Trial

Evaluation of Intensive Community Care Services for young people with psychiatric emergencies

Full Trial Protocol Version 2.3

(19 January 2022)

Protocol Authorisation

Chief Investigator: Professor Dennis Ougrin

Signature: Date: 19/01/2022

Statistician:

Signature ..... Date: 19/01/2022

1. PROTOCOL FULL TITLE:

Comparison of Effectiveness and Cost-Effectiveness of Intensive Community Care Services Versus Treatment As Usual Including Inpatient Care for Young People with Psychiatric Emergencies (IVY): An Internal Pilot followed by a Randomised Controlled Trial Comprising All Intensive Community Service Care Teams in Great Britain

Protocol Short Title/ Acronym: Evaluation of Intensive Community Care Services for young people with psychiatric emergencies (IVY)

Trial Identifiers

ISRCTN:	ISRCTN42999542		
REC Number:	20/WM/0069		
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2. Study Synopsis

TITLE OF CLINICAL TRIAL:	**Comparison of Effectiveness and Cost-Effectiveness of Intensive Community Care Services Versus Treatment As Usual Including Inpatient Care for Young People with Psychiatric Emergencies (IVY): An Internal Pilot followed by a Randomised Controlled Trial Comprising All Intensive Community Service Care Teams in Great Britain**

Protocol Short Title/ Acronym:	IVY
Study Phase If Not Mentioned In Title:	III
Sponsor Name:	King's College London and South London and Maudsley NHS Foundation Trust
Chief Investigator:	Professor Dennis Ougrin
REC Number:	20/WM/0069
Medical Condition Or Disease Under Investigation:	Severe Mental Illness
Purpose Of Clinical Trial:	Randomised controlled trial to establish the effectiveness and cost-effectiveness of Intensive Community Care Services (ICCS) compared to Usual Care - Treatment As Usual (TAU) which might include inpatient care in young people with severe psychiatric disorders
Primary Objective:	Clinical Evaluation of Intensive Community Care Services
Secondary Objective(s):	The cost-effectiveness of ICCS vs TAU at 6 months post randomisation
Trial Design:	Parallel group multi-centre randomised controlled trial
Primary Endpoint:	Time to returning to/time to gaining education/ employment/training, from the day of randomisation to the

	first day of attending either an educational institution, employment or training.
Sample Size:	Randomisation of 252 young people with psychiatric emergencies
Summary Of Eligibility Criteria:	Inclusion criteria: 1. Young people aged 12 years 0 months to 17 years 11 months (if 18 at randomisation then exclude) 2. Young people who can consent* and who are being considered for in-patient psychiatric admission in the participating NHS Trusts * Eligible participants under 16 years of age will require the consent of at least one person with parental responsibility Exclusion criteria will be: 1. Local ICCS teams unable to accept new referrals due to their full capacity being reached 2. Young people unable to consent due to their mental state

	3. The risk profile of the young person is not compatible with ensuring their safety and/or the safety of others in the community. Children Clinical Global Impression (CGAS) score of <20, indicating that the young person must be admitted for inpatient care and is therefore ineligible for randomisation.
Intervention (Description, frequency, details of delivery)	ICCS, as defined for the purposes of this study, will consist of the following essential components: • SMALL CASELOAD: service user/provider ratio of no more, than 10:1. • TEAM APPROACH: Provider group functions as team rather than as individual practitioners; clinicians know and work with all clients. • ICCS TEAM MEETING: ICCS Team meets frequently to plan and review services for each service user. • PRACTICING TEAM LEADER: Supervisor of front-line clinicians provides direct services. • CONTINUITY OF STAFFING: ICCS Team aims to maintain same staffing over time.

	• STAFF CAPACITY: ICCS Team operates at full staffing. • PSYCHIATRIST/ PSYCHIATRIC PRESCRIBER ON STAFF: there is at least one full-time psychiatrist per 100 service users assigned to work with the ICCS Team. • NURSE (RMN) ON STAFF: there are at least two full-time nurses (RMNs) assigned to work with a 100-client ICCS Team. • ICCS TEAM SIZE: team is of sufficient absolute size to provide consistently the necessary staffing diversity and coverage. • EXPLICIT ADMISSION CRITERIA: ICCS Team has clearly identified mission to serve a particular population and has and uses measurable and operationally defined criteria to screen out inappropriate referrals. • INTAKE RATE: ICCS Team takes clients in at a low rate to maintain a stable service environment. • RESPONSIBILITY FOR HOSPITAL ADMISSIONS: ICCS Team is involved in hospital admissions.

	• COMMUNITY-BASED SERVICES: ICCS Team works to monitor status and develop skills in the community rather than function as an office-based team. • NO DROPOUT POLICY: ICCS Team engages and retains service users at a mutually satisfactory level. • ASSERTIVE ENGAGEMENT MECHANISMS: ICCS Team uses community outreach, motivational/ engagement techniques, as well as legal mechanisms or other techniques to ensure ongoing engagement. • INTENSITY OF SERVICE: high amount of face-to-face service time as needed. • FREQUENCY OF CONTACT: high number of face-to-face service contacts as needed. • WORK WITH INFORMAL SUPPORT SYSTEM: with or without service users present, ICCS Team provides support and skills for service user's support network: family, school, extracurricular activities coordinators etc. • ROLE OF SERVICE USERS ON TREATMENT TEAM: Service users are involved in the

	functioning of the team (e.g. as members of the interview panels). • PROVISION OF A DAY SERVICE: ICCS Team provides a form of day service, such as a day school or partial hospitalisation to those service users who need it.
Comparator Intervention:	Usual Inpatient Care
Maximum Duration Of Treatment Of A Subject:	6 months
Version And Date Of Final Protocol:	Version 2.3 20/01/2022
Version And Date Of Protocol Amendments:	Version 2.2 01/11/2020 Version 2.1 13/03/2020

3. Revision History

Document ID - (Document Title) revision X.Y	**Description of changes from previous revision**	**Effective Date**

2.2	• Clarification of primary and secondary outcomes including the variable that is measured, the method of measurement (name of test/scale/questionnaire) • Inclusion criteria clarified/simplified (i.e. word 'psychiatric admission' added) • Added trial registration number (ISRCTN) • Word 'anonymised' changed to 'pseudo-anonymised' as per GDPR • Exclusion of The Columbia Impairment Scale • A directional hypothesis for effectiveness added to section 'Primary endpoints' • Amended Appendix 2: List of measures collected at each stage • EQ5D measure replaced with the CHU-9D • Clarification of the TAU group	Approved as V2.3 following comments from REC
2.3	The REC Committee requested to remove on page 30 of the protocol, 'CGASA score of <20' as it is adequately explained on the following page	Approved 20/01/2022

4. Glossary of terms (Optional)

ICCS=Intensive Community Care Services

CAMHS=Child and Adolescent Mental Health Services

TAU=Treatment As Usual

CI=Chief Investigator

RCT=Randomised Controlled Trial

RW=Research Worker

CI= Chief Investigator

TM=Trial Manager

AE=Adverse Events

LSBU=London South Bank University

5. Protocol Contents

6. Background & Rationale

At least 1 in 10 young people have a mental health disorder (1). Demand for both community and inpatient services continues to grow in the UK. The latest review of Child and Adolescent Mental Health Services (CAMHS; which include specialist and inpatient services) revealed that over 4000 young people required psychiatric inpatient care in 2014(2). This number has more than doubled since 2004. Despite a substantial increase in the number of NHS-funded CAMHS beds from 844 in 1999 to 1450 in 2018, there is currently a national bed crisis with many young people being admitted out of area or to adult wards. The mean length of hospital stay in the UK is 74 days for general admissions, 103 days for Eating Disorders units and 307 days for Secure units, longer than in many other countries. A key contributor to this is an underdeveloped network of services designed to provide alternatives to in-patient care (3). This is despite accumulating evidence, provided largely by our group (4,5), that early discharge with ICCS could provide a cost-effective alternative to inpatient care with similar clinical outcomes.

All CAMHS Specialist Services have been commissioned by NHS England since April 2013. This represents an opportunity to develop a coherent nationwide strategy for dealing with the national bed crisis including the development of innovative models of care which this proposal addresses. According to international standards (6,7), ICCS teams must: a) provide home-based treatment b) have a small caseload (< 5 per full time equivalent) c) offer psychological treatment, including to those patients that are difficult to reach d) provide transition (from clinic to home) case management e) provide early intervention f) offer psychiatric assessment in the community g) provide family support h) focus on vocational and educational goals i) offer psychopharmacological interventions j) offer partial hospitalisation (day hospital) including access to a hospital school k) operate outside of the standard office hours. There are currently 6 services in England and Wales and 1 service in Scotland that conform to the requirements for ICCS - aAll these teams have agreed

to participate in this research. Their treatment adherence will be measured using a modified Dartmouth Assertive Community Treatment Scale (19).

Although inpatient admissions are sometimes unavoidable, there are disadvantages associated with inpatient care as demonstrated by our research group (4,8):

• Prolonged admissions are linked with higher risk of self-harm and poorer school reintegration

• Prolonged admissions are not cost-effective.

The CI and co-investigators have expertise in developing services for adolescents with severe psychiatric disorders both nationally and internationally, including establishing the first adolescent unit in the UK operating a 24/7 admissions policy (all inpatient services providing usual care in the RCT use this model), the most comprehensive day care facility and the first supported discharge service (9,10). The study team comprises world-leading researchers in the field of mental health trial statistics and economics, including child and adolescent mental health. The trial will also provide an in-depth qualitative examination of the experiences of young people in both hospital and ICCS, adding depth to the findings.

The evidence base for the efficacy of ICCS in young people is poor. A Cochrane review (11) found limited evidence that a Homebuilders model for crisis intervention led to a small clinical improvement in comparison to inpatient care. A systematic review by our group (8) found six RCTs examining the efficacy of specialist outpatient treatment, multisystemic therapy, day patient treatment, intensive home treatment and supported discharge service versus inpatient care. Using ICCS was associated with clinical improvements similar to inpatient care in young people but the studies have not focused on preventing admissions in young people with severe psychiatric disorders. There is very limited information on patient satisfaction, patient experiences and cost-effectiveness analyses in the UK. Since the publication of the review, one further RCT by our group was published (4). It demonstrated that early discharge with an ICCS team, in this case, called

Supported Discharge Service (SDS), versus usual inpatient care, leads to similar clinical outcomes, fewer young people reporting multiple self-harm episodes and better school reintegration, and had a higher probability of being cost-effective. However, it is not known whether preventing inpatient admissions with ICCS, rather than early discharge, would perform in a similar way to SDS. In addition, we now have pilot data (n = 20, 12-18) on offering ICCS to prevent admission which indicates good engagement of young people with ICCS and good acceptability.

7. Trial Objectives and Design

7.1 Trial Objectives

The overarching aim of this trial is to evaluate the clinical and cost-effectiveness of Intensive Community Care Services compared with Usual Care, Treatment As Usual (TAU) in young people with severe psychiatric disorders.

Specific Objective:

- To establish the impact of ICCS vs TAU on returning to/time to gaining education, employment or training

PRIMARY ENDPOINTS

Our primary objective is to evaluate the effectiveness of ICCS compared to TAU in reducing the time taken to return to or start education, employment or training (EET) measured from the day of randomisation to the first day of attending either an educational institution, employment or training. This outcome will be collected by contacting the relevant clinical team or the relevant educational, employment or training establishments. The information will be sent to a TM every 2 weeks and the

data will be entered into MACRO by a local Research Assisatnt. This is a continuous variable that comprises of number of days to returning or gaining employment, education or training ("time to EET"). For those not returning/gaining education, employment or training, the time will be censored at the end of the follow-up period (6 months after randomisation) or consent withdrawal. We will contact the relevant clinical team providing care to the participant every two weeks to gather the most up-to-date information regarding the participants' education, employment or training status. We will then contact the relevant establishment and ask them to provide the first day the participant returned/started EET, irrespective of the duration of the attendance.

We will also gather data on the specific dates the participant attended education, employment or training (secondary outcome). If the participant attended more than one establishment on the same date, this will be counted as one attendance.

This outcome measure is not only valuable from a wider societal perspective but was also highlighted by service users and their families as being of preeminent importance. It is also an important marker of improved health, equivalent to employment in adults.

SECONDARY ENDPOINTS

Our secondary objectives are to examine:

1- the impact of ICCS vs TAU on clinical symptoms and functioning and service satisfaction

2- the cost-effectiveness of ICCS vs TAU

3- service users' subjective experiences of receiving ICCS vs TAU, determined from qualitative interviews

4- experiences of mental health professionals in relation to delivering ICCS vs TAU

To achieve objectives 1 and 2 we will collect the following measures:

1. The Strengths and Difficulties Questionnaire – self-reported children will be used in this study to measure common areas of emotional and behavioural problems in young people. Measure will be taken at baseline and 6 months post randomisation.

2. The Children's Global Assessment Scale – we will use this clinicians' rated scale to provide a global measure of functioning in young people. The measure provides a single global rating, on scale of 0-100. Measure will be taken at baseline and 6 months post randomisation.

3. The Clinical Global Impressions/The Clinical Global Impressions Improvement Scale – assessment of the clinician's view of the patient's global functioning prior to and after the study intervention. The Clinical Global Impression Scale will be administered at pre-randomisation and 6 months post randomisation and Clinical Global Impressions Improvement Scale will be measured at 6 months post randomisation.

(Please note that Q1 is asked at both Pre-randomisation and 6 months and Q2 not asked pre-randomisation.)

4. Service Satisfaction Survey (ChASE children self-report questionnare) - will be used to measure patients' satisfaction with services at 6 months post randomisation.

5. The Health of the Nation Outcome Scales for Children and Adolescents – will be used to measure general health and social functioning, the scale is completed by clinicians to indicate the severity of each problem, on a scale of 0-4. Measure will be taken at baseline and 6 months post randomisation.

7. CHU-9D - this is a generic self-reported measure of health-related Quality of Life in children and adolescents. Measure will be taken at baseline and 6 months post randomisation.

8. Self-Harm Questionnaire - a self-reported measure that aims to identify self-harm thoughts and behaviours; measured at baseline and 6 months post randomisation.

9. Time spent in hospital (in days) - we will measure time spent in hospital (in days); we will have full ascertainment of this outcome due to the use of electronic patient records in all participating teams.

10. Child and Adolescent Service Use Schedule (CA-SUS)- this questionnaire will be used to collect information on participants' use of health and social care services (resource-use data). It covers participants' use of these services for the last 3 months (at baseline) and since they last completed the questionnaire (6 months prior) at 6 months post randomisation.

Information on the provision of the intervention and TAU (inpatient services, daypatient services and contact with community CAMHS workers) will be taken from medical notes and recorded in the proforma.

11. Number of days attending education, training or employment in the 6 months following the day of randomisation- this outcome measure will be collected by contacting the relevant clinical team or the relevant educational, employment or training establishments.

All outcomes will be collected at 6-month follow-up by independent researchers unaware of participants' allocation. We will contact the families by mail and include self-addressed envelopes with self-reported outcome measures (or conduct a telephone or remote interview) for those families that do not wish to undertake face-to-face assessments.

To achieve objective 3 and 4 we will undertake in-depth one-to-one interviews with 21 patients randomised to the ICCS group and 21 randomised to TAU. RAs blind to the outcomes will conduct semi-structured in-depth interviews. Young people will participate in a semi-structured visual interview study to examine their experiences of admission, ward-life and treatment. A thematic decomposition analysis will be conducted on the data and specific themes relevant to satisfaction and engagement with services will be examined in-depth. We will aim to understand participant experiences of any organisational problems and barriers, and facilitators of treatments.

We will include 42 healthcare workers, 21 delivering intensive community care and 21 inpatient care to understand in-depth their experience of delivering the services. We will also specifically investigate which outcomes have the greatest importance for young people as part of the existing process evaluation.

7.2 Trial Design

The IVY trial is a two arm, multicentre, blinded RCT examining the hypothesis that the time to returning to/time to gaining education, employment or training (EET) will be significantly faster among the young people randomised to the ICCS group compared to young people who will receive treatment as usual (TAU). This will be tested at 6 months post randomisation (a follow-up).

7.3 Trial Flowchart

See Appendix 1 for the CONSORT diagram

8. Trial Intervention

8.1 Therapy/Intervention Details

ICCS, as defined for the purposes of this study, will consist of the following essential components:

- SMALL CASELOAD: service user/provider ratio of no more, than 10:1.
- TEAM APPROACH: Provider group functions as team rather than as individual practitioners; clinicians know and work with all clients.
- ICCS TEAM MEETING: ICCS Team meets frequently to plan and review services for each service user.

- PRACTICING TEAM LEADER: Supervisor of front-line clinicians provides direct services.
- CONTINUITY OF STAFFING: ICCS Team aims to maintain same staffing over time.
- STAFF CAPACITY: ICCS Team operates at full staffing.
- PSYCHIATRIST/ PSYCHIATRIC PRESCRIBER ON STAFF: There is at least one full-time psychiatrist per 100 service users assigned to work with the ICCS Team.
- NURSE (RMN) ON STAFF: There are at least two full-time nurses (RMNs) assigned to work with a 100-client ICCS Team.
- ICCS TEAM SIZE: Team is of sufficient absolute size to consistently provide the necessary staffing diversity and coverage.
- EXPLICIT ADMISSION CRITERIA: ICCS Team has clearly identified mission to serve a particular population and has and uses measurable and operationally defined criteria to screen out inappropriate referrals.
- INTAKE RATE: ICCS Team takes clients in at a low rate to maintain a stable service environment.
- RESPONSIBILITY FOR HOSPITAL ADMISSIONS: ICCS Team is involved in hospital admissions.
- COMMUNITY-BASED SERVICES: ICCS Team works to monitor status and develop skills in the community rather than function as an office-based team.
- NO DROPOUT POLICY: ICCS Team engages and retains service users at a mutually satisfactory level.

- ASSERTIVE ENGAGEMENT MECHANISMS: ICCS Team uses community outreach, motivational/ engagement techniques, as well as legal mechanisms or other techniques to ensure ongoing engagement.
- INTENSITY OF SERVICE: High amount of face-to-face service time as needed.
- FREQUENCY OF CONTACT: High number of face-to-face service contacts as needed.
- WORK WITH INFORMAL SUPPORT SYSTEM: With or without service users present, ICCS Team provides support and skills for service user's support network: family, school, extracurricular activities coordinators etc.
- ROLE OF SERVICE USERS ON TREATMENT TEAM: Service users are involved in the functioning of the team (e.g. as members of the interview panels).
- PROVISION OF A DAY SERVICE: ICCS Team provides a form of day service, such as a day school or partial hospitalisation to those service users who need it.

The inpatient care aspect of TAU will be based on the model developed by Richard Corrigall, which has since been adopted widely in the UK (9). Community aspects of TAU will include all other CAMHS teams except ICCS.

8.2 Frequency and duration of intervention

In summary, ICCS involves intensive treatment of young people with severe mental illness in community setting. Following the initial assessment, individualised goals are set with the family. The treatment includes a combination of psychological, pharmacological and/or social interventions as needed to achieve the goals. The interventions could be delivered up to several times a day. The treatment is not time limited, but the aim is to achieve the goals within 3 months of the initial assessment. ICCS is followed by standard community treatment.

TAU might include usual inpatient care delivered in hospital or all other community CAMHS except ICCS. Following the initial assessment, young people are treated with a combination of psychological, pharmacological and/or social interventions as needed to achieve the goals set up in collaboration with the family. The treatment is not time limited, but the average duration of treatment is approximately 50 days. The hospital treatment is followed by standard community treatment.

Research assessments will take place following consent and most assessments will need to be completed before randomisation (see Appendix 2). During the baseline assessment, the Kiddie Schedule for Schizophrenia and Affective Disorders (K-SADS) and other assessments as detailed in Appendix 2, will be initiated by experienced researchers trained to fidelity in collaboration with child psychiatrists or psychologists participating in the study. During the follow-up interview at 6-months post-randomisation, patients and their families will be interviewed by one of the project interviewers using the measures listed in Appendix 2 . Information regarding treatment exposure will be recorded in medical records throughout the follow-up period. Treatment data will be recorded in medical records in the form of average weekly doses for all psychotropic drugs, as well as the number and frequency of various types of psychotherapy.

8.3 Intervention records

ICCS treating teams will keep records of the sessions in accordance with the guidelines of the clinical service in which they work and in accordance with professional guidelines.

TAU sessions will be recorded in medical records in accordance with local Trust guidelines and clinical practice.

8.4 Subject compliance

Clinical records will be used to monitor compliance. Clinical records will be accessed at the end of the follow-up period. The study is pragmatic, and any dropouts will be recorded and analysed.

8.5 Study adherence

All teams were selected on the basis of their adherence to the ICCS model using the modified Dartmouth Assertive Community Treatment Scale. We will use the modified scale to test the fidelity of each service at baseline and then 6-monthly. The results of this assessment will be presented at the Trial Steering Committee (TSC) meetings and will be used to provide feedback and to improve the quality of the services. We anticipate some local variations in the services provided, however, we will use the approach developed by Teague et al, (1998) to ensure adequate fidelity across ICCSs. The assessment will involve a telephone consultation with each service leader conducted by a trained independent researcher in order to make 5-point ratings on the critical components of the practice. A rating of 5 will indicate full adherence to the model, and 1 will indicate no adherence. The average of the item ratings will yield a total fidelity score; a total score of 4.0 or greater will indicate high fidelity, scores between 3.0 and 4.0 moderate fidelity, and scores less than 3.0 low fidelity. Items with low fidelity will be highlighted during TSCs and action plans will be developed to address these. The TSC may decide to discontinue the participation of ICCSs with consistently low fidelity scores.

9. Research environment

Consent and outcome measures will be collected within clinical settings at participating NHS Trusts.

10. Selection and Withdrawal of Subjects

10.1 Inclusion Criteria

The following inclusion criteria will be used when identifying potential trial participants:

1. Young people aged 12 years 0 months to 17 years 11 months

2. Young people who can consent* and who are being considered for in-patient psychiatric admission in the participating NHS Trusts

   *Eligible participants under 16-year of age will require the consent of at least one person with parental responsibility.

10.2 Exclusion Criteria

The only 3 exclusion criteria will be:

1. Local ICCS teams unable to accept new referrals due to their full capacity being reached

2. Young people unable to consent due to their mental state

3. The risk profile of the young person is not compatible with ensuring their safety and/or the safety of others in the community *

* We will use the Children Clinical Global Scale (CGAS) to standardise our approach to risk. The CGAS is used to rate the general functioning of young people under the age of 18. It has good validity and reliability. Scores range from 1 to 100, with high scores indicating better functioning. CGAS score of <20 indicates that the young person needs considerable supervision to prevent hurting others or self will be used as a guide to risk, indicating that the young person must be admitted for inpatient care and is therefore ineligible for randomisation.

10.3 Selection of Participants

The target population for this trial is young people with psychiatric emergencies considered for inpatient admission within NHS CAMHS. The diagnosis will be established by the K-SADS-PL

Internal Pilot

We will undertake an internal pilot to ensure that recruitment is feasible as follows:

- Within the first 12 months of the start of the RCT, we will establish if our recruitment projections are in line with the actual recruitment achieved. Achieving 80-100% of the projected recruitment will be a success and the study will proceed as planned. Achieving 60-80% of the projected recruitment will trigger a discussion with the Funder and a plan to remedy recruitment difficulties, such as including more sites if available by that point. Achieving less than 60% of the projected recruitment will indicate that the study should not proceed as planned. All data collected will be published as a service evaluation.
- We will also set specific recruitment targets for each participating service and the same logic will be applied to their recruitment figures.

Progression criteria for the internal pilot

	Red	Amber	Green
Trial recruitment	<60%	60-80%	80-100%
Recruitment rate per site per month	0	0-1	1 or more
Number of sites opened	<3	3 or 4	5, 6 or 7
Total number of participants recruited*	<41	41-54	55-69

only the total number of participants recruited will be used as the progression criterion

10.4 Randomisation Procedure / Code Break

A web-based randomisation system will be designed, using the bespoke King's Clinical Trials Unit (KCTU) randomisation system. The randomisation system will be created in collaboration with the

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

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

The CI team will undertake appropriate reviews of the entered data, in consultation with the project analyst 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.

Randomisation will be at the level of the individual. Young people will be randomised to either the ICCS or the TAU pathway (1:1 ratio). Randomisation will be stratified by the NHS Trust and within Trust blocks with random block sizes will be used to ensure that the site distribution is similar in the two trial arms. Thus, within a Trust all participants randomized to the ICCS will be in contact with the same ICCS team. All research assistants (assessors) gathering outcomes will be kept blind to the treatment allocation of the patients they are gathering follow-up outcomes from. The senior statistician will be fully blind and the second statistician unblind. KCTU will issue authorisations for the trial manager to randomise participants via the online system and which will record all randomisations in an associated KCTU database.

10.5 Withdrawal of Subjects

ICCS will be discontinued if:

- the participant decides they no longer wish to continue
- the trial is terminated at the request of the DMC.

Participants have the right to withdraw from the study at any time, without providing any reason. Should a participant decide to withdraw from the study, he/she will be asked to volunteer a reason for withdrawal but are not at liberty not to state a reason.

Should a patient decide to withdraw from the study, all efforts will be made to report the reason for withdrawal (e.g. adverse events, inability to adhere, inability to attend regularly for treatment or assessment) as thoroughly as possible. This information will be passed onto the other relevant members of the team and the Trial Manager. Should a patient withdraw from study treatment only, efforts will be made to continue to obtain follow-up data, with the permission of the patient.

The research worker attached to the site attended by the patient wishing to withdraw will ascertain whether consent is withdrawn from further trial treatment only, or from both trial treatment and

follow-up. Thus, randomised participants who wish to withdraw from ICCS will be asked to confirm whether they are still willing to:

- provide study-specific data at 6-month follow-up
- participate in the qualitative study

The Research worker attached to that centre will ensure that every effort is made to obtain all outcomes from the participants who drop out of treatment as soon as this occurs. If only one clinical outcome can be collected, then the researchers should make efforts to obtain the CGAS scores. If three outcomes are possible to collect, then researchers should obtain the SDQ and the SHQ scores, if possible, in addition to the CGAS.

If a participant withdraws consent for research follow-up during the trial, we will ask the clinician/research assistant to contact the participant on the same day to find out why the participant wishes to withdraw from research follow-up if they are happy to give a reason.

The reason for a clinician's decision to withdraw a patient from the study must be recorded. When this occurs, the relevant clinician or nominee will need to assess the participant clinically, and arrange appropriate care. Every effort will be made to obtain the primary outcome data. If only one clinical outcome could be collected, then the researchers should make efforts to obtain the CGAS scores. If three outcomes are possible to collect, then researchers should obtain the SDQ and the SHQ scores, if possible, in addition to the CGAS.

Reasons for and dates of withdrawal from the study will be recorded on a withdrawal form, which will describe the circumstances of the withdrawal. We plan to minimise loss to follow-up in a number of ways. We plan to increase compliance with ICCS attendance by encouraging patients to discuss with treating clinicians any difficulties regarding attendance; we will assist patients' participation in the study by providing funds towards travel (for research related appointments) and will provide research appointment reminders. We will also adopt other evidence-based procedures for recruiting

and maintaining participation in the study and encouraging patients to return outcome measures, e.g. the use of incentives (vouchers at the baseline and 6-month follow-up), sending greetings cards, personalising letters, using colour printing and keeping measures short in terms of completion.

10.6 Expected Duration of Trial

6 months per participant 3 ½ years in total. The study will officially end at the last follow-up visit of the last participant.

11. Trial Procedures

11.1 By Visit

Initial assessments/pre-randomisation visit

Eligible young people will be referred for either ICCS or TAU by the relevant clinical crisis teams in each trust. Each member of the crisis teams will be able to explain the study to the eligible participants and their family members and obtain consent. Participants and their family members will be informed that a researcher will contact them prior to randomisation to initiate baseline assessments. In addition to the basic sociodemographic data, the following outcomes will be completed:

The CGAS (Children's Global Assessment Scale)

The CGI (Clinical Global Impression)

The HoNOSCA (Health of the Nation Outcome Scales for Children and Adolescents)

The SDQ (Strengths and difficulties questionnaire, children's and parents' versions)

The CHU-9D (The Child Health Utility 9 dimentions)

Self-Harm Questionnaire

*Child and Adolescent Service Use Schedule (CA-SUS)

*Clinical diagnosis: K-SADS-PL

**could be completed within 2 weeks of the randomisation*

Assessments 6 months post randomisation

We will obtain education/training/employment data from the relevant educational establishments or employers. Research assistants or administrators unaware of the participants' allocation will contact the relevant clinical teams to establish the first day of returning to/time to gaining education, employment or training. We will also contact the relevant educational establishments or employers to obtain the attendance record over the 6-month period.

We will administer all of the above outcome measures except for the K-SADS-PL.

Qualitative interviews will be undertaken by the qualitative researchers, exploring the participants' and clinicians' experiences of ICCS and TAU.

(See Appendix 2 for list of the study measures completed at each stage)

12. Assessment of Efficacy

12.1 Primary Efficacy Parameters

Return to/gaining school/employment/training, from the day of randomisation to the first day of attending either an educational institution, employment or training.

12.2 Secondary Efficacy Parameters (assessed at 6-month follow-up)

1.The Strengths and Difficulties Questionnaire 2. The Children's Global Assessment Scale 3. The Clinical Global Impressions Improvement Scale 4. Service Satisfaction Survey 5. The Health of the Nation Outcome Scales for Children and Adolescents 6. CHU-9D , 7. Self-Harm Questionnaire. 8.

Time spent in hospital (in days). 9 The CA-SUS. 10. The number of days attending education, training or employment in the 6 months following the day of randomisation

For all measures we will contact the families by mail and include self-addressed envelopes with self-reported outcome measures (or conduct a telephone or remote interview) for those families that do not wish to undertake face-to-face assessments.

12.3 Procedures for Assessing Efficacy Parameters

Time (in days) from the point of randomisation to returning/time to gaining education, employment or training (EET) as described above

13. Assessment of Safety

13.1 Specification, Timing and Recording of Safety Parameters.

Safety will be monitored throughout by the clinical teams

13.2 Procedures for Recording and Reporting Adverse Events

The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amended Regulations 2006 gives the following definitions:

- **Adverse Event (AE)**: Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.
- **Adverse Reaction (AR):** Any untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant.
    - **Unexpected Adverse Reaction (UAR)**: An adverse reaction the nature and severity of which is not consistent with the information about the medicinal product in question set out in the summary of product characteristics (SmPC) for that product (for products with a marketing authorisation)
- **Serious adverse Event (SAE), Serious Adverse Reaction (SAR) or Suspected Unexpected Serious Adverse Reaction (SUSAR):** Any adverse event, adverse reaction or unexpected adverse reaction, respectively, that**:**
    - results in death;

- is life-threatening;
- required hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability or incapacity;
- consists of a congenital anomaly or birth defect.

- **Important Medical Events (IME) & Pregnancy:** Events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the participant or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious. Although not a serious adverse event, any unplanned pregnancy will also be reported via the SAE reporting system.

EVALUATING AES AND SAES.

- **Assessment of Intensity**
  The Investigator will make an assessment of intensity for each AE and SAE reported during the study. The assessment will be based on the Investigator's clinical judgement. The intensity of each AE and SAE recorded in the CRF should be assigned to one of the following categories:
  - **Mild** An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities.
  - **Moderate** An event that is sufficiently discomforting to interfere with normal everyday activities.
  - **Severe** An event, which is incapacitating and prevents normal everyday activities.

An AE that is assessed as severe should not be confused with an SAE. Severity is a category utilised for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

- **Assessment of Causality**

The Investigator is obligated to assess the relationship between investigational product and the occurrence of each AE/SAE. The Investigator will use clinical judgment to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product will be considered and investigated.

The causal relationship to the study product assessed by the Investigator (or medically qualified delegate) should be assessed using the following classifications:

- **Not Related** In the Investigator's opinion, there is not a causal relationship between the study product and the AE.
- **Remote**The temporal association between the AE and study product is such that the study product is not likely to have any reasonable association with the AE.

- **Possible** The AE could have been caused by the study Subject's clinical state or the study product.
- **Probable** The AE follows a reasonable temporal sequence from the time of study product administration, abates upon discontinuation of the study product and cannot be reasonably explained by the known characteristics of the study Subject's clinical state.
- **Definitely** The AE follows a reasonable temporal sequence from the time of study product administration or reappears when study product is reintroduced.

There may be situations when an SAE has occurred, and the Investigator has minimal information to include in the initial report to the Sponsor. However, it is very important that the Investigator always assesses causality for every event prior to transmission of the SAE form to the Sponsor. The Investigator may change his/her opinion of causality considering follow-up information, amending the SAE form accordingly. The causality assessment is one of the criteria used when determining regulatory reporting requirements.

- **Assessment of Expectedness**
  A reasonable possibility of a relationship conveys that there are facts, evidence and/or arguments to suggest a causal relationship, rather than a relationship that cannot be ruled out.
  - **Expected** An adverse reaction, the nature or severity of which is consistent with the applicable product information for an unapproved medicinal product).
  - **Unexpected** An adverse reaction, the nature or severity of which is not consistent with information in the relevant source document

FOLLOW-UP OF AES AND SAES

- After the initial AE/SAE report, the Investigator is required to proactively follow each Subject and provide further information to the Sponsor on the Subject's condition.
- All AEs and SAEs documented at a previous visit/contact and are designated as ongoing, will be reviewed at subsequent visits/contacts. All AEs and SAEs will be followed until resolution, until the condition stabilises, until the event is otherwise explained, or until the Subject is lost to follow-up. Once resolved, the appropriate AE/SAE CRF page(s) will be updated. The Investigator will ensure that follow-up includes any supplemental investigations as may be indicated to elucidate the nature and/or causality of the AE or SAE. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals. New or updated information will be recorded on the originally completed SAE form, with all changes signed and dated by the Investigator. The updated SAE form should be presented to the Sponsor.

PREGNANCY

- Any pregnancy that occurs during study participation must be reported using a serious adverse event form. To ensure subject safety, each pregnancy must be reported to the Sponsor within 24 hours of learning of its occurrence. The pregnancy must be followed up to determine outcome (including premature termination) and status of mother and child, which must also be reported to the Sponsor. Pregnancy complications and elective terminations for medical reasons must be reported as an AE or SAE. Spontaneous abortions must be reported as an SAE.

Reporting Responsibilities

All SARs and SUSARs (excepting those specified in this protocol as not requiring reporting) will be reported immediately by the Chief Investigator to the REC and Sponsor (in this case via the SLaM/IoPPN Joint R&D Office). Local PIs will report to the CI.

The Chief Investigator will report relevant SAE's to the ethics committee. Reporting timelines are as follows:

- SUSARs which are fatal or life-threatening must be reported not later than 7 days after the sponsor is first aware of the reaction. Any additional relevant information must be reported within a further 8 days;
- SUSARs that are not fatal or life-threatening must be reported within 15 days of the sponsor first becoming aware of the reaction.

Adverse events that do not require reporting

AEs will be defined as any unfavourable and unintended, symptom, or disease temporally associated with the interventions studied, whether or not related to the interventions. The reporting period for all events and reactions will be from randomisation to 6-month follow-up.

We will define non-serious adverse events as any health event, which was not categorised as an SAE or SAR. Discrepancies will be resolved by consensus between the clinicians.

Examples of expected non-serious adverse events that do not need reporting include:

- Development of new mood disorder (not leading to significant or persistent disability)
- Development of new sleep disturbance
- Worsening of anxiety
- Changes in appetite

Non-serious adverse events will be reported to the DMC via the trial manager/CI/trial statistician and will be included in the safety reporting of the completed trial.

13.3 Stopping Rules

The trial may be prematurely discontinued by the Sponsor or Chief Investigator on the basis of new safety information or for other reasons given by the Data Monitoring & Ethics Committee / Trial Steering Committee regulatory authority or ethics committee concerned.

The trial may also be prematurely discontinued due to lack of recruitment or upon advice from a Trial Steering Committee, who will advise on whether to continue or discontinue the study and make a recommendation to the sponsor. If the study is prematurely discontinued, including if the initial pilot is unsuccessful, active participants will be informed and no further participant data will be collected.

14. Statistics

14.1 Sample Size

Results from our previous study comparing an Intensive Community Care Service (ICCS) called Supported Discharge Service with TAU in inpatient adolescents with psychiatric emergencies showed a difference in the proportion of the young people NEET of around 30% in favour of intensive community care (from 49% at 6 months in the TAU arm). We would expect the relative benefit of offering intensive community care without initial inpatient care to be larger than the

benefit observed in our previous study since the young people might have a lower risk of inpatient admission and might preserve their community links, including the links with school better. However, given the uncertainly of this estimate (95% CI from 13.1% to 47.3%) the reduction in population NEET proportions could be lower. We consider a reduction of 20% or larger to be clinically significant in line with the Adult IAPT targets of achieving 50% recovery versus baseline 30% recovery, and hence chose our minimum clinically significant (proportion) difference (MCID) to be 20%. We have now updated our primary outcome measure as described below. To detect this change in the proportion of young people NEET (TAU: 49%, ICCS: 29%) with 90% power using a two-tailed log-rank test with significance level 5% to analyse the primary outcome "time to return to EET" requires a total sample size of 240 young people. Based on the findings of our recent RCT of Supported discharge versus TAU (4) we anticipate that the primary time-to event outcome (time to EET or 6-month follow-up) will be available for 95%+ of the participants as this data will be sourced from schools or employers and the data availability will not dependent on conducting face-to-face interviews. Adjusting for 5% loss to follow-up increases our requirement to N=252 (126 per trial arm).

14.2 Randomisation

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 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. System access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the randomisation system are not shared, and that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-

specific username and password must be requested via the CI or 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 Trial Manager in the first instance.

Participant initials and date of birth will be entered on the randomisation system, NHS number, email addressed, participant names and 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 by recruiting site staff or by the co-ordinating study team, by authorised staff onto the randomisation system by going to www.ctu.co.uk and clicking the link to access the randomisation system. A full audit trial of data entry will be automatically date and time stamped, alongside information about the user making the entry within the system.

The CI team will undertake appropriate reviews of the entered data, (in consultation with the project analyst) 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.

Randomisation will be at the level of the individual. Young people will be randomised to either the ICCS or the TAU pathway (1:1 ratio). Randomisation will be stratified by the NHS Trust and within Trusts blocks with random block sizes will be used to ensure that the site distribution is similar in the two trial arms. Thus, within a site all participants randomized to the ICCS will be in contact with the same ICCS team. All research assistants (assessors) gathering outcomes will be kept blind to the treatment allocation. The senior statistician will be fully blind and the second

statistician unblind. KCTU will issue authorisations for the trial manager to randomise participants via the online system and which will record all randomisations in an associated KCTU database.

14.3 Analysis

Statistical analyses will follow-the intention-to-treat principle. A detailed statistical analysis plan will be written and agreed by the trial team and oversight committees before analyses commence. Relevant descriptive summaries will be used to describe the trial sample, characterise the pathway interventions received in two trial arms and to summarize outcomes. Cox proportional hazards model will be used to compare the primary time-to-event outcome (time to return to EET) between the two trial arms/pathways. The randomisation stratifier Trust will be included in the model by a set of site-specific dummy variables, i.e. site effects will be modelled by fixed effects. We will consider allowing the pathway effect to vary with site by including respective pathway x site (fixed) interaction terms. We will evaluate the effect of the experimental pathway by estimating its hazard ratio (ICCS vs. TAU pathway) within sites. The proportional hazards assumption will be checked. Continuous secondary outcomes at 6 months will be compared between trial arms using regression modelling. Again, the randomisation stratifier will be represented by a set of dummy variables in these models as will baseline values of the outcome variable to gain extra precision. Distributional assumptions will be checked and nonparametric approaches used where necessary. We do not expect many missing values in the primary outcome. In the case of substantial amounts of missingness in secondary outcomes, baseline predictors of missingness will be investigated empirically, and if identified a modelling approach that is valid under the respective missing at random assumption (conditioning, multiple imputation) will be used. We propose a set of secondary planned moderation analyses for putative moderators: age, the diagnosis of Borderline Personality

Disorder, the diagnosis of Psychosis, Autism Spectrum Disorder and a Black and Minority Ethnic status.

HEALTH ECONOMICS

The primary perspective of the economic evaluation will be the NHS/Personal Social Services perspective preferred by NICE but will additionally include education-based services, given the age of the participants. Resource-use data will be collected using an adapted version of the Child and Adolescent Service Use Schedule (CA-SUS), designed for and successfully implemented in evaluations of services for young people with mental health problems. At baseline, this will include key health and social care resources (hospital and community based services). Only key resources were included so as to keep the CA-SUS brief. This was because it was hypothesized that it would be very difficult to complete all the measures at baseline as participants are in crisis. Additionally, we allowed a 2 week window for completion for the same reason. At follow-up, this will include all cause health and social care resources but will exclude psychiatric inpatient, psychiatric daypatient and CAMHS services, which will be collected directly from medical records using a proforma (to maximise accuracy and minimise unblinding research assessors to group allocation). Services will be costed using the most up-to-date nationally applicable unit costs (13). Our primary economic analysis will be a cost-utility analysis at 6-month follow-up using Quality Adjusted Life Years (QALYs) derived from the CHU9D , found to be valid and responsive in adolescent populations with mental health problems (14). For QALY calculations, appropriate utility weights will be attached to health states (15) and QALYs will be calculated using the total area under the curve approach with linear interpolation between assessment points (16). We will conduct a secondary cost-effectiveness analysis using the primary clinical measure (time to EET).

Costs and outcomes will be compared and presented as mean values by trial arm with standard deviations. Mean differences in costs and 95% confidence intervals will be obtained by non-parametric bootstrap regressions to account for the non-normal distribution commonly found in

economic data (21). Cost-effectiveness will be assessed using the net benefit approach and following standard approaches (25). A joint distribution of incremental mean costs and effects for the two groups will be generated using bootstrapping to explore the probability that ICCS is the optimal choice compared to TAU, subject to a range of possible maximum values (ceiling ratio) that a decision-maker might be willing to pay for unit improvements in outcomes. Cost-effectiveness acceptability curves will be presented by plotting these probabilities for a range of possible values of the ceiling ratio (26) . These curves are a recommended decision-making approach to dealing with the uncertainty that exists around the estimates of expected costs and expected effects associated with the interventions under investigation and uncertainty regarding the maximum cost-effectiveness ratio that a decision-maker would consider acceptable. To provide more relevant treatment-effect estimates, all economic analyses will include adjustment for the variable(s) of interest and baseline covariates (27) , which will be pre-specified and in line with the clinical analyses.

NESTED QUALITATIVE STUDY

21 young people in the experimental group and 21 young people in the control group will be selected, following consultation with responsible clinicians, for an in-depth qualitative interview at 6-month follow-up. We will follow our standard strategy (17). Young people will participate in a semi-structured visual interview study to examine their experiences of admission, ward-life and treatment. In advance of the qualitative interview, participants will be asked to take suitable photographs pertinent to their experience which they can bring for discussion. Participants will not be permitted to take photographs that contain other people. If this occurs, the photographs will be deleted. Guidance on this will be provided in addition to the Information Sheet. Interviews will take place one-on-one and will be conducted by researchers at LSBU trained in qualitative methods. Interviews will be recorded using dictaphones, and the recordings will be saved on an encrypted file in a locked room in LSBU. Transcribes of the interviews will be made, and a thematic

decomposition analysis will be conducted on the data. Specific themes relevant to satisfaction and engagement with services will be examined in-depth. We will aim to understand their experiences of any organisational problems and barriers and facilitators of treatments. In addition to our current plan to interview 42 young people, we have now extended our qualitative study to include 42 healthcare workers delivering both intensive community care and inpatient care to understand in-depth their experience of delivering the services. We will also specifically investigate which outcomes have the greatest importance for young people as part of the existing process evaluation.

15. Trial Steering Committee

We will follow HTA guidelines on appointments to the TSC and its functions. The trial steering committee will meet twice yearly. In addition, the trial management group (Chair – Professor Dennis Ougrin) will meet monthly to six-weekly in the first year and every 2-3 months thereafter.

16. Data Monitoring Committee

We will follow HTA guidelines on appointments to the DMC and its functions. Members will be approved by the HTA.

The DMC will meet twice in the first and second years of the project. It will function according to standard operating procedures stipulated by the HTA. We will appoint a chair and a statistician who meet the HTA's requirements of independence. Following a stipulation by the HTA, in addition to focusing on randomised participants, we will ask the DMC to take on the role of monitoring initial patient recruitment numbers (i.e. numbers recruited at the sites). This pseudo-anonymised data will be made available to the trial statistician who will report it to the DMC on a monthly basis between meetings. Our CTU has standard operating procedures that guide the trial statistician's reporting to the DMC. The DMC will be asked to advise on which sites are giving rise to recruitment difficulties at particular stages of the study and whether particular efforts appear to be required at such sites.

They will also be asked to confirm whether certain sites appear to be more efficient than expected at recruiting participants and whether resources might be reduced in some sites to concentrate on the more effective sites.

17. Direct Access to Source Data and Documents

The Investigator(s) will permit trial-related monitoring, audits and REC review by providing the Sponsor(s), and REC direct access to source data and other documents

18. Ethics & Regulatory Approvals

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research.

This protocol and related documents have been approved by West Midlands and Black Country Research Ethics Committee 20/WM/0069.

The Chief Investigator will submit a final report at conclusion of the trial to the funder, the REC and the Sponsor.

19. Quality Assurance

Monitoring of this trial will be to ensure compliance with Good Clinical Practice and scientific integrity will be managed by the study team in collaboration with DMC, TSC and young people's advisory group.

We will institute a rigorous programme of quality control. The TM will be based at the Institute of Psychiatry, Psychology and Neuroscience, King's College London The TM will supervise a

designated RW employed on the study to undertake data management/cleaning, so that they can provide regular reports on data quality to the CI and the other co-applicants. Quality assurance checks will be undertaken to ensure the integrity of randomisation, to monitor the level of missing data and the timeliness of data entry and check for illogical or inconsistent data. The TM will monitor data collection procedures, ensure that study data entry procedures are followed and undertake source data verification against the paper data collection forms. The trial statistician will be based in the CTU and will be responsible for DMC reports, contribute to the Statistical Analysis Plan and carry out primary analyses.

We will ask the DMC to take on this role of monitoring patients at recruitment. Our CTU has Standard operating procedures that guide the trial statistician's reporting to the DMC.

20. Data Handling

The Chief Investigator will act as custodian for the trial data. The following guidelines will be strictly adhered to. Thus: Patient data will be pseudo-anonymised. All pseudo-anonymised data will be stored on a password-protected computer. All trial data will be stored in line with the Data Protection Act and archived in line with Sponsor requirements.

Each research team will be responsible for transferring non-identifiable data captured on paper Case Report Forms (CRF) into a password protected electronic database (MACRO database) within one month. Prior to CRF data transfer into the electronic database, completed CRFs must be photocopied to minimise data loss.

The data collected from each of the research sites will be stored where the research team is based (either NHS Trust or associated university). All the information collected about participants during the course of the research will be kept strictly confidential and any information that is

stored will have their name and address removed so that participants cannot be recognised. All identifiable data (such as consent forms, email addresses) will be kept in locked filing cabinets, separately from the other research data. Any direct quotation of the study participants will be anonymised. Only researchers directly involved in the study will have access to the passwords or keys.. PIs will be responsible for safe storage of the data.

Access to patient data will be restricted to named individuals, members of the research team conducting the study.

Research staff with access to patient data:

- Trial manager and Research Workers

ICCS staff (to be identified at local sites)

21. 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 analysts and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

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

Participant initials and date of birth will be entered on the EDC. NHS numbers, email addresses, participant names, home 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 or centrally by the co-ordinating study team, typically within 7 days of data collection 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 trail of data entry and any subsequent changes to entered data will be automatically date and time stamped, alongside information about the user making the entry/changes within the system.

The CI team will undertake appropriate reviews of the entered data, in consultation with the project analyst for the purpose of data cleaning and will request amendments as required.

At the end of the trial, the site PI will review all the data for each participant to verify that all the data are complete and correct. At this point, all data can be formally locked for analysis.

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.

Training videos for data entry staff are available at www.ctu.co.uk under the 'Training' section. Users can self-register and should select the MACRO related training videos.

22. Publication Policy

Dissemination will be jointly done by the Trial Management Group and the service user members of the Trial Steering Committee. This RCT will provide new knowledge about the efficacy, cost-effectiveness and patients' experience of the care pathways studied. This has been identified as a priority area by the NIHR, service users and service commissioners. It is vital that young people, their families, professionals and commissioners can use these findings.

Outputs: one of the study reports will be targeted at young people with severe psychiatric disorders and their families, using service users' organisations such as YoungMinds. Other reports will be aimed at mental health professionals who work with young people with severe psychiatric disorders and commissioners, as well as at national government and health agencies. The reports will clearly outline what is needed to implement the research findings in routine NHS care. As well as publication in the scientific journals and conference presentations, we will ensure clinicians can access the findings and the information on the ICCS care model through a segmented marketing strategy, targeting professional bodies such as Royal Colleges and the NHS Confederation. Following a consultation with young people who are ICSS service users, the young people thought the most effective way to disseminate the results of the research is via creating relevant hashtags. The best way to create a highly popular hashtag is via engaging a celebrity followed by many people. The young people thought the two most highly accessed websites with mental health information were Childline and the YoungMinds and any results should be posted on these websites. The young people proposed disseminating the results of the research on the national self-injury awareness day (01/03) with school assemblies and school posters dedicated to self-harm treatment in collaboration with mental health charities such as YoungMinds. The researchers will follow these suggestions in collaboration with the young people.

Impact: the authors of this proposal will develop a campaign strategy identifying who needs to know about the research findings and what they need to do to improve available treatments for young people. The strategy will include campaign recommendations; key audiences and targets; routes to influence; communication channels; PR; and mechanisms and activities for achieving campaign aims. The campaign will have key performance indicators so that it can be fully evaluated. The authors will publish the treatment protocols for the ICCS care pathway. NICE will be informed about the findings and this may influence their guidance on the management of several psychiatric conditions where in-patient admissions are indicated. NHS England and the equivalent

bodies in Scotland and Wales will be informed about the findings and the findings may influence their policy and funding.

23. Insurance / Indemnity

King's College London provides cover under its No Fault Compensation Insurance, which provides for payment of damages or compensation in respect of any claim made by a research subject for bodily injury arising out of participation in a clinical trial or healthy volunteer study (with certain restrictions). The co-sponsor, South London and Maudsley NHS Foundation Trust, takes responsibility for ensuring that appropriate standards, conduct and reporting are adhered to regarding its facilities and staff involved with the project. Financial Aspects.

24. Financial aspect

Funding to conduct the trial is provided by the NIHR HTA Programme reference number NIHR127408

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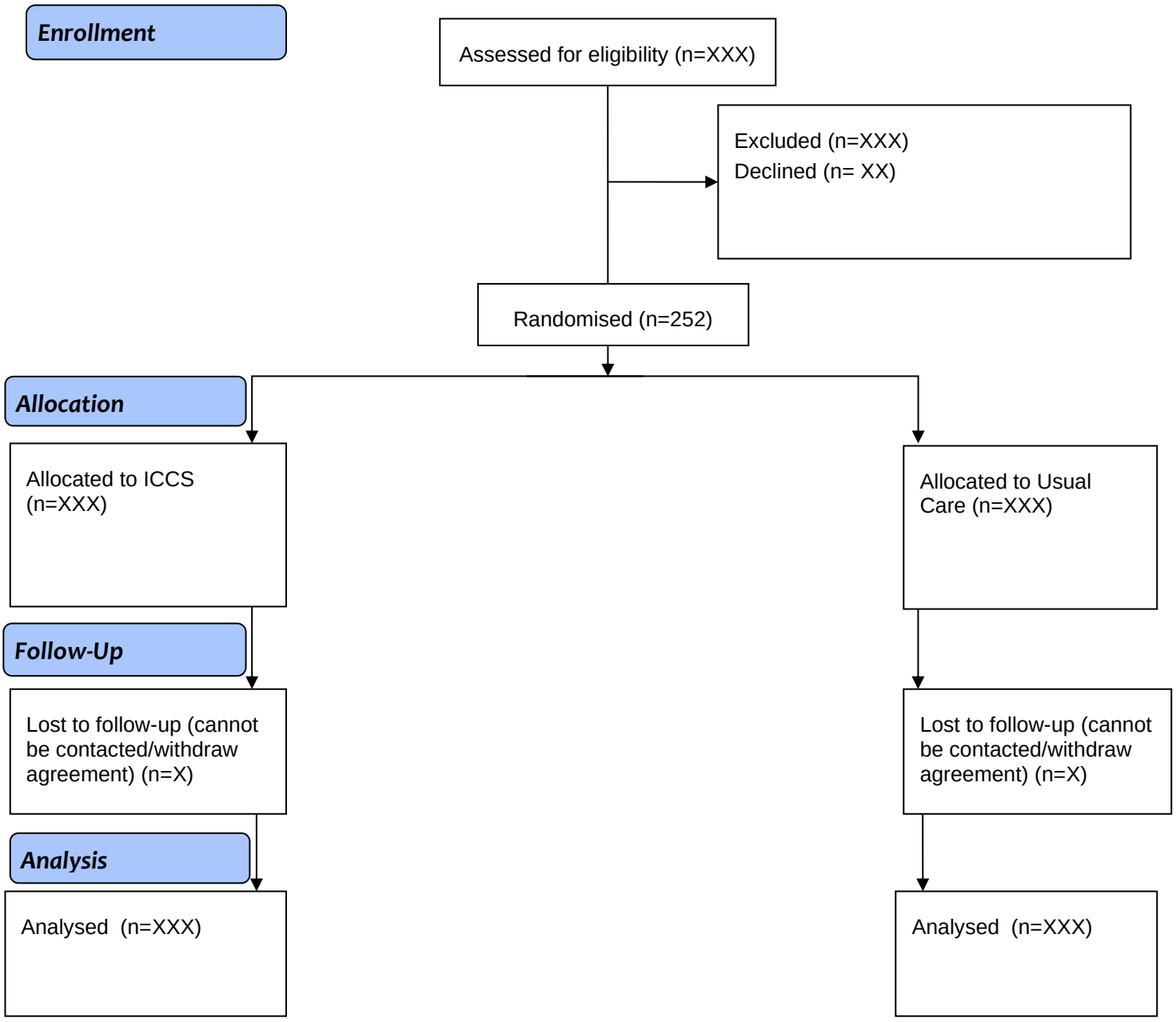
25. Appendixes

Appendix 1

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram IVY



Appendix 2: List of measures collected at each stage

#	Forms/Measures	Pre-randomisation	Within 2 weeks post-randomisation	6-month Follow-up	Type
1	**Patient / Parent Information and Informed Consent**	x			Consent forms
2	**Registration**	x			RA/Clinician
3	**Demographic Form**	x			Participant/EPR
4	**Children's Global Assessment Scale (CGAS)**	x		x	Clinician Rating scale
5	**Clinical Global Impressions Scale (CGI)**	x		X	Clinician Rating scale
6	**Clinical Global Impressions Improvement Scale (CGI-I)**			x	Clinician Rating scale
7	**Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA)**	x		x	Clinician Rating scale
8	**Self-Harm Questionnaire**	x		x	Self-reported questionnaire
9	**Strengths and Difficulties Questionnaire (SDQ)**	x		x	Self-reported questionnaire
10	**Child and Adolescent Service Use Schedule (CA-SUS)**	x	x	x	Questionnaire/proforma from EPR
11	**CHU-9D**	x		x	Self-reported questionnaire
12	**KSADS**	x	x	n/a	Semi-structured interview
13	**Service Satisfaction Survey (ChASE)**			x	Self-reported questionnaire
14	**Employment, Education, Training (EET) Log**			x	Information gathered by RA
15	**Time spent in hospital (in days)**			x	Electronic patient records/ data gathered by RA
16	**Qualitative Study (Healthcare workers and participants)**			x	Interviews by LSBU qualitative researchers
17	**Adverse events**	When required			n/a
18	**Withdrawal form**	When required			n/a