members
Family members do not have to be of African or Caribbean origin. They are generally required to be at least 16 years old, but exceptions can be made if a nominated family member (e.g. a sibling or a child) is under 16 and able to assent, with consent from a guardian. They must have sufficient understanding of the English language to be able to give written, informed consent and complete measures.

Exclusion criteria (service users)

- Other ethnic groups
- Not diagnosed with a schizophrenia spectrum disorder or related non-affective psychoses
- Cognitive impairment
- Substance use as primary diagnosis

Recruitment
Based on our sample size calculation, we will need to recruit 14 participants per month across all 8 NHS Trusts. Data will be collected by RAs blind to delivery of the intervention at 4 time-points: baseline, post-intervention and at 6 and 12 months follow-up.

As recruitment will be within communities previously labelled 'hard-to-reach', we shall adopt engagement and recruitment strategies informed by our PPI work and previous HS&DR (CaFI) study. These may include but are not limited to using local media, working with Faith-Based Organisations (FBOs), voluntary sector agencies and community groups.

Within services, we shall place advertisement posters and flyers in GMMH sites accessible to service users, carers and advocates. We anticipate that the study will be adopted onto the NIHR portfolio. Accordingly, NIHR Clinical Research Network (CRN) Clinical Studies Officers (CSOs) will support recruitment, helping to identify and recruit suitable participants. CSOs and RAs will work collaboratively to publicise the study and inform clinical staff about the inclusion criteria. Recruitment packs, including the study Participant Information Sheet (PIS), will be provided for service users who are deemed well enough to participate by their clinical teams, who have the capacity to consent and who gave permission to be contacted by the research team. Service users who remain interested will

be invited to meet with the RA to receive further information about the study and ask any questions before being consented into the study. Consenting participants will be asked to complete baseline assessments during the initial meeting. An additional meeting will be arranged if this is not feasible.

Data collection and analysis

Quantitative
In our HS&DR pilot trial, we have demonstrated the feasibility of delivering CaFI using the following parameters:

- Recruitment (number approached versus number consented)
- Attendance (number of sessions attended)
- Attrition (number of drop-outs at each time point)
- Retention (the proportion of participants who complete therapy sessions)
- Completeness of outcome measurement

In keeping with our protocol, this has informed our choice of outcomes for the proposed trial. Specifically, we have decided against using hospital admission as a primary outcome measure because changes in practice and service delivery (e.g. fewer inpatient beds, greater emphasis on community care) mean this is no longer a meaningful measure. Instead, we focus on relapse. We have demonstrated the feasibility of collecting relapse data (paper in preparation) and this is a Cochrane-recommended measure[48]. We have also demonstrated the feasibility of collecting all proposed secondary outcomes[59].

Statistical analyses will be performed on an intention-to-treat basis. The log-rank test will be used to compare the survival distributions of the two arms. If its assumptions are met, Cox's proportional hazards model will be fitted, allowing adjustment for covariates.

Economic analysis: An economic evaluation comparing the cost-effectiveness of CaFI with usual care will be performed and reported according to the CHEERS statement. Alongside the cost of delivering CaFI, use of other healthcare resources, informal care and employment status will also be captured and considered (societal perspective).

Qualitative
Internal pilot

Qualitative work (focus groups, individual interviews with 'key informants', expert consensus conference) will be undertaken to ensure the intervention is culturally-adapted for a Black population, which includes both Caribbeans and Sub-Saharan Africans. This work will adopt the methods and procedures used to co-develop CaFI in the feasibility pilot.

Main trial

To explore potential barriers and facilitators to implementing CaFI, semi-structured interviews will be undertaken with approximately 30 service users and family members (biological and FSM); purposively sampled across all sites. The final sample will be informed by findings from the

quantitative study and by iterative data collection processes. It is intended to collect data face-to-face. Where this is not possible, telephone/Skype or similar will be used to ensure maximum variation within the sample. Interviews will be audio-recorded, transcribed verbatim, and analysed using thematic analysis[69].

Understanding why effective interventions such as CaFI are successfully implemented in some settings but not others is a key issue for wider uptake and spread. Process evaluation is an essential part of designing and testing a complex intervention and is required to understand how and under what conditions implementation is effective[70]. There are a large number of theoretical frameworks available to understand the implementation processes[71]. We will draw upon a theoretical approach known as Normalisation Process Theory (NPT) which facilitates understanding of the extent to which new processes become part of routine practice[72]. NPT is comprised of four main constructs that represent individual and collective levels of work involved in the implementation of new practice namely, coherence, cognitive participation collective action and reflexive monitoring.

We will conduct semi-structured interviews with around 30 staff (therapists, care coordinators, NHS senior leaders and service managers, commissioners) purposively sampled across all sites. Interview schedules will be informed by NPT and will focus on understanding:

- Sense making: how CaFI is understood and compared with existing practices
- Implementation: how CaFI is developed and translated into practice
- Embedding: how CaFI becomes or does not become routinely incorporated into the everyday work of professionals
- Integration: how CaFI is sustained as part of normal practice

Interviews will be audio-recorded, transcribed verbatim, and analysis will occur blind to trial outcomes to avoid biased interpretation of the findings. Anonymised transcripts will be analysed using Framework Analysis, allowing for both inductive and deductive coding. Deductive coding will be informed by NPT.

Timetable (months)

Total duration: 54
Setting up main trial (Caribbean) & cultural-adaptation (African): 12
Trial Recruitment: 24
Duration of intervention/participant: 10 weeks within 20 week window
Duration of follow-up: 12
Trial duration/participant: 17 (including follow-up)
Close-out (analyses, write up, initial dissemination): 3

Project management

The project will be managed by a Project & Trial Manager in collaboration with CTU. A Research Management Group (RMG) comprising all applicants plus representative from the host Trust's Research and Innovation department will be established. Via regular monthly meeting, they will provide study management and oversight.

A Study Steering Committee (SSC), at least 75% of whom will be independent of the study (including an independent chair and lay members), will be established. They will provide independent scrutiny

and notify funders of any concerns regarding conduct of the study, including falling behind with recruitment or unexpectedly high rates of adverse events.

A Data Monitoring Committee (DMC), a 100% independent four-member panel of Experts by Profession will provide independent assessment of the study conduct. They will assess the progress of the project and determine on whether the RCT will be continue based on the Stop/Go internal pilot.

As with the CaFI Feasibility Pilot, a Research Advisor Group (RAG) comprising service users and carers will be established. RAG will advise on matters such as cultural-validity of and accessibility of study materials. They will contribute to therapists' cultural competence training. At least one member of RAG will be a member of RMG.

Approval by ethics committees

NHS, HRA and site-specific approvals for each participating NHS Trust will be sought.

Patient and Public Involvement

We have consulted with community members, service users and carers in developing this proposal. Specifically, the RDS bursary award has enabled us to consult about the desirability of CaFI for Sub-Saharan Africans. There is overwhelming support for further refining the intervention with PPI and trialling it with a 'Black' versus Caribbean population.

The study is an example of Community-partnered Participatory Research (CPPR) pioneered in the US[72]. For our feasibility study, we adopted NIHR principles for meaningfully engaging with service users and communities to develop research with versus either for or about them[73]. Our experience indicates that partnering with service users, community members and other key stakeholders to develop interventions has a positive effect on uptake, retention and satisfaction. This is particularly important when developing interventions for so called 'hard-to-reach' communities who are known to mistrust mental health services.

As with our feasibility study, we plan to provide PPIE research training and support. Specifically, we shall deliver sessions on research methods and governance as well as awarding honorary contracts to interested individuals to enable them to undertake further study, thus building capacity. Group and individual supervision will be provided for all involved in testing the intervention.

Team Members & Expertise

Principal Investigator

Dr Dawn Edge: Senior Lecturer, Division of Psychology & Mental Health, at the University of Manchester. Dr Edge will lead the project, overseeing all aspects, including setting up, data collection and analysis, dissemination, ethics and governance. She will supervise the trial manager and RAs and oversee coordination across all sites.

Co-applicants

1. Professor Kathryn Abel: Professor of Psychiatry & Director of Centre for Women's Mental Health, School of Health Science, at the University of Manchester and Hon Consultant Psychiatrist (GMMH). Prof Abel will provide expertise in schizophrenia, trial design and senior oversight of the trial.

2. Dr Lesley-Anne Carter: Research Fellow, Centre for Biostatistics, School of Health Sciences, at the University of Manchester. Dr Carter will provide expertise in trial design and statistics.

3. Dr Katherine Berry: Senior Clinical Lecture, in the Division of Psychology & Mental Health, School of Health Science, at the University of Manchester and Consultant Clinical Psychologist (GMMH). Dr Berry will contribute to trial design and therapists' training. She will lead on clinical supervision of therapists.

4. Professor Linda Davies: Professor of Health Economics Research based in the Division of Population Health, Health Services Research & Primary Care, at the University of Manchester. Prof Davies will provide expertise in health economics.

5. Professor Anthony Morrison: Professor of Clinical Psychology, in the Division of Psychology & Mental Health, at the University of Manchester. Director of Research, Development & Innovation, Greater Manchester Mental Health (GMMH) NHS Foundation Trust (the host Trust). In addition to expertise in trial design, Prof Morrison will facilitate service access and provide expertise in trialling psychological interventions.

6. Reverend Paul Grey: Independent Service User Consultant and 'expert by experience'. As chair of the RAG and member of RMG and TSC in our feasibility, Rev Grey will provide invaluable insight from the service user perspective.

7. Ms Sonia Lindsay: Carer Consultant. A member of the RAG in our CaFI feasibility study, Ms Lindsay will provide expertise from the carer perspective.

8. Mrs Michelle Ayavoro: Community Member and activist. A member of the RAG in our CaFI feasibility study, Mrs Ayavoro will be a community-focused Independent Consultant on this project.

9. Dr Shanaya Rathod: Consultant Psychiatrist & Director of Research, Department of Research & Development, at the Southern Health and Social Care Trust. Dr Rathod's role in this project is to provide expertise in cultural adaptation.

10. Dr Shublade Smith: Consultant Psychiatrist, in the Department of Psychiatry, at the Kings College London. Dr Smith's role in this project is providing expertise in transcultural and forensic psychiatry.

11. Dr Claire Henderson: Consultant Psychiatrist, Department of Psychiatry, at Kings College of London. Dr Henderson's role in this project is to provide expertise in trial design and transcultural psychiatry. She will be the site lead in London.

12. Dr Louisa Codjoe: Psychologist, Department of Psychology, at Kings College of London. Dr Codjoe's role in this project is to provide expertise in transcultural psychology.

13. Professor Swaran Singh: Head of Mental Health and Wellbeing, Warwick Medical School, at the University of Warwick. Prof Singh's expertise is in transcultural psychiatry. Professor Singh will be site lead for Coventry and Warwickshire Partnership NHS Trust.

14. Dr Richard Drake: Consultant Psychiatrist, Division of Psychology & Mental Health, at the University of Manchester. Dr Drake's role will be trial design, liaison with clinical services, and providing expertise in culturally-adapted and other psychosocial intervention trials in schizophrenia.

15. Professor Gillian Doody: Dean of Medical Education, Professor in General Adult Psychiatry and Medical Education, Faculty of Medicine & Health Sciences, at the University of Nottingham. Prof Doody will contribute expertise in trial design. Her experience as member of the AESOP team will be invaluable. She will be site lead for Nottingham.

16. Dr Jonathan Evans: Consultant Senior Lecturer, Centre for Academic Mental Health, School of Population Health Sciences, Bristol Medical School, at the University of Bristol. As site lead in Bristol, Dr Evans will provide expertise in psychosis and liaison with clinical services.

17. Dr Nicholas Kennedy: Consultant Psychiatrist, Birmingham and Solihull Mental Health NHS Foundation Trust. With expertise in transcultural psychiatry, Dr Kennedy's role in this project will be to support participant identification in the trust.

Collaborators

Dr Judith Richardson, NICE: Expertise in Health Service Policy and service implementation.

Professor Peter Bower: Chair in Health Sciences, Health Services Research & Primary Care, Division of Population Health, at the University of Manchester. Prof Bower's role in the project includes providing expertise in clinical trials and population health.

Voluntary sector collaborators

African & Caribbean Mental Health Services, Manchester

Rethink, Manchester

More collaborators will be sought during the project.

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Protocol:

The effect on relapse of Culturally-adapted Family Intervention (CaFI) compared to usual care among Sub-Saharan African & Caribbean people diagnosed with psychosis in the UK: A Randomised Controlled Trial (Phase 2)

Version 1

Date: 21st January 2020

Contents Page

List of abbreviations

ACMHS - African & Caribbean Mental Health Services

AESOP – The Aetiology and Epidemiology of Schizophrenia and Other Psychoses

Brief-IPQ – Brief Illness Perception Questionnaire

CaFI – Culturally-adapted Family Intervention

CaKAP – Culturally-adapted Knowledge About Psychosis

CBT – Cognitive-Behavioural Therapy

CHEERS – The Consolidated Health Economic Evaluation Reporting Standards

CI – Chief Investigator

CONSORT - Consolidated Standards of Reporting Trials

CPPR – Community-Partnered Participatory Research

CQC – Care Quality Commission

CRN – Clinical Research Network

CSOs – Clinical Studies Officers

CTO – Community Treatment Order

DMEC – Data Monitoring and Ethics Committee

DSM-V – Diagnostic and Statistical Manual of Mental Disorders ed. 5

EDC – Electronic Data Capture

EQ-5D – EuroQol-5D

EQ-5D-5L – EuroQol-5D Generic health status measure

FBOs – Faith-Based Organisations

FI – Family Intervention

FSM – Family Support Member

GHQ-12 – General Health Questionnaire

GMMH – Greater Manchester Mental Health NHS Foundation Trust

HCPC – Health and Care Professions Council

HRA – Health Research Authority

HS&DR – The Health Services and Delivery Research Programme

HTA – Health Technology Assessment

ICC – Intraclass Correlation Coefficient

ICD – International Classification of Diseases

ICER – The Incremental Cost-Effectiveness Ratio

IPQ – Illness Perception Questionnaire

KAP – Knowledge About Psychosis Questionnaire

KAPI – Knowledge About Psychosis Interview

KASI – Knowledge About Schizophrenia Interview

KCL – King's College London

KCTU – King's Clinical Trial Unit

NICE – National Institute for Health and Care Excellence

NHS – National Health Service

NIHR - National Institute for Health Research

NPT – Normalisation Process Theory

PANSS – Positive and Negative Syndrome Scale

PCS – Perceived Criticism Scale

PI – Principle Investigator

PIS – Participant Information Sheet

PPI – Patient and Public Involvement

PPIE – Public and Patient Involvement and Engagement

PSP – Personal and Social Performance Scale

QALY – Quality-Adjusted Life Year

RA – Research Assistant

RAG – Research Advisor Group

RCT – Randomised Controlled Trial

RDS – Research Design Service

ReACH - University of Manchester's Researching African Caribbean Health

REC – NHS Research Ethics Committee

RMG – Research Management Group

SES – Service Engagement Scale

SMART - Specific, Measurable, Attainable, Relevant, Timely

SMART-ER - Specific, Measurable, Attainable, Relevant, Timely, Evaluate, Reviewed

SMI – Serious Mental Illnesses

SUI – Service-Use Interview

TAU – Treatment As Usual

TSC – Trial Steering Committee

UK – United Kingdom

WAI – Working Alliance Inventory

.CSV – Comma-Separated Values

Protocol Summary

Full title of project

The effect on relapse of Culturally-adapted Family Intervention (CaFI) compared to usual care among Sub-Saharan African & Caribbean people diagnosed with psychosis in the UK: A Randomised Controlled Trial.

Trial registration

Intended registry: ISRCTN (http://www.isrctn.com/)

Protocol version

Date	Version Number	Author(S)
28/10/2019	0.1	HW / HL / DE / LAC / LD / CH / PW
CI Signature		Dawn Edge
21/01/2020	1	HW / HL / DE / LAC / LD / CH / PW
Acting CI Signature		Claire Henderson

Funding

National Institute for Health Research (NIHR), Health Technology Assessment programme (ref: 16/167/76)

Roles and responsibilities

Chief Investigator

Professor Dawn Edge: Chair in Mental Health & Inclusivity, Division of Psychology & Mental Health, at the University of Manchester. Professor Edge will lead the project, overseeing all aspects, including setting up, data collection and analysis, dissemination, ethics and governance. She will supervise the trial manager and RAs and oversee coordination across all sites.

Co-applicant

Professor Kathryn Abel: Professor of Psychiatry & Director of Centre for Women's Mental Health, School of Health Science, at the University of Manchester and Hon Consultant Psychiatrist (GMMH). Prof Abel will provide expertise in schizophrenia, trial design and senior oversight of the trial.

Co-applicant

Dr Lesley-Anne Carter: Research Fellow, Centre for Biostatistics, School of Health Sciences, at the University of Manchester. Dr Carter will provide expertise in trial design and statistics.

Co-applicant

Professor Katherine Berry: Professor of Clinical Psychology, Division of Psychology & Mental Health, School of Health Science, at the University of Manchester and Consultant Clinical Psychologist (GMMH). Prof Berry will contribute to trial design and therapists' training. She will lead on clinical supervision of therapists.

Co-applicant

Professor Linda Davies: Professor of Health Economics Research based in the Division of Population Health, Health Services Research & Primary Care, at the University of Manchester. Prof Davies will provide expertise in economic evaluation of mental health care.

Co-applicant

Professor Anthony Morrison: Professor of Clinical Psychology, in the Division of Psychology & Mental Health, at the University of Manchester. Director of Research, Development & Innovation, Greater Manchester Mental Health (GMMH) NHS Foundation Trust (the host Trust). In addition to expertise in trial design, Prof Morrison will facilitate service access and provide expertise in trialling psychological interventions.

Co-applicant

Professor Shanaya Rathod: Consultant Psychiatrist & Director of Research, Department of Research & Development, at the Southern Health and Social Care Trust. Prof Rathod's role in this project is to provide expertise in cultural adaptation.

Co-applicant

Dr Shubulade Smith: Consultant Psychiatrist, in the Department of Psychiatry, at the Kings College London. Dr Smith's role in this project is providing expertise in transcultural and forensic psychiatry.

Co-applicant

Dr Claire Henderson: Consultant Psychiatrist, Department of Psychiatry, at Kings College of London. Dr Henderson's role in this project is to provide expertise in trial design and transcultural psychiatry. She will be the site lead in London.

Co-applicant

Dr Louisa Codjoe: Psychologist, Department of Psychology, at Kings College of London. Dr Codjoe's role in this project is to provide expertise in transcultural psychology.

Co-applicant

Professor Swaran Singh: Head of Mental Health and Wellbeing, Warwick Medical School, at the University of Warwick. Prof Singh's expertise is in transcultural psychiatry. Professor Singh will be site lead for Coventry and Warwickshire Partnership NHS Trust.

Co-applicant

Dr Richard Drake: Consultant Psychiatrist, Division of Psychology & Mental Health, at the University of Manchester. Dr Drake's role will be trial design, liaison with clinical services, and providing expertise in culturally-adapted and other psychosocial intervention trials in schizophrenia.

Co-applicant

Professor Gillian Doody: Dean of Medical Education, Professor in General Adult Psychiatry and Medical Education, Faculty of Medicine & Health Sciences, at the University of Nottingham. Prof Doody will contribute expertise in trial design. Her experience as member of the AESOP team will be invaluable. She will be site lead for Nottingham.

Co-applicant

Dr Jonathan Evans: Consultant Senior Lecturer, Centre for Academic Mental Health, School of Population Health Sciences, Bristol Medical School, at the University of Bristol. As site lead in Bristol, Dr Evans will provide expertise in psychosis and liaison with clinical services.

Project and Trial Manager

Mrs Helen Wilson based at Greater Manchester Mental Health NHS Foundation Trust (GMMH), Research and Innovation, Rawnsley Building. Mrs Wilson, will oversee the day to day research

activities across study sites and will ensure the study is run ethically and in accordance with research governance.

Collaborators

Professor Peter Bower: Chair in Health Sciences, Health Services Research & Primary Care, Division of Population Health, at the University of Manchester. Prof Bower's role in the project includes providing expertise in clinical trials and population health.

Reverend Paul Grey: Independent Service User Consultant and 'expert by experience'. As chair of the Research Advisory Group and member of the Research Management Group and Trial Steering Committee in the CaFI feasibility, Rev Grey will be providing invaluable insight from the service user perspective. It is envisaged that her will adopt similar roles in this study.

Ms Sonia Lindsay: Carer Consultant and 'expert by experience'. A member of the RAG in our feasibility study, Ms Lindsay will provide expertise from a carer perspective.

Mrs Michelle Ayavoro: Community Member and Activist. A member of the RAG in our feasibility study, she will be a community-focused Independent Consultant on this project.

Dr Josanne Holloway, Clinical Lead, Greater Manchester Mental Health NHS Foundation Trust, will facilitate access to services via clinical PI and community forensic services.

Dr Nicholas Kennedy: Consultant Psychiatrist, Birmingham and Solihull Mental Health NHS Foundation Trust. With expertise in transcultural psychiatry, Dr Kennedy's role in this project will be to support participant identification in the trust.

Dr Judith Richardson, Programme Director – Quality and Leadership, Health and Social Care, NICE. Dr Richardson will contribute expertise in Health Service Policy and service implementation.

Voluntary sector collaborators

African & Caribbean Mental Health Services, Manchester: Support study promotion across their services, such as drop-in support groups for service users and carers.

Rethink, Manchester: Support study promotion via their support groups, social media and newsletter.

Additional collaborators, including from other sites, will be sought during the project.

Trial sponsor

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Plain English Summary

Schizophrenia and other forms of psychoses are serious mental illnesses that cost the UK around 9 billion pounds every year. Many people with these illnesses cannot work. Families and friends often give 'informal care'. This means that the actual cost of caring for people with these conditions is probably much higher than we think. In addition, supporting people with schizophrenia and psychoses can be stressful. There is often conflict in families. Stress and family tension can affect carers' health so that they get 'burnt out'.

Black people in the UK are diagnosed with psychoses, including schizophrenia, at much higher rates than any other ethnic group. Black people also tend to get into services later than others, so they are at home longer before receiving treatment. This can increase stress and conflict in families. Sometimes families end up calling the police for help. Police involvement and being 'sectioned' under the Mental Health Act is part of a 'negative care pathway' that many Black people experience. Once in psychiatric services, Black people receive more medication and are more often treated in seclusion. They also stay longer in hospital than White British people. When discharged, they get more Community Treatment Orders or 'CTOs'. This means getting treatment in the community whether they want it or not. These things make Black people's treatment both more expensive and less satisfactory.

Getting families to understand service users' experiences and helping service users to understand how their behaviour affects their families can reduce stress and conflict. Family Intervention (FI) is a kind of 'talking treatment' that helps with this. Family Intervention can help service users, their carers and families talk about their needs and feelings and listen to each other. Service users who receive FI are more likely to take their medication and look after themselves better. This lowers the risk of them becoming unwell again and going back into hospital as often.

Unfortunately, many people with schizophrenia and psychoses are not in regular contact with their families. For them to still benefit from FI, we need to do things differently. We have worked with African-Caribbean service users and their families to develop Culturally-adapted FI – 'CaFI' for short. CaFI is based on standard FI but has been designed to make it 'less White' and more relevant to Black people's experiences in the UK. For example, it takes into consideration how things like racism and spirituality affect Black people's mental health. It also makes it possible for service users who are not in regular contact with their families to benefit from CaFI. We did this by asking service users to choose 'trusted individuals' such as close friends or Care Coordinators to work with them. If service users were unable to think of anyone who could do this, we invited community members to support them through the therapy as 'Family Support Members' (FSMs). Half the people who received CaFI when we first tested it did so with this support, showing a clear need for FSMs.

People who tried CaFI really liked it: 24 out of 26 family units who started the therapy completed all ten sessions. CaFI therapists and other health workers also liked it. Everyone who took part thought that other ethnic groups should be able to get CaFI too.

We now plan to test CaFI with people of Sub-Saharan African, Caribbean and 'Mixed' African/Caribbean background. Although there are differences between these groups, we think that being Black or of Mixed heritage means people from these backgrounds have enough in common that developing a therapy for Black service users makes sense. As Black people are more likely to be in forensic care (treatment in 'secure' hospitals after committing a crime), we also plan to test CaFI in these settings. FSMs may be really needed here because people in forensic care are especially likely to lose contact with their families.

Introduction

Background and rationale

The incidence of psychotic disorders was once believed to be similar across all populations, but Kirkbride et al. (2012) confirmed previous findings (Cantor-Graae, 2007; Cantor-Graae & Selten, 2005; Fearon et al., 2006; Sproston & Nazroo, 2006; Takei, Persaud, Woodruff, Brockington, & Murray, 1998) of significantly higher rates among Black populations. The Aetiology and Epidemiology of Schizophrenia and Other Psychoses (AESOP) study (Morgan et al., 2006) reported that, compared with White British people, rates of schizophrenia are around 6 and 9 times greater in Sub-Saharan African and Caribbean groups, respectively.

Although there has been a rapid rise in the number of psychological interventions aimed at meeting the culturally-specific needs of ethnic minorities, they have been mostly among South Asian (Naeem, Ayub, Gobbi, & Kingdon, 2009), Latina (Bernal & Domenech Rodríguez, 2009), and Chinese (Chien & Chan, 2004; Chien & Thompson, 2013) people. Studies in Black populations have been predominantly conducted in the United States (Liu et al., 2012). We undertook a systematic review (Edge et al., 2016) and found no trials of culturally-specific psychological therapies, such as FI, for Black populations.

Implications for current NHS policy and practice

Schizophrenia and related psychoses are serious mental illnesses (SMI) that are associated with considerable economic, societal, and personal burden (Flyckt, Löthman, Jörgensen, Rylander, & Koernig, 2011; Wang et al., 2016). In the UK, the estimated yearly cost of schizophrenia is £8.8bn (Kirkbride et al., 2012). Forty percent of this cost (£3.5bn) is attributable to service provision. Lost employment accounts for an additional 47% (£4.1bn), and informal care provided by family and friends accounts for 13% (£1.2bn). The burden of caring for someone with schizophrenia can adversely affect

carers' physical and mental health (Flyckt et al., 2011), resulting in family conflict. This conflict can, in turn, increase rates of relapse and hospital readmission (Banerjee & Retamero, 2014).

Over several decades, UK research has consistently reported that people of African and Caribbean origin are more likely to be diagnosed with schizophrenia than other ethnic group (Bhui et al., 2003; Harrison et al., 1989; Leff, Bhugra, & Mallett, 1995; Morgan et al., 2006). Despite initiatives to tackle race-based inequalities in mental health (Care Quality Commission, 2011; Department of Health, 2005), Black people continue to experience worse care and outcomes. They have longer inpatient stays and receive higher doses of psychotropic medication. They are also more likely to be discharged on Community Treatment Orders (CTOs), whereby they receive continued supervised treatment, making their care more coercive and costly (The Sainsbury Centre for Mental Health, 2006).

People with SMI become more isolated as their social networks shrink over time, which is detrimental to their mental health (Beels, 1981). Conversely, social support improves mental health and wellbeing and access to care (Tew et al., 2012). Black people diagnosed with SMI are more likely to lose contact with their families and communities (Rabiee & Smith, 2014), reducing their access to FI. Our study will enable such service users to receive CaFI by working with FSMs.

Previous research has highlighted the barriers to implementing FI as part of routine care (Berry & Haddock, 2008; Fadden, 1997). Implementation science in mental health has been described as 'embryonic' (Tansella & Thornicroft, 2009). The intersections of cultural adaptation and implementation science might be particularly helpful for bridging the 'translational gap' and facilitating uptake of interventions (Cabassa & Baumann, 2013). The proposed study includes process evaluation to identify and address the facilitators and barriers to implementation to improve the likelihood of CaFI becoming part of routine practice.

Why this research is needed now

Service users from Sub-Saharan African and Caribbean backgrounds (including those who regard themselves as 'Black British' and 'Mixed') are more likely than other ethnic groups to be diagnosed with schizophrenia (Morgan et al., 2005b). Explanations for this include migration (Morgan, Charalambides, Hutchinson, & Murray, 2010), living in cities ('urbanicity') (Allardyce et al., 2005; Eliacin, 2013), and socioeconomic disadvantage (Morgan et al., 2008). Lower rates of diagnosis in Africa and the Caribbean (Bhugra et al., 1996; Mahy, Mallett, Leff, & Bhugra, 1999), as opposed to in the UK, suggest that personal and institutional discrimination are also important contributory factors (Morgan et al., 2006; Morgan et al., 2009).

Alongside higher rates of diagnosis, Black people also have poorer access to mental healthcare, more negative experiences of services, and worse outcomes (Care Quality Commission, 2011; Department of Health, 2005). They are more likely than other groups to be admitted to hospital with police

involvement under the Mental Health Act (Morgan et al., 2002, 2005b). Once hospitalised, they experience higher rates of seclusion and other forms of coercive care (Mental Health Working Group, 2011). These experiences make Black people fear and mistrust mental health services (Keating & Robertson, 2004). Together with high rates of shame and stigma in these communities (Mantovani, Pizzolati, & Edge, 2017), it is not surprising that Black people tend to avoid contact with mental health services. Research also shows that even when they try to get help, it is often not forthcoming (Morgan et al., 2005a; Morgan, Mallett, Hutchinson, & Leff, 2004). The net result is that Sub-Saharan African and Caribbean people tend to enter into services later in the illness process (Morgan et al., 2004) and are sicker by the time they do so (Morgan et al., 2005a). Long periods with untreated psychosis place great strain on family relationships and may partly explain why people diagnosed with SMI from these communities are especially likely to lose contact with their families (Birchwood et al., 1992). This reduces their access to evidence-based therapies such as Family Intervention (FI).

The National Institute for Health & Care Excellence (NICE) recommend FI for schizophrenia (National Collaborating Centre for Mental Health, 2014). Although there are different models of FI, they share common core components such as psycho-education, problem solving, and stress and crisis management (Pharoah, Mari, Rathbone, & Wong, 2006; Pilling et al., 2002). There is strong evidence that FI is both cost- and clinically-effective (Pharoah et al., 2006; Pilling et al., 2002). For example, FI has been shown to improve medication compliance, self-care and problem-solving, and to reduce the risk and frequency of relapse (Pharoah et al., 2006). As well as improving service users' social functioning and quality of life, FI has been found to reduce carer burden and associated ill-health (Lobban, Postlethwaite, et al., 2013). However, the viewpoint that FI is time intensive and costly means that it is greatly underused in the NHS (Haddock et al., 2014). As Black service users are less likely to be in contact with their families (NICE recommends FI is offered only to people in regular contact with their families), they are even less likely to receive FI (National Collaborating Centre for Mental Health, 2014). This is important, as FI offers advantages over individual therapies, such as Cognitive Behavioural Therapy (CBT), due to family member involvement (Barrowclough & Tarrier, 1992). We therefore propose the opportunity to offer FI to people without family contact via Family Support Members (FSMs). This might be an important step in helping them to reengage with families and community members.

In summary, although FI is recommended by NICE for the treatment of schizophrenia (National Collaborating Centre for Mental Health, 2008), it remains currently underused in the NHS (Berry & Haddock, 2008). NICE have recommended developing culturally-appropriate psychological therapies to improve Black people's access to evidence-based care (National Collaborating Centre for Mental Health, 2008). Without alternative measures of delivering FI, such as involving FSMs, NICE recommendations could inadvertently worsen the inequalities in accessing psychological therapy

currently experienced by Black service users and their families. This is especially pertinent for the forensic population, among whom Black service users without family contact are over-represented (Care Quality Commission, 2011).

Previous related research

Given the lack of research into FI among minority ethnic groups (National Collaborating Centre for Mental Health, 2008), we undertook an NIHR-funded feasibility pilot (Edge et al., 2016) to determine whether it was possible to culturally-adapt, implement, and evaluate FI for Black and 'Mixed' heritage people with Caribbean origins. Our findings demonstrated the feasibility of successfully:

1. recruiting service users and families from this 'hard-to-reach' population
2. recruiting Family Support Members (FSMs) to enable service users not in contact with their families to receive the CaFI intervention
3. delivering CaFI in the NHS in acute, rehabilitation and community settings
4. retaining family units in therapy: 24 of 26 (92%) of those who commenced our Culturally-adapted Family Intervention (CaFI) completed all 10 sessions

CaFI also received high acceptability ratings (above 80%) from service users, family members and health professionals. All groups reported positive benefits, including improved symptoms (as evidenced by better mood and less paranoia) and improvement in social functioning (as evidenced by engaging in volunteering and active planning to return to work and full-time education).

Therapeutic alliance was positively rated by all groups. Improved communication between service users, families and health professionals was also reported. Service users' health utility index improved, especially among individuals who were not in contact with their families and who participated with FSMs. The HTA-funded systematic review (Bhui et al., 2015) highlighted the importance of therapeutic communication and alliance between Black and minority ethnic groups and mental health professionals. Our feasibility pilot achieved therapeutic alliance scores (Tracey & Kokotovic, 1989) comparable or higher to findings from a systematic review of therapeutic alliance in psychological therapies for psychosis (Tryon, Blackwell, & Hammel, 2007), underscoring CaFI's acceptability.

In light of the long history of Black people's negative experiences and relationships within mainstream mental health services, these are important findings. Although the study was not powered to test hypotheses, the results suggest that engaging Black families in psychological therapy has the potential to a) reduce inequalities in accessing evidence-based, NICE-recommended care and b) deliver significant cost savings. Demonstrating the effectiveness of the intervention might also have implications beyond Sub-Saharan African and Caribbean people. For example, the role of FSMs might

be an important means of enabling access to psychological care for others without families in the UK such as refugees.

Comparators

The design does not include a single comparator intervention. Instead, CaFI will be compared against 'usual care'. Our aim is to determine the intervention's cost- and clinical effectiveness versus comparison against a specific treatment.

Study aims

The overarching aim of the study is to evaluate CaFI's effectiveness for service users of Sub-Saharan and Caribbean origin diagnosed with psychoses (ICD 10 F20-F29) and their families compared to usual care.

More specifically, the study has the following aims to:

1. Evaluate CaFI's clinical and cost-effectiveness in Sub-Saharan African and Caribbean populations compared with usual care.

2. Determine how to maximise facilitators and overcome barriers to successful implementation

Research Question

Compared with usual care, will Culturally-adapted Family Intervention (CaFI) improve time to relapse in Sub-Saharan African and Caribbean populations with psychosis in the UK and will CaFI prove cost-effective in improving short term/long term health outcomes for this population?

Objectives

1) Engage key stakeholders (service users, families, clinicians) in further refining the therapy manual and staff training to support the delivery of CaFI with both Sub-Saharan African and Caribbean people.
2) Conduct a large efficacy/cost effectiveness trial of CaFI with 12 months Stop/Go internal pilot.
3) Identify and address implementation barriers and enable facilitators.
4) Create dissemination resources for a range of audiences.

Methods/Design

Study design

This is a mixed-method study comprising a multi-site Randomised Controlled Trial (RCT) with an internal pilot. The study will also include an economic evaluation, integrated into the RCT design, and a Process Evaluation. The main trial will involve testing Culturally-adapted Family Intervention (CaFI) in four geographical locations (seven NHS Trusts plus two contingency Trusts) across England. This will be done with a Caribbean sample, among whom feasibility and acceptability have been established

(HS&DR Feasibility Pilot) (Edge et al., 2016) and people of Sub-Saharan African origin and their families (including those who self-identify as 'Black British' and 'Mixed' heritage) in inpatient, rehabilitation, community and forensic settings.

Study setting

The study will take place in psychiatric hospitals, community and forensic settings in seven NHS Mental Health Trusts across England and two contingency sites. To facilitate recruitment, we have focused on Trusts in urban areas with high proportions of the target population. Greater Manchester Mental Health NHS Foundation Trust will be the host organisation. Reflecting CQC reported variation in service provision, 5 participating Trusts (including the contingency sites) are rated 'good' overall whilst 4 'require improvement' (Care Quality Commission, 2017). Undertaking the trial across a number of geographically dispersed organisations provides the opportunity to identify, compare and address potential barriers to implementation and share good practice in terms of uptake and embedding psychological care.

Sample size

An existing meta-analysis indicates a relative risk of 0.55 for relapse after family intervention without cultural adaptation (Pharoah et al., 2006); 40% of controls relapsed. A reduction in risk of relapse from 40% during follow-up to 24% (i.e. a risk ratio of 0.6) would equate to a clinically-significant difference sufficiently convincing to inform commissioning and facilitate change in practice. We expect 2% of participants to withdraw consent for rating relapse from case notes (Rabiee & Smith, 2014).

Using Stata's 'power logrank' command with Schoenfeld's formula, 171 participants per arm would be required for 90% power to detect a hazard ration of 0.6. However, the design of this study, with therapy offered in the intervention arm only, results in a partially nested data structure. We anticipate little therapist effect, but to allow for variation we recalculated the sample size using 'clsampsi' in Stata with an ICC of 0.01 in the intervention arm. With an average cluster size of 11, 198 participants would be required in each arm for 90% power to detect a difference in relapse of 40% in the control arm and 24% in the intervention arm. Inflating for the expected 2% drop out, we require a total sample size of 404. Based on this sample size, we will need to recruit 17 participants per month across all NHS Trusts (see

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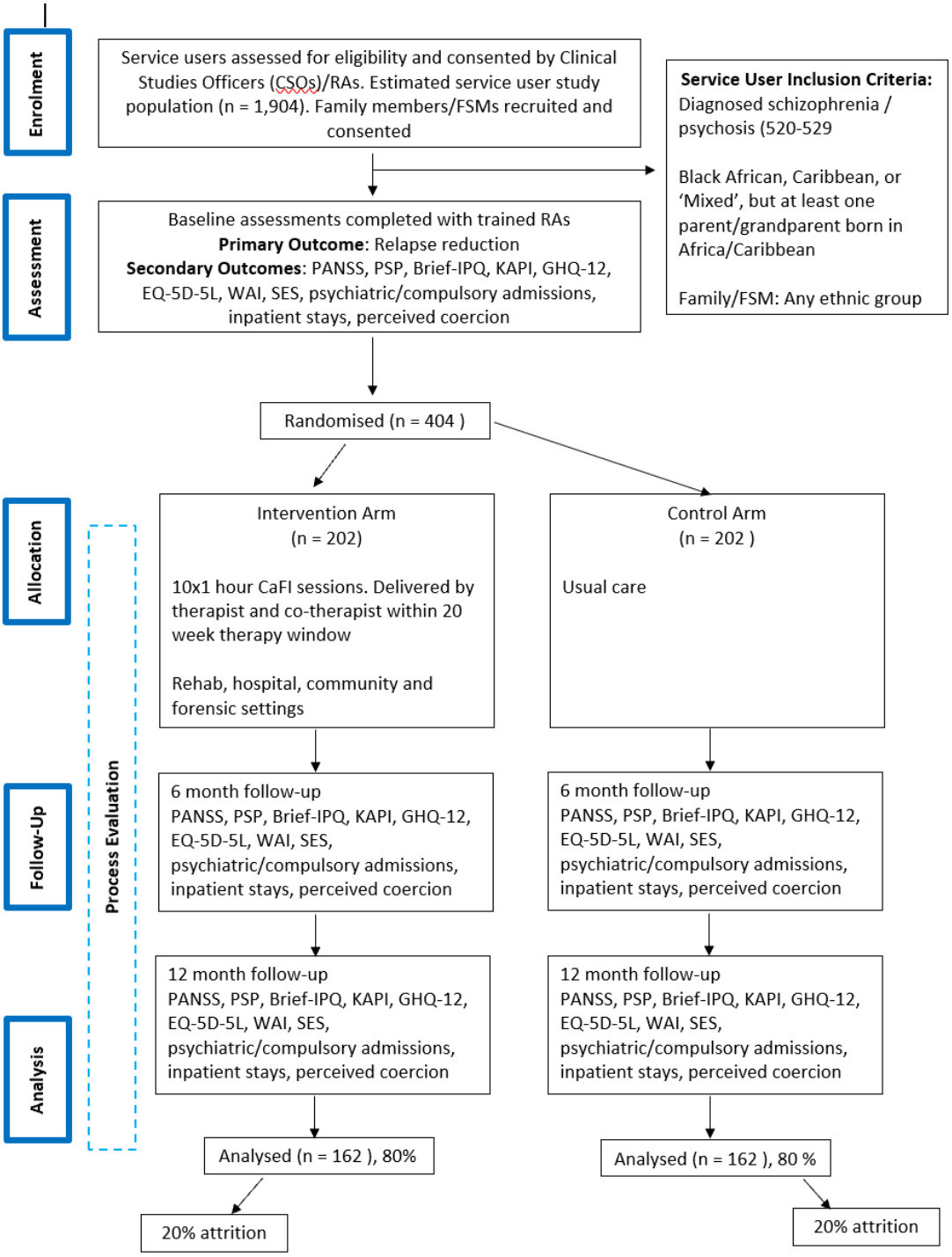

Figure 1. CONSORT diagram of the CaFI RCT procedures.

Participants and recruitment procedures

As recruitment will be within communities previously labelled 'hard-to-reach', we shall adopt engagement and recruitment strategies informed by our PPI work and previous HS&DR (CaFI) study. These may include but are not limited to using local media, working with Faith-Based Organisations (FBOs), voluntary sector agencies and community groups.

Within services, we shall place advertisement posters and flyers in participating sites accessible to service users, carers and advocates. We anticipate that the study will be adopted onto the NIHR portfolio. Accordingly, NIHR Clinical Research Network (CRN) Clinical Studies Officers (CSOs) will support recruitment, helping to identify and recruit suitable participants. CSOs and RAs will work collaboratively to publicise the study and inform clinical staff about the inclusion criteria. Recruitment packs, including the study Participant Information Sheet (PIS), will be provided for service users who are deemed well enough to participate by their clinical teams, who have the capacity to consent and who gave permission to be contacted by the research team. Service users who remain interested will be invited to meet with the RA to receive further information about the study and ask any questions before being consented into the study. Consenting participants will be asked to complete baseline assessments during the initial meeting. An additional meeting will be arranged if this is not feasible.

Target population

Sub-Saharan African and Caribbean origin service users in hospital, community, and forensic settings and their families.

Inclusion & exclusion criteria

Service users

Inclusion criteria

- People of Sub-Saharan African and Caribbean descent, including those who self-identify as 'Black British', 'Black Caribbean', 'Black African', 'African-Caribbean' or 'Mixed' African/Caribbean
- Diagnosis of schizophrenia or related psychoses (ICD F20-29/ DSM-V) (American Psychiatric Association, 2013; World Health Organization, 1992)
- Receiving treatment via psychiatric inpatient services (acute or rehabilitation), forensic or within community services within the seven participating NHS Trusts
- 14 years or older as our target population are in early intervention services and adult service users
- Assessed by key workers as having the capacity to provide informed consent
- Assessed by care teams as being well enough to participate in therapy
- Sufficient understanding of the English language to complete measures. We anticipate that the majority of participants will meet this criterion. However, we shall evaluate it during the acceptability work and early in recruitment and modify if necessary.
- No significant cognitive impairment implicated in aetiology (e.g. organic disorder)
- Do not present a high short-term risk to themselves or others as assessed by care teams.

Exclusion criteria

- Organic brain disorder
- Cognitive impairment sufficient to impact completion of assessment measures
- Substance use as primary diagnosis.
- Currently receiving any form of family intervention

Family members

Inclusion criteria

- Family members do not have to be of African or Caribbean origin but must be able to give informed consent
- Children will be included provided they are able to give assent and have parental/guardian consent.

Exclusion criteria

- Service user does not meet ethnicity or diagnostic criteria
- Cognitive impairment/memory difficulties or substance use sufficient to affect ability to complete measures
- Literacy level does not enable potential participant to be able to give written, informed consent and complete measures.

Family Support Members (FSMs)

Where biological family members are not available, service users can participate with Family Support Members (FSMs) who can be:

- Trusted individuals (e.g. friends, care coordinators, faith/community leaders) nominated by service users
- Former service users as 'befrienders' or 'peer support workers' whom we shall recruit, deploying them where service users without families are unable to nominate anyone.

Design rationale - Randomised Controlled Trial

The RCT is a multi-site study across the UK, in four geographical locations (North West, Midlands, London and South England) in seven NHS Mental Health Trusts, plus two contingency Trusts taking place in psychiatric hospitals, community and forensic settings. Our target population is Sub Saharan African and Caribbean people diagnosed with psychoses and their families (including those who self-

identify as 'Black British' and 'Mixed' heritage). We will recruit 404 family units (all sites combined) which equates to 202 family units in each arm.

The trial will involve testing the Culturally adapted Family Intervention (CaFI) with service users and their families over 10 one-hour sessions within a 20 week 'therapy window' by therapists trained in CaFI therapy delivery. CaFI comprises of five components each delivered over two sessions. The sessions will be delivered by a Lead Therapist (Band 7) and a Co-Therapist (Band 4). The control group will receive usual care.

Our primary outcome is reduction in relapse, as rated from service user records using the definition of a "two-week exacerbation of symptoms leading to a change in management". Our secondary outcomes are Positive and Negative Syndrome Scale (PANSS), Personal and Social Performance Scale (PSP), Perceived Criticism Scale (PCS), Brief Illness Perception Questionnaire (Brief-IPQ), Knowledge About Psychosis Interview (KAPI), General Health Questionnaire (GHQ-12), generic health status measure (EQ-5D-5L), Working Alliance Inventory (WAI) and Service Engagement Scale (SES).

As CaFI was not established with Sub Saharan African people, neither its acceptability nor the feasibility of recruitment and retention has been tested in this population. We plan on testing CaFI with African families in an internal pilot, which will be embedded in the RCT. Depending on the outcome of the pilot, we will either continue with a Caribbean only sample at this stage or incorporate the African sample in to the main study.

Qualitative adaptation work

In preparing this trial, we consulted with members of the Sub-Saharan African community and relevant agencies, such as African & Caribbean Mental Health Services (ACMHS), Manchester. These consultations suggested that CaFI is desired by this population and that there are sufficient similarities between the experiences of African and Caribbean people within mental health services to justify further refinement of the intervention to ensure that it meets the needs of both groups. Specifically, the individuals we consulted felt that it was not the intervention itself that would require further adaptation. Rather, the therapy manual and supporting resources would need to include African-specific material and that this would need to be reflected in therapists' cultural competence training. We shall therefore undertake work alongside setting up the main trial to culturally-adapt the intervention with a Sub-Saharan African sample, using the processes and procedures used to develop CaFI (Edge et al., 2016).

Internal pilot

As CaFI was not established or evaluated with African people, neither its acceptability nor the feasibility of recruitment and retention have been tested in this population. We shall then test the feasibility of recruitment, retention, and data collection in this population by running an internal pilot. Depending on the outcome, we shall either continue with a Caribbean-only sample at this stage or incorporate Sub-Saharan Africans into the main study.

Intervention

The trial will involve testing Culturally-adapted Family Intervention (CaFI) (Edge et al., 2016), which is delivered in 10x1 hour within a 20 week 'therapy window' by therapists trained in therapy delivery. Deriving from the Barrowclough and Tarrier (1992) Family Intervention (FI) model and incorporating findings from our study to culturally-adapt an extant approach to FI, CaFI consists of five components: Engagement and Assessment; Shared Learning; Communication; Stress Management, Coping and Problem-Solving; and Maintaining Gains.

Session content

Sessions 1 & 2: Service User and Family Engagement & Assessment

Sessions will begin by building a positive relationship with families, which includes improving communication between family members. Therapists will assess family dynamics, tailoring the intervention to meet the needs of each family and identifying (SMART – specific, measurable, attainable, relevant, timely) goals with the family.

Sessions 3 & 4: Shared Learning (Psycho-education)

Therapists will create a collaborative environment in which the therapist, relatives, and service users can share their perceptions and knowledge about schizophrenia and psychosis, including different illness models and cultural attributions. Sessions will also explore mental health systems and ways to interact with them. A 'Shared Learning' approach also recognises power dynamics within therapy and promotes strategies to minimise their impact.

Sessions 5 & 6: Communication

The aim of these sessions is to enable effective communication, building on existing communication skills within the family. This will empower participants to express their needs and better engage with mental health services and any partner agencies. These sessions will also support carers and family members in advocating for service user members of their families.

Sessions 7 & 8: Stress management, Coping & Problem-solving

The purpose of these sessions is to promote positive cycles around thoughts, feelings, and behaviours by identifying stressful situations and conceptualising alternative coping strategies based on the initial (SMART-ER – specific, measurable, attainable, relevant, timely, evaluate, reviewed) goals.

Sessions 9 & 10: Staying Well & Maintaining Gains

The final recovery-focused sessions will be used to develop a long-term plan for maintaining wellbeing, including setting realistic expectations for preventing relapse. Sessions will conclude with a 'goodbye letter', highlighting the family's strengths and achievements.

Trial therapists

Trial therapists will be recruited within the participating Trusts via advertisements published on NHS Jobs (jobs.nhs.uk) and other appropriate websites. The intervention will be delivered by trained therapist dyads. The Band 7 Lead Therapists will likely be Clinical Psychologists, but other appropriate Health and Care Professions Council (HCPC)-registered candidates with suitable experience will be considered. To address challenges in finding suitably qualified therapists, we will recruit psychiatry trainees, first as co-therapists and then as leads. Band 4 Co-Therapists will be from diverse health and care professional backgrounds, such as Assistant Psychologists, Support Workers and Healthcare Assistants. For flexibility we shall employ the Lead Therapists and Co-Therapists on a sessional basis as successfully trialled in the CaFI feasibility study.

Control arm – Treatment as usual

Service users in both treatment and control groups will receive usual care. This usually involves medication with support from nurses. Lack of FI generally (Fadden, 1997) and specifically for Black people (National Collaborating Centre for Mental Health, 2008) were confirmed by our feasibility trial (Edge et al., 2016). We also know that some of our proposed sites do not have resources for psychological interventions in psychoses so usual care is not psychologically based. Accordingly, we do not anticipate that participants will concurrently be offered structured FI or similar psychological intervention although this is subject to potential changes in commissioning. We shall make structured FI an exclusion criterion but allow informal family support or FI occurring more than 6 months previously and record FI as part of usual care post-randomisation.

Assignment of interventions

Randomisation will be stratified by recruitment site (Greater Manchester Mental Health NHS Foundation Trust, Pennine Care NHS Trust, Mersey Care NHS Trust, Coventry & Warwickshire Partnership NHS Trust, Birmingham & Solihull Mental Health NHS Foundation Trust, South London

& Maudsley NHS Foundation Trust, & Southern Health NHS Foundation Trust), ethnic background (African, Caribbean or mixed A/C) and therapy partner (family member or FSM).

Within each stratum, participants (service users and relatives/carers) will be individually randomised to CaFI or treatment as usual (TAU) on a ratio of 1:1, using randomly permuting block sizes. Family Support Members will not be randomised. Instead, they will be matched to service users, who are unable to nominate a relative/carer, randomised to the intervention arm.

A web-based randomisation system will be designed using the bespoke KCTU randomisation system. The randomisation system will be created in collaboration with the trial statistician and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

The CI or delegate will request usernames and passwords from the KCTU. System access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the randomisation system are not shared, and that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested via the CI or delegate (e.g. Trial Manager) from the KCTU team and a request for access to be revoked must be requested when staff members leave the project. Study site staff experiencing issues with system access or functionality should contact the CI or delegate (e.g. Trial Manager) in the first instance.

Participant initials and date of birth will be entered on the randomisation system, NHS number, email addresses, participant names, addresses, and full postcodes will not be entered into the randomisation system. No data will be entered onto the randomisation system unless a participant has signed a consent form to participate in the trial. Randomisation will be undertaken centrally by the co-ordinating study team, by authorised staff onto the randomisation system by going to www.ctu.co.uk and clicking the link to access the randomisation system. A full audit trial of data entry will be automatically date and time stamped, alongside information about the user making the entry within the system.

The CI team will undertake appropriate reviews of the entered data, in consultation with the Trial Manager and statisticians for the purpose of data cleaning. No data can be amended in the system, however CI or delegate (e.g. Trial Manager) may request King's Clinical Trials Unit to add notes against individual subject entries to clarify data entry errors.

Upon request, KCTU will provide a copy of the final exported dataset to the CI in .csv format and the CI will onward distribute as appropriate.

Blinding

As it is infeasible to blind participants to treatment allocation in this study, only the outcome assessors will be blinded. Participants will be asked not to discuss the details of their care to avoid breaking that blind. We will report the level of success of our attempts of blinding.

Quantitative data: Quantitative outcome data will be collected by RAs blind to delivery of the intervention at four-time points: baseline, post intervention (within 1 month) and at 6 and 12-months follow-up. We will ask study participants to complete a self-report socio-demographic questionnaire which is a non-standardised measure. We will collect primary and a variety of secondary outcome data using standardised measures.

Socio-demographic questionnaire

A self-report socio-demographic questionnaire will be used to collect data on key variables such as age, gender, ethnic group and religion will be completed by service users, family members and FSMs. Additional questions for service users will include diagnosis, relationship with the family member/FSM, length of time since first contact with services, inpatient history and medication.

Primary outcome

Time in relapse as rated from service user records (case-notes) defined as a 2-week exacerbation of symptoms leading to a change in management (Barrowclough et al., 1999). This is a Cochrane-recommended measure (Pharoah et al., 2006), which was endorsed as a desired outcome by participants in the CaFI feasibility study as preventing relapse and readmission were significant motivators for engaging in therapy. Past studies (Barrowclough et al., 1999) have demonstrated the ability to predict rating of relapse via case-notes in 98% of cases. We confirmed the feasibility of collecting relapse data in our HS&DR study (Edge et al., 2016).

Secondary outcomes

Other outcomes that were important to our feasibility study participants relate to service use (frequency of admission) and experiences of coercive care, including compulsory detention under the Mental Health Act, length of hospital admission, and use of Community Treatment Orders (CTOs). We shall collect these data from patient records so their collection will not add to the assessment burden. Our previous study also proved the feasibility of collecting the following standardised service user and family secondary outcomes, which will be used in the trial:

Psychosis symptom severity (service users)

The Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987) is a widely used 30-item semi-structured interview designed to assess positive, negative and general symptoms in

service users with schizophrenic spectrum diagnoses. The PANSS has good psychometric properties of reliability and validity and is sensitive to change (Kay, Opler, & Lindenmayer, 1988). Trained RAs will rate the PANSS. Inter-rater reliability will be reported.

Social functioning (service users)

The Personal and Social Performance Scale (PSP) (Morosini, Magliano, Brambilla, Ugolini, & Pioli, 2000) is a 100-point, observer-rated, single-item scale. The PSP measures social functioning across the past month in four areas: i) socially useful activities including ii) work and study, iii) personal and social relationships, iv) self-care, disturbing and aggressive behaviours. It is reliable, valid, sensitive to change and correlates with PANSS scores (Patrick et al., 2009). Ratings will be made by trained RAs based on service users' reports of symptoms, service users' behaviour during PANSS interviews, and reports from care staff and significant others.

Perceived coercion (service users)

The MacArthur Admission Experience Survey: Short Form (Gardner et al., 1993) is a 16-item measure of service users' subjective experience of hospital admission. The PCS comprises 4 sub-scales: i) perceived coercion scale ii) Negative Pressures Scale iii) Voice Scale iv) Affective Reactions to Hospitalisation.

Knowledge about psychosis (family members)

The Knowledge About Psychosis Interview (KAPI) (Smith, Gregory, & Higgs, 2007) is a revised version of the Knowledge About Schizophrenia Interview (KASI) (Barrowclough & Tarrier, 1992). As KASI and KAPI are culturally-insensitive and use somewhat outdated language; we developed and validated an updated version of these instruments, the Knowledge About Psychosis (KAP) questionnaire, for use in a general population sample. We also produced a Culturally-adapted Knowledge About Psychosis (CaKAP) version for the African-Caribbean community (Edge et al., 2016). The proposed study affords the opportunity to validate the CaKAP measure for African and Caribbean people.

Family stress/burden (family members)

The 12-item General Health Questionnaire (GHQ-12) (Goldberg & Williams, 1988) is one of the most widely used and valid measures of emotional distress and is frequently used to detect the risk of psychiatric morbidity. It will be used as a measure of burden and general stress among family members.

Illness beliefs (service users, family members)

The modified version of the 12-item Brief Illness Perception Questionnaire (Brief-IPQ) (Broadbent, Petrie, Main, & Weinman, 2006) will be used to assess illness perceptions in service users and family members at baseline. Like the original IPQ (Addington, 2003) from which it was derived, the Brief-IPQ is a measure of physical health problems but can be adapted for mental health problems (Lobban, Barrowclough, & Jones, 2005). Modifications made for the feasibility were in line with previous adaptations (Lobban, Solis-Trapala, Tyler, Chandler, & Morriss, 2013) e.g. replacing the word 'illness' with 'mental health problems. Scores on the 11 illness perception items can be summed to compute a total score, with higher scores indicating a more negative model of illness. The Brief-IPQ has demonstrated good reliability and validity (Broadbent et al., 2006) and has previously been used in psychosis research (Broadbent, Kydd, Sanders, & Vanderpyl, 2008).

Working alliance (service users, family members)

The Working Alliance Inventory (WAI)-short-form (Adam O. Horvath & Greenberg, 1989) is a 12-item self-report measure of the quality of staff-service user relationships and comprises three subscales; agreement on goals, agreement on tasks and emotional bond. The WAI short-form has good psychometric properties (Tracey & Kokotovic, 1989). Working alliance has also been shown to influence outcome in therapy (A. O. Horvath & Bedi, 2002; A. O. Horvath & Luborsky, 1993; Norcross, 2002).

Health status and QALY (service users, family members)

The EQ-5D-5L (Herdman et al., 2011) is a generic self-report measure of health, covering five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Individuals' responses to the EQ-5D-5L will be used to calculate a single index utility value and estimate QALYS. The utility tariff will be that recommended by NICE at the time of the analysis. The EQ-5D- has been validated in diverse populations (Janssen et al., 2013) and is recommended by NICE (National Institute for Health and Care Excellence, 2013). In in our previous study, we assessed the feasibility of using the EQ-5D- for this RCT.

Service use interview (SUI)

Service use data will be collected from patient records (hospital inpatient, outpatient and accident & emergency services) and from a Service-Use Interview (SUI) with participants and family at baseline and at each follow up assessment. The SUI will include questions about whether the participant has used any primary, secondary or community-based health and social care and how often they used the service in the last 3 months (baseline study visit) or since the last assessment (follow-up study visits).

The SUI will ask participants to record whether they have used any hospital inpatient, outpatient or emergency services and the name of the hospital, to facilitate the review of patient records.

The SUI will also include time spent by family as informal carers, use of other public services (e.g. criminal justice system) and time in paid and unpaid employment/productive activity. These data will be used to estimate costs for a broader societal perspective for sensitivity analysis.

Timetable (months) and participant timeline

Total duration: 42 months

1-22 months: Recruiting people to test CaFI and making sure CaFI is acceptable to both Sub Saharan Africa and Caribbean descent

1-40 months:

- Recruiting more people to test CaFI and delivering CaFI to family units
- Collecting information before receiving CaFI
- Collecting information directly after receiving CaFI
- Collecting information 6 months after receiving CaFI
- Collecting information 12 months after receiving CaFI
- Analysing the collect information

31-42 months: share findings with the public (including service users and families), health professionals, policy makers and academics

Participant timeline

Participant recruitment: 22

Duration of intervention/participant: 10 weeks within 20-week therapy window

Duration of follow-up: 12

Trial duration/participant: 17 (including follow-up)

Table 1. Schedule of participant enrolment, interventions and assessments in the CaFI study.

	STUDY PERIOD					
	Enrolment	**Allocation**	**Post-allocation**			**Close-out**
TIMEPOINT**	$-t_1$ *Baseline*	t_1	t_2 ***Post-intervention***	t_3 *6-month follow-up*	t_4 *12-month follow-up*	t_x

ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Randomisation		X				
INTERVENTIONS:						
Culturally-adapted Family Intervention		←	→			
Treatment as Usual		←	→			
ASSESSMENTS:						
Relapse data (health records)	X		X	X	X	
Number of psychiatric and compulsory admissions (health records)	X		X	X	X	
Length of inpatient stays (health records)	X		X	X	X	
Positive and Negative Syndrome Scale (PANSS)	X		X	X	X	
Perceived Coercion	X		X	X	X	
Personal and Social Performance Scale (PSP)	X		X	X	X	
Brief Illness Perception	X		X	X	X	

Questionnaire (Brief-IPQ)						
Knowledge About Psychosis Interview (KAPI)	X		X	X	X	
General Health Questionnaire (GHQ-12)	X		X	X	X	
EQ-5D-5L	X		X	X	X	
Service use interview SUI	X		X	X	X	
Working Alliance Inventory (WAI)	X		X	X	X	
Service Engagement Scale	X		X	X	X	
Qualitative interview (process evaluation)						X

Qualitative data

Qualitative interviews will be conducted with approximately 30 service users and family members and approximately 30 staff purposively sampled across all sites in a process evaluation exploring potential barriers and facilitators of implementing CaFI. Interview schedules with gather views on: sense making, implementation, embedding and integration.

Process evaluation

To explore potential barriers and facilitators to implementing CaFI, semi-structured interviews will be undertaken with approximately 30 service users and family members (biological and FSM); purposively sampled across all sites. The final sample will be informed by findings from the quantitative study and by iterative data collection processes. It is intended to collect data face-to-face. Where this is not

possible, telephone/Skype or similar will be used to ensure maximum variation within the sample. Interviews will be audio-recorded, transcribed verbatim, and analysed using thematic analysis (Tait, Birchwood, & Trower, 2002).

Understanding why effective interventions such as CaFI are successfully implemented in some settings but not others is a key issue for wider uptake and spread. Process evaluation is an essential part of designing and testing a complex intervention and is required to understand how and under what conditions implementation is effective (Moore et al., 2015). There are a large number of theoretical frameworks available to understand the implementation processes (Nilsen, 2015). We will draw upon a theoretical approach known as Normalisation Process Theory (NPT) which facilitates understanding of the extent to which new processes become part of routine practice (May & Finch, 2009). NPT is comprised of four main constructs that represent individual and collective levels of work involved in the implementation of new practice namely, coherence, cognitive participation collective action and reflexive monitoring.

We will conduct semi-structured interviews with around 30 staff (therapists, care coordinators, NHS senior leaders and service managers, commissioners) purposively sampled across all sites. Interview schedules will be informed by NPT and will focus on understanding:

- Sense making: how CaFI is understood and compared with existing practices
- Implementation: how CaFI is developed and translated into practice
- Embedding: how CaFI becomes or does not become routinely incorporated into the everyday work of professionals
- Integration: how CaFI is sustained as part of normal practice

Data Analysis

Statistical analyses will be performed on an intention-to-treat basis. The log-rank test will be used to compare the survival distributions of the two arms. If its assumptions are met, Cox's proportional hazards model will be fitted, allowing adjustment for covariates. All analyses will be appropriately adjusted for therapist clustering.

Qualitative data will be will be digitally-recorded, transcribed verbatim, and analysis will occur blind to trial outcomes to avoid biased interpretation of the findings. Anonymised transcripts will be analysed using Framework Analysis, allowing for both inductive and deductive coding. Deductive coding will be informed by NPT.

An economic evaluation comparing the cost-effectiveness of CaFI with usual care will be performed and reported according to the CHEERS statement. The perspective for the primary analysis will be that of the NHS and Social Care for direct costs (as recommended by NICE) and patient participants for health benefit. The time horizon will be 12 months from baseline to end of follow up.

When the data are analysed, the most recent, published, national unit costs will be used to cost each of the services used (Department of Health and Social Care, 2014; Personal Social Services Research Unit, 2019). The costs of the intervention will be estimated from staff time (training, delivery, and supervision), facilities, and consumables and cost using national unit costs.

The measure of health benefit for the primary analysis is the QALY (EQ-5D-5L and the published utility tariffs recommended by NICE at the time of the analysis). Single imputation will be used to account for missing cost data at baseline and missing data from the outcome measures used at baseline. A missing indicator will be used to account for missing data about a participant's demographic characteristics (e.g. age, gender, ethnicity) at baseline. The methods used to deal with missing follow-up data will be determined according to the extent and pattern of missing data (e.g. multiple imputation, missing indicator or propensity score methods) (Faria, Gomes, Epstein, & White, 2014; White, Horton, Carpenter, & Pocock, 2011; White & Thompson, 2005). A pooled descriptive statistical analysis of baseline data will be used with information from previous economic evaluations to inform the final methods used for (i) methods to account for missing follow-up data (ii) the type of regression models and key covariates for the analyses of the 12-month follow-up data. The regression analysis will be used to estimate net costs and net QALYs (or health benefit) for the intervention compared to TAU. All analyses will be adjusted for key covariates which will be identified prior to analysis of the follow-up data.

The estimates of net costs and QALYs from the regression analyses will be bootstrapped (National Institute for Health and Care Excellence, 2013) to simulate 10,000 pairs of incremental cost and QALY outcomes of the CaFI intervention. These capture the relationship between costs and QALYs and will be used to generate a cost effectiveness acceptability analyses to capture both parameter uncertainty and uncertainty about the value to decision makers of an additional QALY gained. This will include: (i) plotting the distribution of pairs of net costs and QALYs on a cost-effectiveness plane, to assess parameter uncertainty, (ii) generate a cost-effectiveness acceptability curve to estimate whether the additional cost of a QALY gained by an intervention is acceptable to decision makers (iii) estimate the probability that the CaFI intervention is cost-effective compared to TAU (iv) estimate a net benefit statistic. The cost-effectiveness acceptability approach requires revaluing QALY by an estimate of how much decision makers are prepared to pay to gain one QALY. However there is no universally agreed threshold willingness to pay value and reported thresholds for the UK range from £8,000 to £30,000

per QALY gained (Claxton et al., 2015; McCabe, Claxton, & Culyer, 2008; National Institute for Health and Care Excellence, 2013). Accordingly, we plan to use a mid-estimate willingness to pay threshold value of £15,000 per QALY gained to estimate the probability that CaFI is cost effective and the net benefit statistic, with a range of £0 to £30,000 threshold values for the cost-effectiveness acceptability curve. The final mid-estimate and range of threshold values will be determined on the basis of published guidance at the time of analysis.

Sensitivity analysis will be used to test the impact of assumptions and data on the ICER and results of the cost-effectiveness acceptability analysis. The planned sensitivity analyses will explore the intervention's cost-effectiveness using (i) cost per relapse avoided and cost per relapse free year; (ii) broader cost perspectives to include non-NHS and social care costs and indirect costs of lost productivity; (iii) broader health benefit perspectives to include family health benefits; (iv) complete case analysis (v) alternative methods of dealing with missing follow-up data.

Interim analyses and stopping guidelines

Based on our sample size calculation, we will need to recruit 16 participants per month across all seven NHS Trusts to reach target. Recruitment will be rigorously monitored throughout the recruitment period. 12 months from starting recruitment, we expect to have recruited 60-80% of our family units. As with most trials, we anticipate recruitment may be slow initially. If at 6 months we have recruited 60 families (10 per month), will consider options for boosting uptake. At the 9 months review, if we have recruited less than 60% of the 9 month target we shall consider opening one or both contingency sites. If we have achieved 80% or more of the 12 months target, we will continue without change. Similarly, if recruitment is less than 50% at the 12 months review, the trial may be stopped after discussion with the Trial Steering Committee, Data Monitoring and Ethics Committee (DMEC), and funders.

Data management: A web based electronic data capture (EDC) system will be designed, using the InferMed Macro 4 system. The EDC will be created in collaboration with the trial analyst/s and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

The CI or delegate will request usernames and passwords from the KCTU. Database access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the EDC are not shared, and that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested via the CI or delegate (e.g. Trial Manager) from the KCTU team and a request for access to be revoked must be requested when staff members leave the project. Study site staff

experiencing issues with system access or functionality should contact the CI or delegate (e.g. Trial Manager) in the first instance.

Participant initials and date of birth will be entered on the EDC, NHS number, email addressed, participant names and addresses, and full postcodes will not be entered into the EDC. No data will be entered onto the EDC system unless a participant has signed a consent form to participate in the trial. Source data will be entered by recruiting site staff according to the KCTU guidelines by authorised staff onto the EDC by going to www.ctu.co.uk and clicking the link to access the MACRO 4 EDC system. A full audit trial of data entry and any subsequent changes to entered data will be automatically date and time stamped, alongside information about the user making the entry/changes within the system.

The CI team will undertake appropriate reviews of the entered data, in consultation with the trial statistician for the purpose of data cleaning and will request amendments as required. No data will be amended independently of the study site responsible for entering the data.

At the end of the trial, data will be reviewed for each participant. At this point, all data can be formally locked for analysis.

Data Monitoring and Ethics Committee (DMEC)

A Data Monitoring and Ethics Committee (DMEC), a 100% independent four-member panel of Experts by Profession will provide independent assessment of the study conduct. They will assess the progress of the project and determine on whether the RCT will be continued based on the Stop/Go internal pilot.

Trial Steering Committee

A Trial Steering Committee (TSC), at least 75% of whom will be independent of the study (including an independent chair and lay members), will be established. They will provide independent scrutiny and notify funders of any concerns regarding conduct of the study, including falling behind with recruitment or unexpectedly high rates of adverse events.

Research Management Group

The project will be managed by a Project & Trial Manager in collaboration with KCTU. A Research Management Group (RMG) comprising all applicants, a representative from the host Trust's Research and Innovation department, and trial staff (Research Assistants and Administrator), Service Users, Carers and Community Consultants will be established. Via regular monthly meetings, they will provide study management and oversight.

Research Advisor Group

As with the CaFI Feasibility Pilot, a Research Advisor Group (RAG) comprising service users and carers will be established. RAG will advise on matters such as cultural-validity of and accessibility of study materials. They will contribute to therapists' cultural competence training. At least one member of RAG will be a member of RMG. They will meet biannually and receive regular study updates.

Patient and Public Involvement

We have consulted with community members, service users and carers in developing this proposal. Specifically, the RDS bursary award has enabled us to consult about the desirability of CaFI for Sub-Saharan Africans. There is overwhelming support for further refining the intervention with PPI and trialling it with a 'Black' versus Caribbean population.

The study is an example of Community-partnered Participatory Research (CPPR) pioneered in the US (May & Finch, 2009). For our feasibility study, we adopted NIHR principles for meaningfully engaging with service users and communities to develop research with versus either for or about them (Mahy et al., 1999). Our experience indicates that partnering with service users, community members and other key stakeholders to develop interventions has a positive effect on uptake, retention and satisfaction. This is particularly important when developing interventions for so called 'hard-to-reach' communities who are known to mistrust mental health services.

As with our feasibility study, we plan to provide PPIE research training and support. Specifically, we shall deliver sessions on research methods and governance as well as awarding honorary contracts to interested individuals to enable them to undertake further study, thus building capacity. Group and individual supervision will be provided for all involved in testing the intervention.

Harms

We will actively collect information at each assessment of the study about adverse events and serious adverse events. In addition to recording events in the standard way, we will include events particularly relevant to this trial, such as significant changes in family situation and deterioration in mental health. There are standard operating procedures for reporting serious adverse events to the Trial Steering Committee (TSC), DMEC and research management group, sponsor, funder and NHS Research Ethics Committee (REC).

Auditing

Study conduct is monitored by regular auditing visits from the sponsor, annual reports to the NHS REC, bi-annual reports to the funder and regular Trial Steering Committee meetings.

Research ethics approval

NHS Research Ethics Committee, HRA and site-specific approvals for each participating NHS Trust will be sought. Phase 1 of the study (qualitative cultural adaptation phase) has previously been approved by the NHS North West Greater Manchester South Research Ethics Committee (19/NW/0385).

Protocol amendments

Protocol amendments will be formally documented and communicated to the Research Management Group, NHS REC, funder (HTA NIHR), DMEC, TSC and recorded in the trial registration site.

Consent or assent

Informed consent (participants aged 16+) and assent (participants aged 14-15) will be obtained by Project & Trial Manager and trial Research Assistants. Consent from parents/legal guardians of participants under 16 will also be obtained. Consent and assent will be obtained using a consent form (Appendix 3a and 3b) and an age-appropriate assent form (Appendix 3c).

Confidentiality, Anonymity & Data Protection

Given levels of stigma within these communities, we shall strive to preserve confidentiality. Whilst adhering to principles of confidentiality, participants will be informed that certain disclosures (such as intent to harm themselves or others) will be reported after discussion with them. Anonymity will be carefully protected unless participants choose to reveal their identity – e.g. by participating in dissemination events and resources that will be shared with wider audiences such as videos. All personal information, such as names of people or places, will be removed from interview and focus group data, and anything that could identify participants (known as 'personally-identifiable information') such as their address will be kept separately. Data will be stored securely in accordance with the General Data Protection Regulation, Data Protection Act (2018) and Caldicott Principles. Personal identifiable data will be stored in a locked filing cabinet separate from any other information about participants. Only the research team will have access to participants' data and related information. All data held on computers and any other devices (e.g. digital recorders, external hard drives, USB devices) will be encrypted and password-protected. The data will be stored for 15 years after the completion of the trial.

Declaration of interests

None to declare

Dissemination plan to communicate trial findings

We shall disseminate study findings to all relevant stakeholders, including service users, carers, community members, mental health professionals, NHS managers, service commissioners and policy makers. We shall work with CRN, University of Manchester and NHS Trusts' Communications teams to maximise dissemination. Study details and key findings will be hosted on the University of Manchester's Researching African Caribbean Research (ReACH) website: http://research.bmh.manchester.ac.uk/ReACH and the CaFI website: https://sites.manchester.ac.uk/cafi/ . The website will also provide links to our study outputs including publications, presentations and plain English lay summaries. Additionally, study participants who agreed to receive study findings will get these via post or email depending on preference. Findings will also be shared via local and national media, specifically targeting Black newspapers, community radio and television. We shall also share findings via voluntary sector (e.g. African & Caribbean Mental Health Services) and campaigning groups (e.g. Sane, The Mental Elf) and social media. The CaFI video we created with service users and carers to share findings feasibility study has proved a very popular means of disseminating our findings at community events. The video has been shared via YouTube, broadening reach beyond clinical and academic audiences. A similar approach will be taken to sharing findings from this study. For example, we shall collaborate with local creatives with experience of co-producing arts with marginalised groups (e.g. ethnic minorities and service users). The outputs will include a range of media, such as videos, performing arts and spoken word. We shall host dissemination events in venues accessible to members of the communities in our recruitment sites as well as a national conference. We shall prepare interim reports for NIHR and publish our report in the NIHR HTA Journal and target other high impact peer reviewed journals such as British Journal of Psychiatry/Schizophrenia Bulletin (main study findings) and Psychiatric Services (service organisation and development journals). We shall also produce papers specifically for frontline staff such as Journal of Advanced Nursing and Behavioural and Cognitive Psychotherapy Journal. We shall co-produce papers, blogs, opinion pieces and conference presentations with service users and carers. The latter will include The British Psychological Society Division of Clinical Psychology, Caribbean Studies Association, World Psychiatric conference, and International Society of Psychiatric Nurses annual conferences)

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