Appendix 1 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: Study protocol for a Randomised Controlled Trial (RCT)

Version 3

Date: 15.06.2021

Contents Page

List of Figures and Tables

List of abbreviations

ACMHS - African & Caribbean Mental Health Services

AE – Adverse Event

AR – Adverse Reaction

AESOP – The Aetiology and Epidemiology of Schizophrenia and Other Psychoses

BSMHFT – Birmingham & Solihull Mental Health NHS Foundation Trust

Brief-IPQ – Brief Illness Perception Questionnaire

CaFI – Culturally-adapted Family Intervention

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

CWPT – Coventry and Warwickshire Partnership NHS Trust

DMEC – Data Monitoring and Ethics Committee

DSM-V – Diagnostic and Statistical Manual of Mental Disorders – 5th Edition

EDC – Electronic Data Capture

EQ-5D – EuroQol-5D

EQ-5D-5L – European Quality of Life in Five Dimensions Generic health status measure

FBOs – Faith-Based Organisations

FI – Family Intervention

FSM – Family Support Member

GHQ-12 – General Health (12 Item) 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 – Principal 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 Advisory 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

SAE – Serious Adverse Event

SAR – Serious Adverse Reaction

SES – Service Engagement Scale

SMART - Specific, Measurable, Attainable, Relevant, Timely

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

SMI – Serious Mental Illnesses

SUQ – Service-Use Questionnaire

SUSAR – Suspected Unexpected Serious Adverse Reaction

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

ISRCTN (http://www.isrctn.com/) 12622538.

Protocol version

Date	Version Number	Author(S)
28/10/2019	0.1	DE/ HW / HL / LAC / LD / CH / PW
CI Signature		Dawn Edge
21/01/2020	1	HW / HL / DE / LAC / LD / CH / PW
Acting CI Signature (26th November 2019 – 31st March 2020)		Claire Henderson
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CI Signature		Dawn Edge

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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 Research Assistants 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: Lecturer in Biostatistics, Centre for Biostatistics, School of Health Sciences, at the University of Manchester. Dr Carter will provide expertise in trial design and statistics and supervise statistics RA.

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. She will supervise Health Economics RA on the Trial.

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 and site lead for Southern Health, Southampton.

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. Dr Drake will provide input on the peer support component on the study.

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

The Trial Manager will be based at Greater Manchester Mental Health NHS Foundation Trust (GMMH), Research and Innovation, Rawnsley Building. S/he 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 he 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 (GMMH), 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 (BSMHFT). 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 (SMI) 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 admitted to inpatient 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 are more likely to be placed on Community Treatment Orders or 'CTOs'. This means getting psychiatric 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 in the UK 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. The COVID-19 pandemic has hit Black, Asian and minority ethnic (BAME) communities especially hard. Taking this into consideration, we have developed an online version of CaFI called 'CaFI:Digital'. This will make it possible for people to take part in the study and receive the CaFI therapy even if they are unable to meet with therapists in person. CaFI:Digital is an important part of trying to make it as easy as possible for Black people to receive psychological therapy or 'talking treatments'.

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 (Degnan et al., 2018) 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 groups (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; (Mental Health Working Group, 2011).

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), compared with the UK, suggest that personal and institutional discrimination are important additional 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 recommend 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).

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' to determine the intervention's cost and clinical effectiveness.

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 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 trial of CaFI's clinical and cost effectiveness 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 (North West, Midlands, London, and South) across England. The study population will comprise people of Caribbean origin, among whom feasibility and acceptability have been established via an HS&DR-funded 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 NHS Mental Health Trusts across England. 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 (GMMH) will be the host organisation. Reflecting CQC reported variation in service provision, 5 of the 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 and using digital technology provides the opportunity to

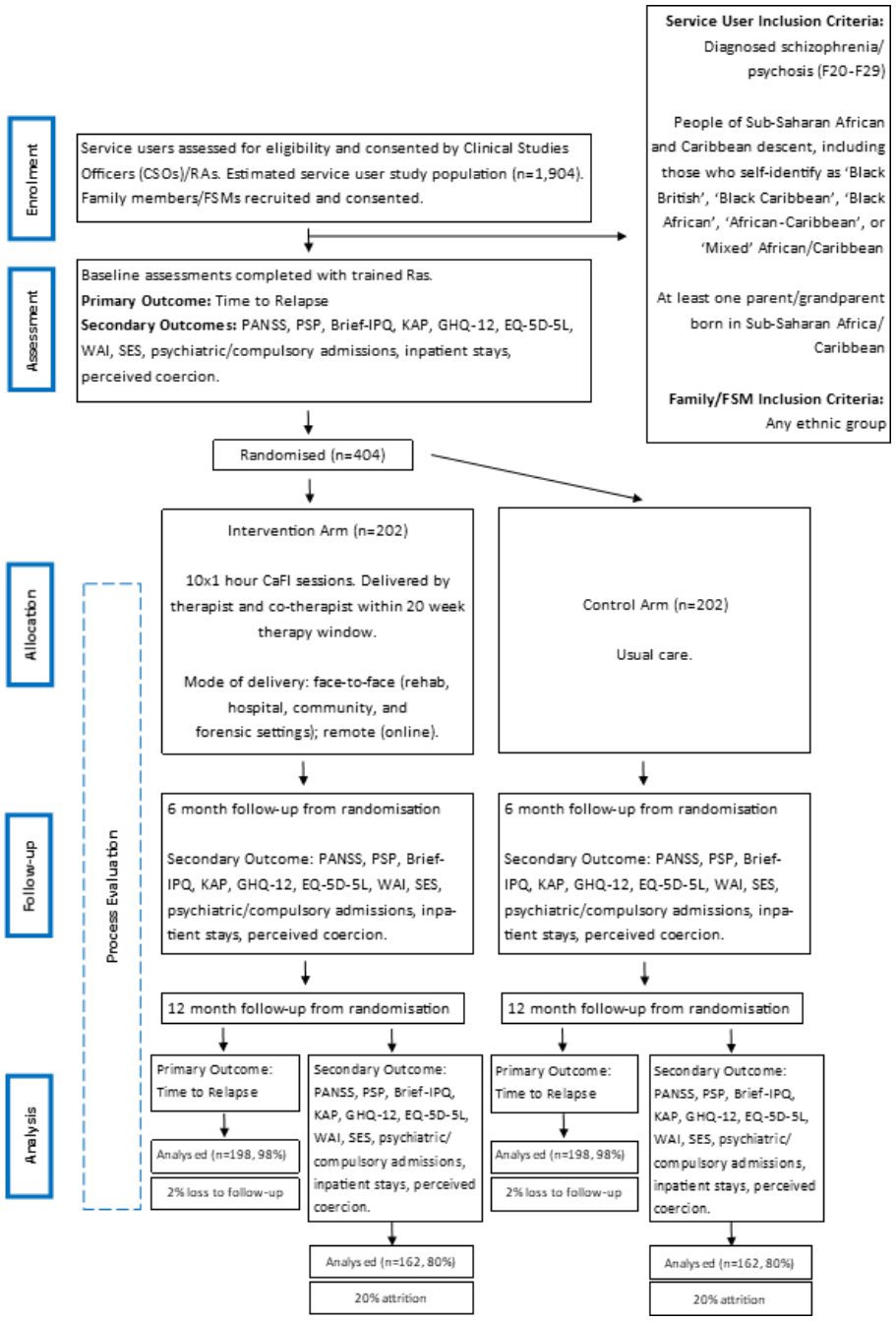
identify, compare, and address potential barriers to implementation and sharing good practice in terms of uptake and embedding psychological care.

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 ratio 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.

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. The study has been 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. Additional meetings 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
- At least one parent/ grandparent born in a Sub-Saharan African/ Caribbean country
- 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 a participating NHS Trust
- 14 years or older in keeping with the age groups served by Early Intervention Services and adult services
- Assessed by researchers 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
- No significant cognitive impairment implicated in aetiology (e.g. organic disorder)
- Does 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 and nominated Family Support Members (FSMs)

Family members and nominated family support members do not have to be of African or Caribbean origin.

Inclusion criteria

- Assessed by researchers as having the capacity to provide informed consent
- Children will be included provided they are able to give assent and have parental/guardian consent
- Sufficient proficiency in English to enable completion of measures

Exclusion criteria

- Service user does not meet ethnicity or diagnostic criteria
- Cognitive impairment sufficient to impact completion of assessment measures
- Inability to understand study information or to give informed consent and complete measures

Definition of Family Support Members (FSMs)

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

- Nominated Family Support Members (nFSM) – 'trusted individuals' (e.g. friends, care coordinators, faith/community leaders) designated by service users to enable them to participate in CaFI.
- Allocated Family Support Member (aFSM) – a person allocated to the service user by the study team to enable them to participate in CaFI. The pool of aFSMs will include 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. Service users will be provided with demographic and other pertinent information to enable their selection of aFSMs from those available.

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). The study will involve service users 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 compared with usual care. In light of the recent COVID-19 pandemic, CaFI will be offered as a face-to-face therapy *and* as an online version to service users and their families allowing them choice and flexibility in therapy delivery. CaFI comprises five components delivered over 10 one-hour sessions delivered by a Lead Therapist (Band 7 or above) and a Co-Therapist (Band 4 or above). The control group will receive usual care.

Our primary outcome is time to relapse, as rated from service user records using the definition of relapse as 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), the modified version of the 12-item Brief Illness Perception Questionnaire (Brief-IPQ), Knowledge about Psychosis Questionnaire (KAP), General Health Questionnaire (GHQ-12), generic health status measure (EQ-5D-5L), Working Alliance Inventory (WAI), Service Engagement Scale (SES) and Service Use Questionnaire (SUQ).

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 have therefore undertaken work in preparation for setting up the main trial to culturally-adapt the intervention with a Sub-Saharan African sample, using the processes and procedures used to develop and pilot test CaFI (Edge et al., 2016).

Internal pilot

As CaFI was not established or evaluated with Sub-Saharan African people, neither its acceptability nor the feasibility of recruitment and retention have been tested in this population. We shall therefore test the feasibility of recruitment, retention, and data collection in this population by conducting a 12-month 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., 2018), which comprises 10x1 hour sessions delivered within a 20-week 'therapy window' by therapists trained in CaFI 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 (Edge et al., 2018), CaFI consists of five components: Engagement and Assessment; Shared Learning; Communication; Stress Management, Coping and Problem-Solving; and Maintaining Gains. A CaFI therapy session is considered to have been attended/completed if lasting over 30 minutes. Additional therapy slots will be offered where booked sessions were not attended/completed. If FM/nFSMs drop out of the study, they can be replaced in the intervention arm to allow continuation with the therapy. Outcome data will be sought from the original FM/nFSM only.

CaFI will be offered both as a face-to-face option and as online version called 'CaFI Digital'. The latter option has been developed to mitigate the likely impact of the COVID-19 pandemic on the trial and our study population which has been disproportionately affected by the virus. An online version of CaFI ('CaFI Digital') will provide flexibility and choice in therapy delivery. It also allows the study to continue if we enter any further lockdowns either regionally or nationally. The CaFI:Digital offer may also support trial therapist recruitment. This could be critical for attracting a diverse workforce.

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 related psychoses, including different illness models and cultural attributions. Sessions will also explore mental healthcare systems and ways to navigate and interact with them. A 'Shared Learning' approach (versus 'psychoeducation') explicitly acknowledges and seeks to address power dynamics within therapy by promoting 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 and themselves.

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), other appropriate websites and media that promote diversity among therapists. The intervention will be delivered by trained therapist dyads. The Band 7 or above 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 promote cultural competence in mental healthcare and address potential challenges in finding suitably qualified therapists, we will recruit psychiatry trainees, first as co-therapists and then as leads. Band 4 or above Co-Therapists will be from diverse health and care professional backgrounds, such as Assistant Psychologists, Support Workers and Healthcare Assistants. We shall also seek to recruit people from diverse ethnic and cultural backgrounds. For flexibility, we shall employ the Lead Therapists and Co-Therapists on a sessional basis as successfully trialled in the CaFI feasibility study.

Mode of delivery

CaFI face-to-face: comprises a minimum of four people; a service user, family member(s) (also referred to as a Family Unit), a Lead Therapist and a Co-Therapist who deliver the intervention in a mutually agreed space. A paper-based therapy manual and accompanying resources will be used to facilitate the sessions. They will serve as the 'Therapy Tool Box', enabling the therapists and family unit to work collaboratively using relevant resources linked to each of the five therapy components over the 10 sessions (outlined below). In practice, this means the resources used will vary depending on the needs of individual family units and agreement on areas to be addressed in therapy.

CaFI Digital: comprises a minimum of four people working virtually i.e. Family Unit (minimum two people) and two Therapists (Lead and Co-Therapist) remotely. We envisage that the Family Unit and Therapists will connect remotely from the most accessible locations/ venues. In practice, this is likely to mean that service user and family members will connect from their homes (together or separately) and Therapists either from an NHS/office setting or their homes depending on prevailing social distancing restrictions. The CaFI therapy manual and resources will be identical in content to that used in face-to-face therapy, differing only in mode of delivery. Content will be digitised to enable remote access, sharing and engagement. This will be via an NHS compliant platform such as Microsoft Teams (MS Teams) with therapists directing Family Units to resources located on the purpose built, secure CaFI Digital website. Study outcome data will also be collected via a videoconferencing platform, such as MS Teams, and entered into the bespoke study database in line with standard operating procedures agreed with King's Clinical Trials Unit (KCTU). We will provide study participants with a tablet/ smartphone and WiFi to enable access and provide appropriate training/ technical support where needed to facilitate accessibility.

Control arm – Treatment as usual

Service users in both treatment and control groups will receive usual care. This usually involves medication with support from care coordinators, who are generally nurses or social workers. Lack of FI generally (Fadden, 1997) and specifically for Black people (National Collaborating Centre for Mental Health, 2008) were confirmed by our feasibility trial (Degnan et al., 2018). 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 service 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/nFSM or aFSM).

Due to the large number of strata, minimisation will be used over block randomisation to reduce imbalance in the two treatment arms. Allocated Family Support Members (aFSMs) 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, user-specific usernames and passwords 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 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.

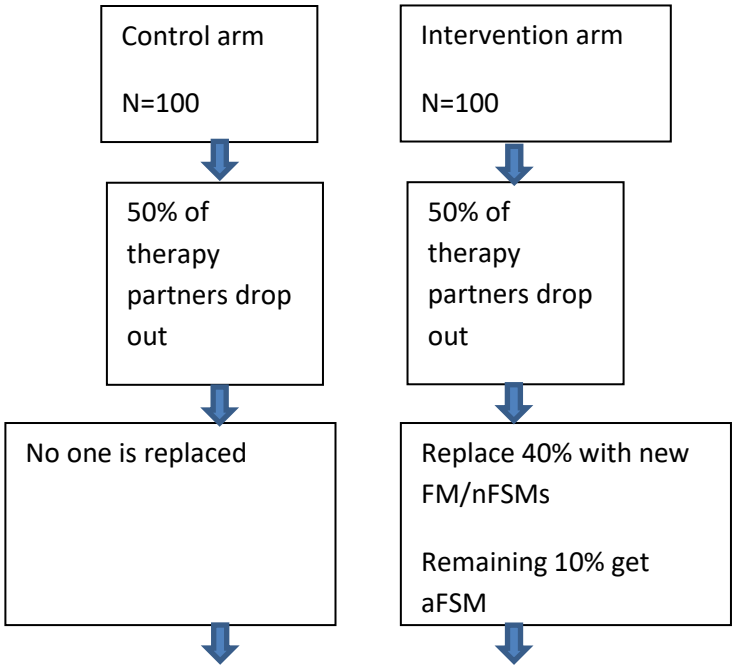
Upon request, KCTU will provide a copy of the final exported dataset to the CI in .csv format and the CI will onward distribute as appropriate.

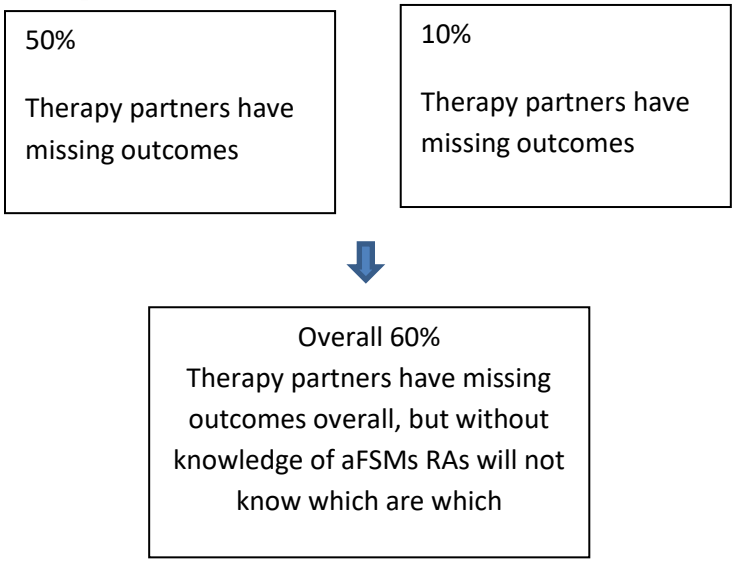
Blinding

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 reduce the risk of unblinding.

However, we recognise the potential for unblinding when the RAs completing the CRF ask whether the service user has a family member/nominated family support member; if the answer is "no" this could lead RAs to believe that the SU is in the control arm. This is because the intervention arm will have to replace FM/nFSMs who drop out to continue with therapy, but the control arm will not. However, a FM/nFSM can be replaced with an aFSM in the intervention arm. As such, RAs cannot *know* whether a SU is in the control arm unless they *know* which SUs have an allocated FSM (which they shouldn't as this is stored in a blinded database) or whether there are, in fact, **no** aFSMs in this study (based on the feasibility study, this is highly unlikely). In other words, whilst RAs may think that many of these service users are probably in the control arm, they cannot know for sure unless the above conditions are met. If a blind break does occur, a different researcher will complete any further follow-ups. We shall report the level of success of our attempts maintain blinding. Please see Figure 2 for worked example.

Figure 2. Worked example of blinding of outcome assessors to participant treatment arm





Quantitative data collection

Quantitative outcome data will be collected by RAs blind to delivery of the intervention at three-time points: baseline, 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 as detailed below and schedule outline in Table 1.

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 nFSMs/aFSMs. Additional questions for service users will include diagnosis, relationship with the family member/nFSM, length of time since first contact with services, history of service use, and medication.

Primary outcome

Time to first 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., 2018). As well as collecting time to first relapse data, we shall record

the number of subsequent relapses that occur to support our understanding and interpretation of participants' experiences during the study.

Secondary outcomes

Other outcomes that were important to our feasibility study participants and work to refine the intervention 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. PSP 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.

Knowledge about psychosis (family members/ nominated family support 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.

Family stress (family members/ nominated family support 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 general stress among family members.

Illness beliefs (service users/ family members/ nominated family support 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 condition'. 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/ therapist/ care coordinators)

The Working Alliance Inventory (WAI)-short-form (Horvath & Greenberg, 1989) is a 12-item self-report measure of the quality of staff-service user relationships, comprising 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 (Horvath & Bedi, 2002; Horvath & Luborsky, 1993; Norcross, 2002).

Health status and QALY (service users/ family members/ nominated family support 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 our previous study, we assessed the feasibility of using the EQ-5D- for this RCT.

Service engagement (Care Coordinator)

The Service Engagement Scale (SES) (Tait, Birchwood, & Trower, 2002) is a 14-item self-report measure assessing participants' engagement with services from a key worker perspective. The

measure has four subscales: availability, collaboration, help-seeking, and treatment adherence. The SES has been validated in a psychosis sample and has evidence of good psychometric properties.

Service Use Questionnaire (SUQ)

Service use data will be collected from patient records (hospital inpatient, outpatient, and Accident & Emergency services) and from a Service-Use Questionnaire (SUQ) to be completed with participants and family at baseline and at each follow up assessment. The SUQ will include questions about whether the participant has used any primary, secondary or community-based health and social care and how often they used these services in the last 3 months (baseline study visit) or since the last assessment (follow-up study visits). The SUQ will ask participants to record whether they have used any hospital inpatient, outpatient, or emergency services and the name of the relevant hospital/services, to facilitate the review of patient records.

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

Table 1. Table of Measures for the CaFI RCT.

	SU	FM	nFSM	aFSM	Therapist	Care Co.
Baseline Only						
Sociodemographic Information	X	X	X	X		
Baseline, 6 Months, and 12 Months						
BRIEF-IPQ	X	X	X			
KAP		X	X			
EQ-5D-5L	X	X	X			
GHQ-12		X	X			
PANSS	X					
PSP	X					
SES						X
SUQ	X					
WAI	X	X	X		X	X
Treatment Arm: Therapy Session 3 and 8						

Timetable (months) and participant timeline

Total duration: 42 months1-12 months: Internal pilot to test whether CaFI is feasible and acceptable to people of Sub-Saharan African descent in addition to those of Caribbean descent

1-24 months: Recruiting people to test CaFI and delivering CaFI to family units

1-40 months:

- Collecting information before receiving CaFI
- Collecting information 6 months after randomisation
- Collecting information 12 months after randomisation
- 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: 24 months

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

Duration of follow-up: 12 months

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

Table 2. Schedule of Participant Enrolment, Interventions and Assessments in the CaFI Study

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**		**Close-out**
TIMEPOINT**	***-T_1*** ***Baseline***	**T_0**	***T1*** ***6-month follow-up***	***T2*** ***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	
Number of psychiatric and compulsory admissions (health records)	X		X	X	
Length of inpatient stays (health records)	X		X	X	

Positive and Negative Syndrome Scale (PANSS)	X		X	X	
Personal and Social Performance Scale (PSP)	X		X	X	
Brief Illness Perception Questionnaire (Brief-IPQ)	X		X	X	
Knowledge about Psychosis (KaP)	X		X	X	
Knowledge About Psychosis Questionnaire (KAP)	X		X	X	
General Health Questionnaire (GHQ-12)	X		X	X	
EQ-5D-5L	X		X	X	
Service use questionnaire SUQ	X		X	X	
Working Alliance Inventory (WAI) **(Care Coordinator & Service User)**	X		X	X	
Working Alliance Inventory (WAI) **(Therapist & Service User)**		Therapy session 3 X	Therapy session 8 X		

***Working Alliance Inventory (WAI)* (Therapist & FSM/nFSM)**		Therapy session 3 X	Therapy session 8 X		
Service Engagement Scale	X		X	X	
Qualitative interview (Process Evaluation)		X	X	X	X

Note. Data collected at baseline (-T1), 6-month follow-up (T1), and 12-month follow-up (T2).

Process evaluation (Qualitative data)

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/nFSM) and approximately 30 staff purposively sampled across all sites. Interview schedules with gather views on: sense making, implementation, embedding and integration. 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 in a practice setting

Process evaluation will also be investigated by assessing therapeutic alliance with CaFI therapist and whether this changes over time (week 3 to week 8 of therapy). The relationship between therapeutic alliance and outcome in the interventions group will also be explored, controlling for known confounders. This is intended as an exploratory analysis of WAI, and not a treatment effect modifier.

Data Analysis

Statistical analyses will be performed on an intention-to-treat basis and will follow the CONSORT statement for non-pharmacological interventions. Within the first six months of the trial, the trial statistician will develop a detailed statistical analysis plan which will be presented to and agreed with the DMEC and TSC prior to the allocation codes being released and commencement of any data analysis.

A consort diagram will be presented detailing participant flow and reasons for drop out where available. Baseline socio-demographic data will be presented by arm to demonstrate the extent of comparability between randomised groups.

For the primary outcome, a 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 used in the minimisation process. All analyses will be appropriately adjusted for therapist clustering.

Secondary outcomes as defined above will be analysed using linear mixed models, adjusting for baseline outcome and minimisation covariates, with random effects for therapist and treatment allocation (Roberts & Roberts, 2005). Where residuals are found to be skewed, standard errors and confidence intervals for the treatment effects will be estimated by applying a bootstrap procedure (Efron and Tibshirani, 1994) using the percentiles based on the results of 5000 replications (using the trial participant as the sampling unit).

Qualitative data 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 thematically analysed using a modified framework approach (Gale 2013). This produces a matrix of summarised data providing a structure for analysis and interpretation. We will initially take an inductive approach to theme generation, with subsequent deductive theme refinement, guided by Normalisation Process Theory.

An economic evaluation comparing the cost-effectiveness of CaFI with usual care will be performed and reported according to the The Consolidated Health Economic Evaluation Reporting Standards (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 costed 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 combined 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. Regression analyses 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 Stop/Go guidelines

Based on our sample size calculation, we will need to recruit 17 participants per month across all participating NHS Trusts to reach target. Recruitment will be rigorously monitored throughout the recruitment period. Twelve months from starting recruitment, we expect to have recruited 60-80% of our family units into the Stop/Go internal pilot. As with most trials, we anticipate recruitment may be slow initially. We have increased monitoring in-line with recent changes to study design, specifically – offering a CaFI Digital version. The Trial Steering Committee (TSC) will meet at least twice within the first 6 months at the start of recruitment, by which time at least 60 families should have been recruited. We will also monitor engagement and participation in therapy sessions during this time. In the feasibility study attendance rate at therapy sessions was 80%. At each review point during the 6 months period if attendance rates are 50% or less this would be cause for concern. 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. If, however, 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.

Each participant's initials and date of birth will be entered on the EDC. NHS number, email address, 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 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. After review, all data will be formally locked for analysis.

Data Monitoring and Ethics Committee

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 Advisory Group

As with the CaFI feasibility pilot, a Research Advisory 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 with Sub-Saharan Africans. There is overwhelming support for further refining the intervention with PPI and trialling it with a wider 'Black' versus Caribbean-only 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 point about adverse events (AEs) or adverse reactions (ARs)and serious adverse events (SAEs) or serious adverse reactions (SARs) which occur between the dates of each participant's commencement and completion of the study (not the end of the trial). In addition to recording AEs/ARs in the standard way, we will include events particularly relevant to this trial and study population, such as significant changes in family situation and deterioration in mental health. Standard operating procedures will be consulted for reporting SAEs/SARs to the Trial Steering Committee (TSC), DMEC and research management group, sponsor, funder and NHS Research Ethics Committee (REC). Definitions of AEs/ARs are:

Expected AE/AR – not reportable

An unfavourable medical occurrence or response to such occurrence experienced by a participant receiving psychological therapy and/or assessment.

It is expected that people in this study population may require a change in medication.

Expected AE/AR/SAE/SAR – standard reporting

Participants in this study may experience a change in medical treatment. The change in treatment may not be due to the study intervention but the possibility cannot be ruled out; it should therefore be reported.

Related or unexpected SAE/SAR – expedited reporting

An SAE is a related or unexpected medical occurrence which:

- results in death;
- is life-threatening as a consequence of the occurrence;
- necessitates inpatient hospital admission or prolongs an existing admission;
- results in persistent or significant disability or incapacity.

A SAR is an AE which is considered both serious and reasonably likely to be due to the psychological therapy and/or assessment. All related or unexpected SAEs/SARs experienced by a participant receiving psychological therapy and/or assessment during their participation in the study will be reported within 24 hours of site staff becoming alerted to the event.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

A serious AR which by nature and severity is not consistent with any effects of psychological therapy and/or assessment.

Withdrawal process

Participants can withdraw from the study at any time without giving a reason, without detriment to themselves and without any medical care and legal rights being affected. Data collected up until the point of withdrawal will still be used in the analyses if participants consented to this as recorded on the original consent form.

Auditing

Study conduct is monitored by regular auditing visits from the sponsor, annual reports to the NHS REC, biannual 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 and an age-appropriate assent form.

Confidentiality, Anonymity & Data Protection

Given levels of stigma within these communities, it is especially important that we 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/ Information will also be shared via a dedicate site the host Trust's Psychosis Research Unit website https://www.psychosisresearch.com/cafi2/.

These websites 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) and social media (e.g. @TheMentalElf).

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 and our CaFI consultants (Ayavoro, Lindsay and Grey) who have experience of co-producing arts with marginalised groups (e.g. ethnic minorities and service users). 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 Association, and International Society of Psychiatric Nurses annual conferences.

References

Addington, J. (2003). An integrated treatment approach to substance use in an early psychosis programme. In H. L. Graham, A. Copello, M. Birchwood, & K. T. Mueser (Eds.), *Substance Misuse in Psychosis: Approaches to Treatment and Service Delivery* (pp. 121–135). Chichester, UK: John Wiley & Sons, Ltd.

Allardyce, J., Gilmour, H., Atkinson, J., Rapson, T., Bishop, J., & McCreadie, R. G. (2005). Social fragmentation, deprivation and urbanicity: Relation to first-admission rates for psychoses. *British Journal of Psychiatry*, *187*(1), 401–406.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Washington, DC: American Psychiatric Association Publishing.

Banerjee, A. G., & Retamero, C. (2014). Expressed emotion – a determinant of relapse in schizophrenia: a case report and literature review. *Journal of Psychiatry and Brain Functions*, *1*(4), 1–3. https://doi.org/10.7243/2055-3447-1-4

Barrowclough, C., & Tarrier, N. (1992). *Families of Schizophrenic Patients: Cognitive Behavioural Intervention*. Hampshire, UK: Cengage Learning EMEA.

Barrowclough, C., Tarrier, N., Lewis, S., Sellwood, W., Mainwaring, J., Quinn, J., & Hamlin, C. (1999). Randomised controlled effectiveness trial of a needs-based psychosocial intervention service for carers of people with schizophrenia. *British Journal of Psychiatry*, *174*(6), 505–511. https://doi.org/10.1192/bjp.174.6.505

Beels, C. C. (1981). Social networks and the treatment of schizophrenia. *International Journal of Family Therapy*, *3*(4), 310–315. https://doi.org/10.1007/BF00924358

Bernal, G., & Domenech Rodríguez, M. M. (2009). Advances in Latino family research: Cultural adaptations of evidence-based interventions. *Family Process*, *48*(2), 169–178. https://doi.org/10.1111/j.1545-5300.2009.01275.x

Berry, K., & Haddock, G. (2008). The implementation of the NICE guidelines for schizophrenia: Barriers to the implementation of psychological interventions and recommendations for the future. *Psychology and Psychotherapy: Theory, Research and Practice*, *81*(4), 419–436. https://doi.org/10.1348/147608308X329540

Bhugra, D., Hilwig, M., Hossein, B., Marceau, H., Neehall, J., Leff, J., … Der, G. (1996). First-contact incidence rates of schizophrenia in Trinidad and one-year follow-up. *British Journal of Psychiatry*, *169*(5), 587–592. https://doi.org/10.1192/bjp.169.5.587

Bhui, K., Aslam, R. W., Palinski, A., McCabe, R., Johnson, M. R. D., Weich, S., … Szczepura, A. (2015). Interventions designed to improve therapeutic communications between black and minority ethnic people and professionals working in psychiatric services: A systematic review of the evidence for their effectiveness. *Health Technology Assessment*, *19*(31), 1–173. https://doi.org/10.3310/hta19310

Bhui, K., Stansfeld, S., Hull, S., Priebe, S., Mole, F., & Feder, G. (2003). Ethnic variations in pathways to and use of specialist mental health services in the UK: Systematic review. *British Journal of Psychiatry*, *182*, 105–116. https://doi.org/10.1192/bjp.182.2.105

Birchwood, M., Cochrane, R., Macmillan, F., Copestake, S., Kucharska, J., & Cariss, M. (1992). The influence of ethincity and family structure on relapse in first-episode schizophrenia. *British Journal of Psychiatry*, *161*(6), 783–790. https://doi.org/10.1192/bjp.161.6.783

Broadbent, E., Kydd, R., Sanders, D., & Vanderpyl, J. (2008). Unmet needs and treatment seeking in high users of mental health services: Role of illness perceptions. *Australian and New Zealand Journal of Psychiatry*, *42*(2), 147–153. https://doi.org/10.1080/00048670701787503

Broadbent, E., Petrie, K. J., Main, J., & Weinman, J. (2006). The Brief Illness Perception Questionnaire. *Journal of Psychosomatic Research*, *60*(6), 631–637. https://doi.org/10.1016/j.jpsychores.2005.10.020

Cabassa, L. J., & Baumann, A. A. (2013). A two-way street: Bridging implementation science and cultural adaptations of mental health treatments. *Implementation Science*, *8*(1), 90–104. https://doi.org/10.1186/1748-5908-8-90

Cantor-Graae, E. (2007). Ethnic minority groups, particularly African-Caribbean and Black African groups, are at increased risk of psychosis in the UK. *Evidence-Based Mental Health*, *10*(3), 95–95. https://doi.org/10.1136/ebmh.10.3.95

Cantor-Graae, E., & Selten, J. P. (2005). Schizophrenia and migration: A meta-analysis and review. *American Journal of Psychiatry*, *162*(1), 12–24. https://doi.org/10.1176/appi.ajp.162.1.12

Care Quality Commission. (2011). *Count me in 2010 - Results of the 2010 national census of inpatients and patients on supervised community treatment in mental health and learning disability services in England and Wales*. London, UK.

Care Quality Commission. (2017). *The state of care in mental health services, 2014 to 2017: Findings from CQC's programme of comprehensive inspections of specialist mental health services*. London, UK.

Chien, W. T., & Chan, S. W. C. (2004). One-year follow-up of a multiple-family-group intervention for Chinese families of patients with schizophrenia. *Psychiatric Services*, *55*(11), 1276–1284. https://doi.org/10.1176/appi.ps.55.11.1276

Chien, W. T., & Thompson, D. R. (2013). An RCT With three-year follow-up of peer support groups for Chinese families of persons with schizophrenia. *Psychiatric Services*, *64*(10), 997–1005. https://doi.org/10.1176/appi.ps.201200243

Claxton, K., Martin, S., Soares, M. O., Rice, N., Spackman, D. E., Hinde, S., … Sculpher, M. (2015). Methods for the estimation of the NICE cost effectiveness threshold. *Health Technology Assessment*, *19*(14), 1–503.

Degnan, A., Baker, S., Edge, D., Nottidge, W., Noke, M., Press, C. J., Husain, N., Rathod, S., & Drake, R. J. (2018). The nature and efficacy of culturally-adapted psychosocial interventions for schizophrenia: a systematic review and meta-analysis. Psychological Medicine, 48(5), 714-727. doi: https://doi.org/10.1017/S0033291717002264.

Department of Health. (2005). *Delivering race equality in mental health care: An action plan for reform inside and outside services and the government's response to the Independent inquiry into the death of David Bennett*. London, UK. https://doi.org/10.1192/apt.bp.107.004986

Department of Health and Social Care. (2014). NHS reference costs. Retrieved October 29, 2019, from https://www.gov.uk/government/collections/nhs-reference-costs/

Edge, D., Degnan, A., Cotterill, S., Berry, K., Drake, R., Baker, J., … Abel, K. (2016). Culturally-adapted Family Intervention (CaFI) for African-Caribbeans diagnosed with schizophrenia and their families: A feasibility study protocol of implementation and acceptability. *Pilot and Feasibility Studies*, *2*(39), 1–14. https://doi.org/10.1186/s40814-016-0070-2.

Edge D, Degnan A, Cotterill S, et al. Culturally adapted Family Intervention (CaFI) for African-Caribbean people diagnosed with schizophrenia and their families: a mixed-methods feasibility study of development, implementation and acceptability. Southampton (UK): NIHR Journals Library; 2018 Sep. (Health Services and Delivery Research, No. 6.32.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK525363/ doi: 10.3310/hsdr06320.

Efron, B., & Tibshirani, R. J. (1994). *An introduction to the bootstrap*. CRC Press.

Eliacin, J. (2013). Social capital, narratives of fragmentation, and schizophrenia: An ethnographic exploration of factors shaping African-Caribbeans' social capital and mental health in a north London community. *Culture, Medicine and Psychiatry*, *37*(3), 465–487.

https://doi.org/10.1007/s11013-013-9322-2

Fadden, G. (1997). Implementation of family interventions in routine clinical practice following staff training programs: A major cause for concern. *Journal of Mental Health*, *6*(6), 599–612. https://doi.org/10.1080/09638239718464

Faria, R., Gomes, M., Epstein, D., & White, I. R. (2014). A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. *Pharmacoeconomicseconomics*, *32*, 1157–1170.

Fearon, P., Kirkbride, J. B., Morgan, C., Dazzan, P., Morgan, K., Lloyd, T., … Murray, R. M. (2006). Incidence of schizophrenia and other psychoses in ethnic minority groups: Results from the MRC AESOP Study. *Psychological Medicine*, *36*(11), 1541–1550. https://doi.org/10.1017/S0033291706008774

Flyckt, L., Löthman, A., Jörgensen, L., Rylander, A., & Koernig, T. (2011). Burden of informal care giving to patients with psychoses: A descriptive and methodological study. *International Journal of Social Psychiatry*, *59*(2), 137–146. https://doi.org/10.1177/0020764011427239

Gale, N.K., Heath, G., Cameron, E. et al. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol 13, 117 (2013). https://doi.org/10.1186/1471-2288-13-117

Gardner, W., Hoge, S. K., Bennett, N., Roth, L. H., Lidz, C. W., Monahan, J., & Mulvey, E. P. (1993). Two scales for measuring patients' perceptions for coercion during mental hospital admission. *Behavioral Sciences and the Law*, *11*(3), 307–321. https://doi.org/10.1002/bsl.2370110308

Goldberg, D., & Williams, P. (1988). *A user's guide to the General Health Questionnaire*. Windsor, UK.

Haddock, G., Eisner, E., Boone, C., Davies, G., Coogan, C., & Barrowclough, C. (2014). An investigation of the implementation of NICE-recommended CBT interventions for people with schizophrenia. *Journal of Mental Health*, *23*(4), 162–165. https://doi.org/10.3109/09638237.2013.869571

Harrison, G., Holton, A., Neilson, D., Owens, D., Boot, D., & Cooper, J. (1989). Severe mental disorder in Afro-Caribbean patients: Some social, demographic and service factors. *Psychological Medicine*, *19*(3), 683–696. https://doi.org/10.1017/S0033291700024284

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., … Badia, X. (2011).

Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*, *20*, 1727–1736. https://doi.org/10.1007/s11136-011-9903-x

Horvath, A. O., & Bedi, R. P. (2002). The alliance. In J. C. Norcross (Ed.), *Psychotherapy Relationships That Work: Therapist Contributions and Responsiveness to Patients* (pp. 37–70). New York, New York: Oxford University Press.

Horvath, A. O., & Luborsky, L. (1993). The role of the therapeutic alliance in psychotherapy. *Journal of Consulting and Clinical Psychology*, *61*(4), 561–573. https://doi.org/10.1037/0022-006X.61.4.561

Horvath, Adam O., & Greenberg, L. S. (1989). Development and validation of the working alliance inventory. *Journal of Counseling Psychology*, *36*(2), 223–233. https://doi.org/10.1037/0022-0167.36.2.223

Janssen, M. F., Pickard, A. S., Golicki, D., Gudex, C., Niewada, M., Scalone, L., … Busschbach, J. (2013). Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *Quality of Life Research*, *22*(7), 1717–1727. https://doi.org/10.1007/s11136-012-0322-4

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261–276. https://doi.org/10.1093/schbul/13.2.261

Kay, S. R., Opler, L. A., & Lindenmayer, J.-P. (1988). Reliability and validity of the positive and negative syndrome scale for schizophrenics. *Psychiatry Research*, *23*(1), 99–110. https://doi.org/10.1016/0165-1781(88)90038-8

Keating, F., & Robertson, D. (2004). Fear, black people and mental illness: A vicious circle? *Health and Social Care in the Community*, *12*(5), 439–447. https://doi.org/10.1111/j.1365-2524.2004.00506.x

Kirkbride, J. B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., … Jones, P. B. (2012). Incidence of schizophrenia and other psychoses in England, 1950-2009: A systematic review and meta-analyses. *PLoS ONE*, *7*(3), e31660. https://doi.org/10.1371/journal.pone.0031660

Leff, J., Bhugra, D., & Mallett, R. (1995). Raised incidence of schizophrenia in UK Afro-Caribbeans-clues to aetiology. *Schizophrenia Research*, *15*(1), 193. https://doi.org/10.1016/0920-9964(95)95595-Z

Liu, J. J., Davidson, E., Bhopal, R. S., White, M., Johnson, M. R. D., Netto, G., … Sheikh, A. (2012). Adapting health promotion interventions to meet the needs of ethnic minority groups: Mixed-methods evidence synthesis. *Health Technology Assessment*, *16*(44). https://doi.org/10.3310/hta16440

Lobban, F., Barrowclough, C., & Jones, S. (2005). Assessing cognitive representations of mental health problems. II. The illness perception questionnaire for schizophrenia: Relatives' version. *British Journal of Clinical Psychology*, *44*(2), 163–179. https://doi.org/10.1348/014466504X19785

Lobban, F., Postlethwaite, A., Glentworth, D., Pinfold, V., Wainwright, L., Dunn, G., … Haddock, G. (2013). A systematic review of randomised controlled trials of interventions reporting outcomes for relatives of people with psychosis. *Clinical Psychology Review*, *33*(3), 372–382. https://doi.org/10.1016/j.cpr.2012.12.004

Lobban, F., Solis-Trapala, I., Tyler, E., Chandler, C., & Morriss, R. K. (2013). The role of beliefs about mood swings in determining outcome in bipolar disorder. *Cognitive Therapy and Research*, *37*(1), 51–60. https://doi.org/10.1007/s10608-012-9452-9

Mahy, G. E., Mallett, R., Leff, J., & Bhugra, D. (1999). First-contact incidence rate of schizophrenia on Barbados. *British Journal of Psychiatry*, *175*(1), 28–33. https://doi.org/10.1192/bjp.175.1.28

Mantovani, N., Pizzolati, M., & Edge, D. (2017). Exploring the relationship between stigma and help-seeking for mental illness in African-descended faith communities in the UK. *Health Expectations*, *20*(3), 373–384. https://doi.org/10.1111/hex.12464

May, C., & Finch, T. (2009). Implementing, embedding, and integrating practices: An outline of normalization process theory. *Sociology*, *43*(3), 535–554. https://doi.org/10.1177/0038038509103208

McCabe, C., Claxton, K., & Culyer, A. J. (2008). The NICE cost-effectiveness threshold. *Pharmacoeconomics*, *26*, 733–744.

Mental Health Working Group. (2011). *Completing the revolution: Transforming mental health and tackling poverty*. London, UK.

Moore, G. F., Audrey, S., Barker, M., Bond, L., Bonell, C., Hardeman, W., … Baird, J. (2015). Process evaluation of complex interventions: Medical Research Council guidance. *BMJ (Online)*, *350*, 1–7. https://doi.org/10.1136/bmj.h1258

Morgan, C., Abdul-Al, R., Lappin, J. M., Jones, P., Fearon, P., Leese, M., … Murray, R. (2006).

Clinical and social determinants of duration of untreated psychosis in the ÆSOP first-episode psychosis study. *British Journal of Psychiatry*, *189*(.), 446–452. https://doi.org/10.1192/bjp.bp.106.021303

Morgan, C., Charalambides, M., Hutchinson, G., & Murray, R. M. (2010). Migration, ethnicity, and psychosis: Toward a sociodevelopmental model. *Schizophrenia Bulletin*, *36*(4), 655–664. https://doi.org/10.1093/schbul/sbq051

Morgan, C., Dazzan, P., Morgan, K., Jones, P., Harrison, G., Leff, J., … Fearon, P. (2006). First episode psychosis and ethnicity: Initial findings from the AESOP study. *World Psychiatry*, *5*(1), 40–46. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16757995%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC1472260

Morgan, C., Fisher, H., Hutchinson, G., Kirkbride, J., Craig, T. K., Morgan, K., … Fearon, P. (2009). Ethnicity, social disadvantage and psychotic-like experiences in a healthy population based sample. *Acta Psychiatrica Scandinavica*, *119*(3), 226–235. https://doi.org/10.1111/j.1600-0447.2008.01301.x

Morgan, C., Hutchinson, G., Bagalkote, H., Morgan, K., Dazzan, P., Samele, C., & Murray, R. (2002). GP referral and ethnicity in the AESOP (Aetiology and Ethnicity in Schizophrenia and Other Psychoses) first onset study. *Schizophrenia Research*, *53*(3), 49.

Morgan, C., Kirkbride, J., Hutchinson, G., Craig, T., Morgan, K., Dazzan, P., … Fearon, P. (2008). Cumulative social disadvantage, ethnicity and first-episode psychosis: A case-control study. *Psychological Medicine*, *38*(12), 1701–1715. https://doi.org/10.1017/S0033291708004534

Morgan, C., Mallett, R., Hutchinson, G., Bagalkote, H., Morgan, K., Fearon, P., … Leff, J. (2005a). Pathways to care and ethnicity. 2: Source of referral and help-seeking: Report from the ÆSOP study. *British Journal of Psychiatry*, *186*, 290–296. https://doi.org/10.1192/bjp.186.4.290

Morgan, C., Mallett, R., Hutchinson, G., Bagalkote, H., Morgan, K., Fearon, P., … Leff, J. (2005b). Pathways to care and ethnicity. I: Sample characteristics and compulsory admission: Report from the ÆSOP study. *British Journal of Psychiatry*, *186*, 281–289. https://doi.org/10.1192/bjp.186.4.281

Morgan, C., Mallett, R., Hutchinson, G., & Leff, J. (2004). Negative pathways to psychiatric care and ethnicity: The bridge between social science and psychiatry. *Social Science and Medicine*, *58*(4), 739–752. https://doi.org/10.1016/S0277-9536(03)00233-8

Morosini, P. L., Magliano, L., Brambilla, L., Ugolini, S., & Pioli, R. (2000). Development, reliability and acceptability of a new version of the DSM- IV Social Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatrica Scandinavica*, *101*(4), 323–329. https://doi.org/10.1034/j.1600-0447.2000.101004323.x

Naeem, F., Ayub, M., Gobbi, M., & Kingdon, D. (2009). Development of Southampton Adaptation Framework for CBT (SAF-CBT): A framework for adaptation of CBT in non-western culture. *Journal of Pakistan Psychiatric Society.*, *6*(2), 79–84.

National Collaborating Centre for Mental Health. (2008). *Schizophrenia: Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care*. London, UK.

National Collaborating Centre for Mental Health. (2014). *Psychosis and schizophrenia in adults*. London, UK.

National Institute for Health and Care Excellence. (2013). *Guide to the methods of technology appraisal 2013*. London, UK. Retrieved from https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781%0Ahttps://www.nice.org.uk/process/pmg9/chapter/foreword

Nilsen, P. (2015). Making sense of implementation theories, models and frameworks. *Implementation Science*, *10*(53), 1–13. https://doi.org/10.1186/s13012-015-0242-0

Norcross, J. C. (2002). *Psychotherapy Relationships that Work: Therapist Contributions and Responsiveness to Patients*. (J. C. Norcross, Ed.). New York, New York: Oxford University Press.

Patrick, D. L., Burns, T., Morosini, P., Rothman, M., Gagnon, D. D., Wild, D., & Adriaenssen, I. (2009). Reliability, validity and ability to detect change of the clinician-rated Personal and Social Performance scale in patients with acute symptoms of schizophrenia. *Current Medical Research and Opinion*, *25*(2), 325–338. https://doi.org/10.1185/03007990802611919

Personal Social Services Research Unit. (2019). Unit costs of health and social care. Retrieved October 29, 2019, from https://www.pssru.ac.uk/project-pages/unit-costs/

Pharoah, F., Mari, J., Rathbone, J., & Wong, W. (2006). Family intervention for schizophrenia. In F. Pharoah (Ed.), *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd. https://doi.org/10.1002/14651858.CD000088.pub2

Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Orbach, G., & Morgan, C. (2002).

Psychological treatments in schizophrenia: I. Meta-analysis of family intervention and cognitive behaviour therapy. *Psychological Medicine*, *32*(5), 763–782. https://doi.org/10.1017/S0033291702005895

Rabiee, F., & Smith, P. (2014). Understanding mental health and experience of accessing services among African and African Caribbean Service users and carers in Birmingham, UK. *Diversity and Equality in Health and Care*, *11*, 125–134.

Roberts, C., & Roberts, S. A. (2005). Design and analysis of clinical trails with clustering effects due to treatment. *Clinical Trials*, *2*(2), 152-162.

Smith, G., Gregory, K., & Higgs, A. (2007). *An integrated approach to family work for psychosis: A manual for family workers*. London, UK: Jessica Kingsley Publishers.

Sproston, K., & Nazroo, J. (2006). *Ethnic Minority Psychiatric Illness Rates in the Community (EMPIRIC). UK Data Archive*. London, UK.

Tait, L., Birchwood, M., & Trower, P. (2002). A new scale (SES) to measure engagement with community mental health services. *Journal of Mental Health*, *11*(2), 191–198. https://doi.org/10.1080/09638230020023570-2

Takei, N., Persaud, R., Woodruff, P., Brockington, I. F., & Murray, R. M. (1998). First episodes of psychosis in Afro-Caribbean and White people. *British Journal of Psychiatry*, *172*(2), 147–153. https://doi.org/10.1192/bjp.172.2.147

Tansella, M., & Thornicroft, G. (2009). Implementation science: Understanding the translation of evidence into practice. *British Journal of Psychiatry*, *195*(4), 283–285. https://doi.org/10.1192/bjp.bp.109.065565

Tew, J., Ramon, S., Slade, M., Bird, V., Melton, J., & Le Boutillier, C. (2012). Social factors and recovery from mental health difficulties: A review of the evidence. *British Journal of Social Work*, *42*(3), 443–460. https://doi.org/10.1093/bjsw/bcr076

The Sainsbury Centre for Mental Health. (2006). *The costs of race inequality*. London, UK. Retrieved from http://www.scie-socialcareonline.org.uk/the-costs-of-race-inequality/r/a11G00000017xdSIAQ

Tracey, T. J., & Kokotovic, A. M. (1989). Factor structure of the Working Alliance Inventory. *Psychological Assessment*, *1*(3), 207–210. https://doi.org/10.1037/1040-3590.1.3.207

Tryon, G. S., Blackwell, S. C., & Hammel, E. F. (2007). A meta-analytic examination of client-

therapist perspectives of the working alliance. *Psychotherapy Research, 17*(6), 629–642. https://doi.org/10.1080/10503300701320611

Wang, H., Naghavi, M., Allen, C., Barber, R. M., Carter, A., Casey, D. C., … Zuhlke, L. J. (2016). Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet, 388*(10053), 1459–1544. https://doi.org/10.1016/S0140-6736(16)31012-1

White, I. R., Horton, N. J., Carpenter, J., & Pocock, S. J. (2011). Strategy for intention to treat analysis in randomised trials with missing outcome data. *BMJ, 342*, d40.

White, I. R., & Thompson, S. G. (2005). Adjusting for partially missing baseline measurements in randomized trials. *Statistics in Medicine, 24*, 993–1007.

World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines.* Geneva.