OPTYC: Online PTSD Treatment for Young People and Carers

CASE SERIES PROTOCOL

Version 2

20th February 2019

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Roles and responsibilities

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Trial steering committee

Role	Name	Responsibilities
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Declaration of interests

Smith, Clark, and Yule are co-authors of a book on which the interventions are based, and they receive royalties from sales of the book.

Smith, Dalgleish, and Meiser-Stedman occasionally deliver clinical workshops about the face to face intervention and may receive fees for doing so.

There are no other potential conflicts of interest.

Contents

Study Synopsis

Full Title	OPTYC: Online PTSD Treatment for Young People and Carers
Acronym	OPTYC
Protocol version number and Date	Version 2 20th February 2019
Study Duration	4 months (May 2019 to September 2019)
Study Design	Case series
Sponsor/Co-sponsors	Joint IoPPN / SLaM R&D Office
Chief Investigator	Patrick Smith
REC number	TBC
Primary objective	To develop and evaluate an Internet-delivered Cognitive Therapy (iCT) programme for the treatment of PTSD in adolescents.
Secondary objective (s)	To run an uncontrolled case series
Number of subjects	N = 6
Main inclusion criteria	Young people (12-17 years) whose main presenting problem is PTSD (diagnosed according to DSM-5 criteria) following a single-event trauma (e.g. serious accidents or assaults) will be included.

Main exclusion criteria	Young people with brain damage, learning difficulty, ongoing trauma-related threat, recently started treatment with medication, or receiving another psychological treatment, will be excluded.
Statistical methodology and analysis	We will report on Reliable Clinical Change on a standardised questionnaire measure of PTSD symptoms (CPSS-5, detailed below); and we will obtain qualitative feedback from young people, carers, and therapists about their experience of using the programme.

1. Introduction

The proposed study

The primary objective is to develop and evaluate an Internet-delivered Cognitive Therapy (iCT) programme for the treatment of PTSD in adolescents.

First, we will develop a secure, interactive, multi-media, iCT software program, designed specifically for adolescents, to be delivered on computers, tablets, and smart phones.

Second, we will evaluate this new iCT programme in a case series. In the case series, the new iCT programme will be used to treat N = 6 patients with PTSD. The objective of the case series is to gauge acceptability of the programme to young people, carers, and therapists; to measure adherence to the programme; to gauge acceptability of the battery of measures; and to measure clinical change on symptoms measures.

The population to be studied

Young people (12-17 years) whose main presenting problem is PTSD (diagnosed according to DSM-5 criteria) following a single-event trauma (e.g. serious accidents or assaults) will be included.

Summary of findings from previous studies

PTSD is prevalent among young people, and is distressing and impairing. Face-to-face trauma-focused CBT (TF-CBT) is an effective short-term therapy for PTSD in young people. Our group has developed Cognitive Therapy for PTSD (CT-PTSD) in children and young people, and shown in 2 published RCTs that it is efficacious. However, most young people with PTSD do not receive effective, evidence-based treatments. This is in part due to under-capacity in NHS CAMHS, and in part due to the burden and inconvenience to young people in attending face-to-face appointments in a clinic. In this project we propose to make CT for PTSD widely available to young people by delivering the therapy via the internet, with therapist support. The rationale for this approach is that (1) young people will engage with internet-delivered therapy, and online therapies for other disorders such as depression have demonstrated efficacy in clinical trials; (2) effective online therapies for adults with PTSD have been developed and evaluated; (3) no online treatments for young people with PTSD have yet been developed.

2. Study Objectives and Design

2.1. Study Objectives

2.1.1 Primary Objective

To develop and evaluate an Internet-delivered Cognitive Therapy (iCT) programme for the treatment of PTSD in adolescents.

Our initial evaluation of this new iCT-PTSD intervention will be made using a case series design.

2.1.2 Secondary Objectives

The objectives of the case series are:

1. to gauge acceptability of the programme to young people, carers, and therapists
2. to measure adherence to the programme
3. to gauge acceptability of the battery of measures
4. to obtain estimates of reliable clinical change on a standardised measure of PTSD symptoms (CPSS-5, see below)

2.2. Study Design

We will complete a development case series with N=6 young people. The inclusion and exclusion criteria are described below.

We will allow iterative development of the intervention and its delivery during the case series, if needed. We will achieve this by staggering the start of treatment as far as practical so that feedback from patients who start early can be used to amend modules for patients who start later.

2.3. Study Outcomes

2.3.1 Acceptability of iCT

To gauge acceptability of iCT-PTSD, we will carry out post-treatment qualitative interviews with N=6 young people, their carers, and their therapists. We will summarise interview data using content analysis. Young people will also be asked to complete ratings of acceptability at the end of treatment, using a 0–100 scale (to measure design appeal, ease of use, comprehension, likelihood of recommending to a friend with similar problems).

2.3.2 Adherence to iCT

To gauge adherence to iCT, we will report:

1. Number of times logged into the programme per week and in total;
2. Time spent logged in per week and in total and according to device used (phone, tablet, computer);
3. Number of modules completed in total and according to device used (phone, tablet, computer);
4. Number of therapist phone calls per week and in total;
5. Time spent on phone calls per week and in total;
6. Number of messages to / from therapist per week and in total.

2.3.3 Outcome measures

Clinical interview with young people and carers:

1. Clinician Administered PTSD Scale for Children and Adolescents CAPS-CA-5 (Pynoos et al 2015), administered by trained reliable interviewers.

Questionnaire measures of PTSD, anxiety, and depression completed by young people:

2. Child Post Traumatic Stress Scale (CPSS-5; Foa et al. 2001)
3. Children's Revised Impact of Event Scale (CRIES; Perrin et al 2005)
4. Revised Children's Anxiety and Depression Scale RCADS-C; Chorpita & Ebesutani 2014)
5. Child Post Traumatic Cognitions Inventory (CPTCI, McKinnon et al 2016)

Questionnaire measures of emotional and behaviour problems, and depression and anxiety completed by carers:

6. Revised Children's Anxiety and Depression Scale (RCADS-P Chorpita & Ebesutani 2014)
7. Strength & Difficulties Questionnaire (SDQ-P; Goodman, 2001)

We will also collect economic data on health utilities and resource uses using the

8. Child Health Utility Index (CHU-9D, Stevens, 2012)
9. Child & Adolescent Service Use Schedule (CA-SUS, Shearer, 2018)

2.3.4 Acceptability of questionnaire battery

Acceptability of the questionnaire battery will be assessed by asking young people to complete an end-of-treatment rating using a 0–100 scale (rating the extent to which they agree with the statement, “I think other people of my age would be willing to fill in the questionnaire pack before and after treatment”), and including a space for free text feedback.

2.3.5 Clinical change

We will report appropriate descriptive statistics for all outcomes at each time point (e.g. mean and standard deviations for continuous outcomes where possible; counts and percentages for categorical outcomes). Initial signal of clinical effect will be indexed using Reliable Change on the CPSS (see below) i.e. a change of >= 14 points on this scale. The purpose of re-administering the questionnaire pack at 10 month follow up is to determine whether any treatment gains are maintained for these 6 young people.

2.4. **Study Timeline for the case series**

MEASURE	STUDY PERIOD (w = week; m = month)					
	Screen 0-1w	Pre 0w	Weekly	Mid 0+6w	Post 0+4m	Post 0+10m
ENROLMENT						
Eligibility screen	x					
Provide study information	x					
Gain informed consent		x				
ONLINE ASSESSMENT						
DAWBA		x				
INTERVIEW						
DEMOGRAPHIC INTERVIEW		x				
CAPS-CA-5		x			x	
		x				
CGAS		x			X	
ADOLESCENT QUESTIONNAIRES						
CPSS-5		x			X	X
CRIES-8		x	x	x	x	X
RCADS-C		x			x	X
CPTCI		x		x	x	X
CHU-9		x			x	X
Adverse events				x	x	X
CARER QUESTIONNAIRES						
SDQ-P		x			x	X
RCADS-P		x			x	X
CA-SUS		x			x	X
Adverse events				x	x	X
QUALITATIVE INTERVIEWS						
Adolescents					x	
Carers					x	
Therapists					x	

DAWBA Development and Well-Being Assessment (online assessment)
CAPS-CA-5, diagnostic interview for PTSD
CGAS, clinician rated global measure of functioning
CPSS-5, severity of PTSD symptom (27 items)
CRIES-8, severity of PTSD (8 items)
RCADS-C, severity of anxiety and depression (47 items)
CPTCI, appraisals potential mediator (10 items)
CHU-9, health state preferences (quality of life) (9 items)
SDQ-P, emotional and behavioural problems (33 items)
RCADS-P, severity of anxiety and depression (47 items)
CA-SUS, service use and costs (50 items)

3. Participants

Participants will be recruited from CAMHS services in the South London and Maudsley NHS Foundation Trust.

3.1.1 Inclusion criteria assessed at baseline interview

1. Participant is aged 12-17 years old

2. Main presenting problem is PTSD and there is a not a co-morbid problem that would preclude treatment of PTSD.

   Potential PTSD will be diagnosed using CAPS-CA-5. The assessment of potential co-morbid disorders that would preclude treatment of PTSD will be informed by the online DAWBA questionnaire (completed online prior to baseline interview) and based on clinical judgement at the face-to- face clinical interview. The overall assessment of comorbidity will therefore be based on clinical judgement. A standard operating procedure (SOP) will be prepared detailing how this clinical assessment should be made, to improve reliability across clinicians.

3. PTSD symptoms related to a single trauma

4. Participant has access to compatible smartphone and larger computing device (e.g. laptop, desktop computer, iPad) with internet access.
5. Participant is proficient in speaking and writing in the English language, sufficient to participate in treatment without an interpreter.

3.1.2 Exclusion criteria assessed at baseline interview

1. Brain damage assessed by clinical interview with parents / carers

2. Intellectual disability assessed by clinical interview with parents / carers

3. Pervasive developmental disorder or neurodevelopmental disorder assessed by clinical interview with parents / carers

4. Other psychiatric diagnosis that requires treatment before PTSD, determined by clinical interview and questionnaires

5. Moderate to high risk to self assessed in clinical interview
6. Ongoing trauma-related threat assessed in clinical interview
7. Started treatment with psychotropic medication, or changed medication, within the last 2 months, assessed in clinical interview
8. Currently receiving another psychological treatment, assessed in interview
9. . Have already received Trauma Focused CBT in relation to the same traumatic event that they are currently seeking treatment for.

4. Analysis

4.1. Acceptability

We will carry out qualitative interviews at the end of iCT (approximately 13 weeks after the baseline interview). If participants drop out of treatment early, we will endeavour to interview them as well as interviewing participants who complete a full course of treatment. The views and experiences of patients, parents/caregivers, and clinicians will be sought in order to gain a multi-perspective view of acceptability. Both commonalities and variations within and between these respondents will be explored. We will summarise interview data using content analysis.

We will report appropriate descriptive statistics for the acceptability ratings of the intervention and the questionnaire pack, completed by young people at the end of treatment (e.g. means and standard deviations for continuous outcomes; counts and percentages for categorical outcomes).

We will report completion rates for all measures (number and percentage of measures completed, out of total number of measures; and percentage of items completed for each measure).

4.2. Adherence

We will report descriptive summary statistics for the adherence metrics listed above in 2.3.2.

4.3. Clinical change

We will report descriptive statistics for all measures at each time point. We will categorise participants based on Reliable Change in Child Post-Traumatic Stress Scale (CPSS-5). We will report the number and proportion of participants who achieve:

(i) Significant improvement of PTSD symptoms at post-treatment, defined as a reduction of >= 14 points on this scale; and

(ii) No significant worsening of PTSD symptom scores at post-treatment, defined as an increase of >= 14 points on this scale.

5. Study procedures

5.1. Intervention

All participants will undergo internet Cognitive Therapy for PTSD (iCT-PTSD) treatment. iCT-PTSD comprises therapist-supported online delivery of all components from our face-to-face CT manual.

A course of iCT will deliver the same treatment components as face-to-face CT. These include: psycho-education about PTSD and its treatment, behavioural activation, developing a narrative of the trauma, re-appraisal of trauma-related cognitions, updating the trauma memory, dealing with reminders, developing a relapse-prevention blueprint, and working with parents.

All patients will meet their therapist face-to-face at the baseline assessment. Patients will be supported throughout treatment with regular (at least weekly) phone contact with their therapist and frequent messaging with their therapist.

We will make full use of online multi-media to maximise delivery of treatment, including use of appealing graphics and animation, videos of young people. Our design and development of the inline intervention includes frequent input from and testing with young people and patients.

5.2. Schedule of treatment for each visit

Following a face to face baseline assessment, participants will receive iCT over 12 weeks, supported by a weekly 15-minute phone call from their therapist. At the end of the 12-week treatment period, they will be invited for a post-treatment assessment face to face, and invited to take part in a qualitative interview to gauge acceptability of iCT.

5.3. Informed Consent Procedures

All recruitment documents, Participant Information Sheets and consent forms will be reviewed by the project Young Advisor Group and modified accordingly.

Participants will be initially approached about the project by a member of their clinical care team. If they appear to be eligible, they will be given Patient Information Sheets to read, and their consent obtained to pass their details to the project team.

The project team will follow up with a phone call to the young person and carer after at least 48 hours. The study will be explained in detail, and any questions the young person or carer has about the study will be answered by a member of the research team. The Investigator will explain to the potential participant that they are free to refuse any involvement within the study or alternatively withdraw their consent at any point during the study and for any reason.

The researcher will screen for eligibility against inclusion criteria 1 (aged between 12 – 17), 3 (experience of a traumatic event), and 4 (access to a smart-phone and computer); and exclusion criteria 7 and 8 (currently receiving treatment).

If the young person meets these initial inclusion criteria, consent will be sought. If they choose to take part, the young person and carer will be asked to formally record their consent using a secure online system.

After consenting, an appointment will be arranged for a detailed face to face interview, and they will be invited to complete an online assessment (DAWBA) of anxiety and depression. At the face to face meeting, participants will be asked to confirm their consent in writing by signing the consent form. If the detailed face to face clinical assessment confirms that they are eligible for the study, then they will be offered iCT to start the following week.

During treatment, if there is any further safety information which may result in significant changes in the risk/benefit analysis, the Patient Information Sheet will be reviewed and updated accordingly. All participants who are actively enrolled on the study will be informed of the updated information and given a revised copy of the PIS to confirm their wish to continue on the study.

5.4. Risks/burdens

Participants who take part in the case series may experience some upset while updating their trauma memory during therapy. Our experience is that such distress is temporary and support will be provided as necessary as part of therapy.

6. Data handling

6.1. Confidentiality

Information about study participants will be kept confidential and managed in accordance with the Data Protection Act, GDPR policies, NHS Caldicott Guardian, The Research Governance Framework for Health and Social Care, and Research Ethics Committee Approval.

- Personally-identifiable information will be collected from participants including name and contact details. This information will be stored securely and separately from all other study-generated data, which will be pseudo-anonymised (i.e. participants will be assigned a study ID).

- The treating clinician and research team involved in day to day trial management will have access to personally identifiable data. This is so that they can maintain contact with participants throughout the study.

- The Chief Investigator is the 'Custodian' of the data.
- Participant identifiable details will not be transferred outside the EU.
- Participants retain the right to revoke their authorisation for the use of their identifiable information.
- Participants will be anonymised with regards to any future publications relating to this study.

6.2. Data collection

- Baseline and interviews will be conducted by unblind members of the study team.
- Post-treatment interviews will be conducted by blinded outcome assessors.
- All clinical assessors will be trained to a standard on the CAPS-CA-5.

6.3. Case Report Forms

- All interviewers will record participant responses on a paper case report form (CRF).
- The interviewer will then re-enter this information into the electronic database, described below.
- Please see Table below for parameters captured by the Case Report Forms, including when data is gathered (study time point), how (interview or questionnaire) and by whom (research team, treating clinician, or blind assessor).

Time Point	**CRF#**	**Parameter**	**Questionnaire or Interview**	**Responsible Person**	**Method of delivery**
Enrolment					
	1	Registration	N/A	Study RA	F2F/phone
	2	Eligibility/exclusion screen	N/A	Study RA	F2F/phone
	3	Demographics-C	N/A	Study RA	F2F/phone
	4	Demographics-P	N/A	Study RA	F2F/phone
	5	Consent Form	N/A	Study RA	F2F
	6	Delays Form	N/A	Study RA	N/A
Baseline					
	7	PTSD diagnosis	CAPS-CA-5	Clinician	F2F
	8	Global Functioning	CGAS	Clinician	F2F
	9	PTSD symptoms	CPSS-5	Clinician/ Study RA	F2F

	10	PTSD symptoms	CRIES-8	Clinician/ Study RA	F2F
	11	Anxiety and Depression symptoms	RCADS-C	Clinician/ Study RA	F2F
	12	PTSD symptoms	CPTCI-s	Clinician/ Study RA	F2F
	13	Quality of Life	CHU-9D	Clinician/ Study RA	F2F
	14	Behavioural and Emotional difficulties (parent-rated)	SDQ-P	Clinician/ Study RA	F2F
	15	Anxiety and Depression symptoms (parent-rated)	RCADS-P	Clinician/ Study RA	F2F
	16	Use of services	CA-SUS	Clinician/ Study RA	F2F
Weeks 1-12					
		PTSD symptoms	CRIES-8	Clinician	Online/F2F
		Mood rating (0-10)	N/A	Clinician	Online/F2F
Mid (0+6 weeks)					
	17	PTSD symptoms	CRIES-8	Clinician	Online/F2F
	18	PTSD appraisals	CPTCI-s	Clinician	Online/F2F
	19	Adverse Events-C	N/A	Clinician	F2F/Phone
	20	Adverse Events-P	N/A	Clinician	F2F/Phone
Post (0+16 weeks)					
	21	PTSD diagnosis	CAPS-CA-5	Clinician	F2F
	22	Global Functioning	CGAS	Clinician	F2F
	23	PTSD symptoms	CPSS-5	Clinician/ Study RA	F2F
	24	PTSD symptoms	CRIES-8	Clinician/ Study RA	F2F
	25	Anxiety and Depression symptoms	RCADS-C	Clinician/ Study RA	F2F
	26	PTSD symptoms	CPTCI-s	Clinician/ Study RA	F2F
	27	Quality of Life	CHU-9	Clinician/ Study RA	F2F
	28	Adverse Events-C	N/A	Clinician/	F2F

				Study RA	
	29	Behavioural and Emotional difficulties (parent-rated)	SDQ-P	Clinician/ Study RA	F2F
	30	Anxiety and Depression symptoms (parent-rated)	RCADS-P	Clinician/ Study RA	F2F
	31	Use of services	CA-SUS	Clinician/ Study RA	F2F
	32	Adverse Events-P	N/A	Clinician/ Study RA	F2F
	33	Experience of the intervention and trial (YP-rated)	Qualitative-C	Study RA	F2F
	34	Experience of the intervention and trial (parent-rated)	Qualitative-P	Study RA	F2F
	35	Experience of the intervention and trial (therapist-rated)	Qualitative-therapist	Study RA	F2F
Follow up (0+10m)					
	36	PTSD symptoms	CPSS-5	Clinician/ Study RA	Online/post/phone
	37	PTSD symptoms	CRIES-8	Clinician/ Study RA	Online/post/phone
	38	Anxiety and Depression symptoms	RCADS-C	Clinician/ Study RA	Online/post/phone
	39	PTSD symptoms	CPTCI-s	Clinician/ Study RA	Online/post/phone
	40	Quality of Life	CHU-9	Clinician/ Study RA	Online/post/phone
	41	Adverse Events-C	N/A	Clinician/ Study RA	Online/post/phone
	42	Behavioural and Emotional difficulties (parent-rated)	SDQ-P	Clinician/ Study RA	Online/post/phone
	43	Anxiety and Depression symptoms (parent-rated)	RCADS-P	Clinician/ Study RA	Online/post/phone
	44	Use of services	CA-SUS	Clinician/ Study RA	Online/post/phone
	45	Adverse Events-P	N/A	Clinician/ Study RA	Online/post/phone
	46	SAE-child	N/A	Clinician/ Study RA	Online/post/phone

	47	SAE-parent	N/A	Clinician/ Study RA	Online/post/phone
	48	Withdrawal from study	N/A	Clinician/ Study RA	Online/post/phone

*Study RA if follow up questionnaire data collected online or by post; Blind assessor if follow up questionnaire data collected by phone or in person

6.4. Data storage

All outcomes will be stored in SPSS databases. These databases will be stored on a secure KCL network drive, accessible to the study team only. The study team will provide data extracts to the trial statisticians, upon request.

Data validation will be carried out at the time of data entry (in SPSS) to ensure that entered values are valid (e.g. for dates, within an allowed period; for continuous variables, within an allowed range; for categorical, within a list of allowed responses). These validity criteria will be specified in a database specification document, stored in the trial master file.

Databases will be stored in a version control system, such that changes made over time can be examined and recovered.

All databases will be registered in the King's Data Protection Register (KDPR).

6.5. Record Retention and Archiving

During the course of the study, all records are the responsibility of the Chief Investigator and will be kept in secure conditions in accordance with the King's College London data security policy. The primary data-sets and secondary data analyses will be retained for a minimum of ten years.

6.6. Compliance

The PI will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework, Trust and Research Office policies and procedures and any subsequent amendments.

7. Assessment of Safety

Procedures for Recording and Reporting Adverse Events

7.1.1 Definitions

Adverse Event (AE)	Any untoward occurrence in a trial participant, including events that are not necessarily caused by or related to trial procedures.
Adverse Reaction (AR)	Any untoward and unintended response in a trial participant which is related to trial procedures.
Unexpected Adverse Reaction (UAR)	An adverse reaction the nature and severity of which is not consistent with the information known about the therapy in question in the view of the investigator.
Serious Adverse Event (SAE), Serious Adverse Reaction (SAR) or Unexpected Serious Adverse Reaction (USAR)	Any adverse event, adverse reaction or unexpected adverse reaction, respectively, that: • Results in death; • Is life-threatening; • Required hospitalisation or prolongs existing hospitalisation; • Results in persistent or significant disability or incapacity.

7.1.2 Types of adverse events

Adverse Events (AEs) do not require reporting to the REC or sponsors but will be reported routinely to the Project Management Group.

Some AEs are expected and possible within this study population. These include:

- Self-harm not requiring medical attention (e.g. minor scratching)
- Increase in suicidal ideation (assessed by clinical interview)
- Worsening of PTSD symptoms (defined as 7-point increase in CRIES-8)

AEs may include non-medical events, for example:

- Children's schooling or carers' work is adversely affected (e.g. due to time spent in therapy or assessments encroaching on school or homework time)

- A sustained and significant increase in detrimental behaviours (e.g. safety seeking behaviours) as determined by any of the outcome measures collected throughout the study

Serious Adverse Events will be reported to the Independent Chair of the TSC, the Research Ethics Committee, and the R&D sponsor

Serious adverse events (SAE) are defined above. They may represent a worsening of AE symptoms. For example:

- Self-harm requiring medical attention e.g. cutting with a blade
- Suicidal behaviours or suicide attempts e.g. overdose of medication

Contact details for the sponsor are on page 2. Contact details for the Chair of the TSC are on page 3.

7.2. Monitoring of adverse events

Adverse events will be assessed at each face-to-face assessment time point. Risk monitoring including adverse event monitoring will be carried out during clinical contact (approximately weekly). AEs will be monitored and recorded from pre-treatment to final follow-up (10-month follow-up).

7.3. Reporting Responsibilities

- Assessors and therapists must report all SAEs to the Chief Investigator first where possible.
- All SAEs will be reported to the sponsor and the independent chair of the TSC by the Chief Investigator within 7 days.
- All SARs and USARs will be reported by the Chief Investigator to the Research Ethics Committee, using the NRES template, within 15 days of the CI becoming aware of the event.
- The Coordinator of the main REC will acknowledge receipt of safety reports within 30 days.
- A copy of the SAE notification and REC acknowledgement receipt will be copied to the sponsor.
- All AEs will be reported in the Annual Progress Report to the ethics committee and copied to the sponsor.
- All AEs and SAEs will be recorded and reported in the trial report.

7.4. Stopping Rules

The case series may be prematurely discontinued by the Sponsor or Chief Investigator based on new safety information or for other reasons given by the Ethics Committee, Trial Steering Committee or other regulatory authority concerned.

The case series may also be discontinued due to lack of recruitment or upon advice from the 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, active participants will be informed. In consultation with the Independent Chair, next steps will be agreed upon. It is most likely that data collection would continue but that participants would no longer receive the intervention.

8. Study oversight arrangements

8.1. Project Management Group

Project oversight will be provided by a **Project Management Group (PMG).** The PMG is chaired by the PI and attended by all CIs. The PMG will meet monthly and is responsible for all aspects of project management including:

- Monitoring the delivery of the scientific results needed to progress the project
- Monitoring the project against budget/schedule
- Monitoring the project against agreed milestones and identification of risks to achieving milestones as well as solutions for managing risks and issues resolution
- Providing access to appropriate resources necessary for project progression, including internal and outsourced resources and the management of these resources
- Identification and capture of project generated intellectual property (IP) and the development of a protection and exploitation strategy
- Development of requests for change to the plan if milestones are at risk

8.2. Trial Steering Committee

Study oversight will be provided by a Trial Steering Committee (TSC).

We have convened a TSC at this stage in preparation for the planned feasibility RCT. We will be submitting a separate application for ethical approval to proceed to a feasibility RCT.

The role of the TSC will be to review and agree this protocol, to agree the analysis plan, and to safeguard the interests of trial participants.

The independent members of the TSC will be independent from the sponsor and funder.

The membership, responsibilities, frequency of meetings, activity (including trial conduct and data review) and authority will be described in the TSC Charter. The Charter will be prepared and signed off by all committee members shortly after the second TSC meeting.

The first TSC was held in October 2018 (to give advice on this protocol and REC applications). The second is planned for Summer 2019 (after the case series). Subsequent TSC meetings are planned for January 2020 (6 months after trial recruitment has started) and September 2020 (to monitor trial recruitment and implementation).

8.3. Protocol amendments

Protocol amendments will be discussed and approved by TSC. They will be reported in subsequent TSC closed reports (i.e. to be prepared by the unblinded trial statistician and seen only by TSC members, not by study team members, including the blinded senior statistician). Any approved amendments will be submitted to the REC for approval, and to the sponsor.

9. Ethics & Regulatory Approvals

The CI will ensure that REC Favourable Opinion, HRA approval, and Trust Confirmation of Capacity and Capability will be in place before recruiting from the Trust. Should it be necessary to add research sites at a later stage, the sponsor will be approached to review an amendment for submission to the HRA, and Confirmation of Capacity and Capability will be obtained from the new NHS sites before starting recruitment from research sites.

Amendments

The CI is aware that all amendments must be notified to the sponsor, and agreement from the study sponsor is required before an amendment is submitted to the REC/HRA. The CI will check the detailed guidance on amendments on the HRA website beforehand to familiarise himself with the process: http://www.hra.nhs.uk/research-community/during-your-research-project/amendments/

10. Finances

This project is being carried out with funding awarded from the MRC DPFS scheme (Total FEC £1.3m). King's College London receives and manages the funding on behalf of all sites and collaborating institutions.

11. Dissemination policy

The main findings of the case series will be communicated to participants via an adolescent-friendly newsletter.

A report will be prepared for the sponsor and funders.

We plan to publish a peer-reviewed paper reporting iCT development and findings from the case series.

12. Appendix 1: Information with regards to Safety Reporting in Non-CTIMP Research

	Who	When	How	To Whom
SAE	Chief Investigator	Within 15 days of CI becoming aware of the event	SAE Report form for Non-CTIMPs, available from NRES website.	Main REC with a copy to the sponsor
Urgent Safety Measures	Chief Investigator	Immediately Within 3 days	By phone Notice in writing setting out reasons for the urgent safety measures and the plan for future action.	Main REC Main REC with a copy sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC with a copy to the sponsor
Declaration of the conclusion or early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) The end of study should be defined in the protocol	End of Study Declaration form available from the NRES website	Main REC with a copy to the sponsor
Summary of final Report	Chief Investigator	Within one year of conclusion of the Research	No Standard Format However, the following Information should be included:-	Main REC with a copy to be sent to the sponsor

			Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to subjects	