JRMO Non-CTIMP Protocol Template

1. TITLE PAGE

Full Title	*Development, Piloting and Evaluation of a Phone-Delivered Psychological Intervention (t-CETA) for Syrian Refugee Children in Lebanon: Phase II*
Short Title/Acronym	t-CETA
Sponsor	*Name the sponsor organisation and contact person:* ▪ *Queen Mary University of London* *Contact person of the above sponsor organisations is:* *Dr. Mays Jawad* *R&D Governance Operations Manager* *Joint Research Management Office* *5 Walden Street* *London* *E1 2EF* *Phone: 020 7882 7260* *Email:* research.governance@qmul.ac.uk
REC Reference	**SBS-2018-0582** (*IRB of American University of Beirut, Lebanon*).
Chief Investigator	*Prof. Michael Pluess* *Reader in Developmental Psychology* *Head of Department* *Biological and Experimental Psychology* *School of Biological and Chemical Science* *Queen Mary University of London* *Mile End Road* *London E1 4NS* *Phone 0207882 8004* *Email: m.pluess@qmul.ac.uk*
Local Principle Investigator	*Dr. Tania Bosqui* Assistant Professor in Clinical Psychology *American University of Beirut* *P.O.Box 11-0236* *Department of Psychology* *Riad El-Solh / Beirut 1107 2020*

Lebanon
Phone +961 1 350 000 ext: 4370
Email: tb33@aub.edu.lb

Study Team

- **PI** Prof. Michael Pluess, Reader in Developmental Psychology at Queen Mary University of London, UK
- **Study coordinator (London)** Dr. Fiona McEwen, Postdoctoral Researcher at Queen Mary University of London, UK.
- **Field work coordinator (Lebanon)** Ms Patricia Moghames, Médecins du Monde, Lebanon
- **Trial coordinator (Lebanon)** Mr Nicolas Chéhadé (TBC), Médecins du Monde, Lebanon
- **Co-I (acting as local PI in Lebanon)** Dr Tania Bosqui, Assistant Professor in Clinical Psychology at American University of Beirut, Lebanon
- **Advisor** Dr Alaa Hijazi, Assistant Professor in Clinical Psychology at American University of Beirut, Lebanon
- **Co-I** Dr Laura Murray, Clinical Psychologist at Johns Hopkins Bloomberg School of Public Health, US
- **CETA trainer and supervisor** Stephanie Skavenski, Research Associate at Johns Hopkins Bloomberg School of Public Health, US
- **Co-I** Dr Paul Bolton, Senior Scientist at Johns Hopkins Bloomberg School of Public Health, US
- **Co-I** Prof. Roland Weierstall, Professor of Clinical Psychology and Psychotherapy at Hamburg Medical School, Germany
- **Co-I** Stéphanie Legoff, General Coordinator Lebanon at Médecins du Monde, Lebanon
- **Co-I** Zeina Hassan, Regional Mental Health Coordinator at Médecins du Monde, Lebanon

Insert as applicable list of

A) Sites
   a. Queen Mary University of London
   b. Médecins du Monde, Lebanon
   c. American University of Beirut, Lebanon
   d. Johns Hopkins Bloomberg School of Public Health, US
   e. Hamburg Medical School, Germany

B) Laboratories and/or technical departments: N/A

C) Central facilities: N/A

Contents Page

2. GLOSSARY of Terms and Abbreviations

AE	Adverse Event
AR	Adverse Reaction
ASR	Annual Safety Report
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
EC	European Commission
GAfREC	Governance Arrangements for NHS Research Ethics Committees
ICF	Informed Consent Form
JRMO	Joint Research Management Office
NHS REC	National Health Service Research Ethics Committee
NHS R&D	National Health Service Research & Development
Participant	An individual who takes part in a clinical trial
PI	Principal Investigator
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
SSA	Site Specific Assessment
TMG	Trial Management Group
TSC	Trial Steering Committee

3. SIGNATURE PAGE

Chief Investigator Agreement

The clinical study as detailed within this research protocol **(Version 2.3, dated 23rd April 2019)**, or any subsequent amendments will be conducted in accordance with the Research Governance Framework for Health & Social Care (2005), the World Medical Association Declaration of Helsinki (1996) and the current applicable regulatory requirements and any subsequent amendments of the appropriate regulations.

Chief Investigator Name: Michael Pluess

Chief Investigator Site: Queen Mary University of London

Signature and Date: 23/04/2019

Principal Investigator Agreement *(if different from Chief investigator)*

The clinical study as detailed within this research protocol **(Version 2.3, dated 23rd April 2019)**, or any subsequent amendments will be conducted in accordance with the Research Governance Framework for Health & Social Care (2005), the World Medical Association Declaration of Helsinki (1996) and the current applicable regulatory requirements and any subsequent amendments of the appropriate regulations.

Principal Investigator Name: Tania Bosqui

Principal Investigator Site: American University of Beirut

Signature and Date: 23/04/2019

4. SUMMARY/SYNOPSIS

Short Title	*t-CETA*
Methodology	*This study involves the development, piloting and evaluation of a phone delivered intervention (t-CETA) in Syrian refugee children in Lebanon. An existing treatment, Common Elements Treatment Approach (CETA), will be culturally adapted for Syrian refugees and adapted for phone delivery. It will then be evaluated using a randomised controlled trial, comparing t-CETA to treatment as usual.* *The study will be carried out in Lebanon with 200 Syrian children, aged 8-17 years, who were displaced by the war in Syria. In Phase I up to 60 children will participate in face-to-face CETA and this will be used to adapt CETA for telephone administration (t-CETA). t-CETA will be piloted in 10-20 children and qualitative interviews used to determine acceptability and feasibility. In Phase II up to 120 children will be randomised to receive t-CETA or treatment-as-usual (standard treatment provided by Médecins du Monde). Both children and primary caregivers will be interviewed to assess the child's mental health, including measures of psychopathology (anxiety, depression, PTSD, and externalising behaviour problems) and wellbeing. Independent assessment will be conducted at baseline (pre-intervention assessment), immediately after treatment, and at 3 month follow up. t-CETA will be delivered in weekly or twice weekly sessions of 30-60 minutes over the span of 8-16 weeks.* *The proposed interdisciplinary project includes research groups in the UK, Lebanon, US, and Germany.*
Research Sites	• *Queen Mary University of London* • *Médecins du Monde, Lebanon* • *American University of Beirut, Lebanon* • *Johns Hopkins University, US* • *Hamburg Medical School, Germany*
Objectives/Aims	• *Objective 1: Development of telephone-delivered CETA (t-CETA) by adapting the existing face-to face CETA intervention (completed during Phase I; IRB approval on 8th November 2017: FAS.TB.06/SBS-2017-0429)* • *Objective 2: Scientific evaluation of the effectiveness of t-CETA with a pilot randomised controlled trial.*
Number of	*120 Syrian children and their primary caregiver*

Participants/Patients	
Main Inclusion Criteria	*Lebanon-based Syrian refugee children of Arabic ethnicity aged 8-17 years and scoring above threshold on standard measures of psychopathology*
Statistical Methodology and Analysis (if applicable)	*Randomised controlled trial: comparison of t-CETA to treatment as usual on key outcome measures.* *Please see section on statistical analyses for more details.*
Proposed Start Date	Funded from1st September 2017 Phase I - recruitment from May 2018 Phase II - recruitment from April 2019
Proposed End Date	Funded period: 1st September 2019 Study end (including no-cost extension): 1st March 2020
Study Duration	***Funded period: 2 years*** ***Including no-cost extension: 2.5 years***

5. INTRODUCTION

Current State: There are currently more than 2 million internationally displaced Syrian refugee children in countries surrounding Syria, with more than 500,000 living in Lebanon [1]. In addition to the ongoing conflict in Syria, every year millions of children from other countries are faced with the severe consequences associated with war and political conflict [2]. Empirical studies confirm that refugee children are at great risk of developing psychological problems, including post-traumatic stress disorder, depression and behavioural problems [3, 4]. The few studies on mental health of Syrian refugee children suggest that about 45% of surveyed Syrian refugee children in Turkey meet criteria for PTSD and about 20% present with clinical depression [5].

The significant need for psychological treatment among Syrian refugee children stands in stark contrast to the limited availability of services in most low and middle income host countries. Lebanon, for example, already suffered from a shortage of mental health services before the Syria crisis [6]. The total number of specialised mental health professionals working with refugees in Lebanon is extremely low with about 7-9 psychiatrists and 30-40 psychologists for a refugee population of more than 1 million [7]. In addition, access to services is very challenging for many refugees due to high mobility, cultural factors (e.g., stigma of mental illness) as well as living far away from mental health services (i.e., transportation costs).

Research Gap: While there is an overwhelming need for the psychological treatment of refugee children, available mental health services, particularly those specialised for children, are often insufficient and very difficult to access for the refugee population. These challenges are not unique to Lebanon and the Syria crises. Organisations aiming at improving mental health in low and middle income countries tend to be confronted with at least three significant obstacles:

1. Lack of funding to cover the high costs of setting up new mental health services
2. Difficulty in recruiting local qualified mental health professionals
3. Restricted access of refugee population to primary health care centres

These challenges are very difficult to address with conventional mental health services, which tend to be provided by mental health specialists in centralised primary health care centres [7]. However, over the last years access to mobile phone technology has improved across the globe and even people in remote areas with very limited resources have access to mobile phones which opens up a new and innovative avenue to overcome the three listed obstacles: ***The provision of mental health and psychological support services over the phone with the help of trained lay counsellors.*** Recent studies provide empirical evidence that cognitive behavioural therapy can be administered effectively over the phone in Western countries [8, 9]. Furthermore, transdiagnostic interventions delivered by trained non-specialists have been shown to be effective in the treatment of various psychological problems [10, 11]. **What has not been tested yet, is whether trained local non-specialists can deliver effective psychological treatment over the phone in an emergency setting in low and middle income countries.**

Impact: The proposed study focuses on the development of a new innovative approach for the delivery of effective mental health treatment to children in low resourced settings. Delivery of psychological services over the phone will improve

health results by making psychological intervention much more accessible at a significantly reduced cost compared to current standard approaches. Children are the most vulnerable victims of war and displacement. However, psychological treatment for traumatised children is often not easily accessible and generally provided in group settings that don't allow addressing individual needs [7]. Although most people in emergency settings have access to mobile phones, this technology has not yet been utilised for the delivery of mental health and psychosocial support. The proposed study is the first to explore this promising possibility in emergency settings and will provide important empirical findings regarding the feasibility and efficacy of telephone-administered psychological treatment delivered by trained local non-specialists who are familiar with both language and culture of the refugee population. The **C**ommon **E**lement **T**reatment **A**pproach (CETA) utilises the most effective CBT components. After identifying the most relevant CETA components through face-to-face delivered CETA among Syrian refugees in the Beqaa valley, these psychotherapy elements will be adapted for the use over phone and tested in a randomised controlled trial. Our study will yield the following specific results:

1. Identification of the most relevant CETA components for Syrian refugee children
2. Manual and training material for telephone-delivered CETA (t-CETA)
3. Detailed protocols to ensure child protection, safety and privacy
4. Empirical data on the efficacy of t-CETA based on a randomised controlled trial
5. Information on acceptance and implementation of t-CETA

Long Term Impact: If found to be successful, telephone-administered psychological treatment (t-CETA) will provide an innovative, promising, highly economical and widely scalable alternative approach for the provision of mental health and psychological support services in emergency situations. Importantly, this approach can easily be applied to other and future settings where children have experienced trauma and therefore represents a new and important addition to the tool box of humanitarian organisations and agencies faced with the challenge of providing mental health services in under-resourced emergency settings. Importantly, we plan to test t-CETA in large multinational follow-up studies and to develop a global network of t-CETA training- and supervision centres.

Improving Health results: The newly developed treatment approach will improve mental health in the long-term by providing access to those that are not able to receive psychological treatment due to a lack of such services in the first place or constrained access to them (i.e., long distance from primary health care centres, lack of transport, mental health stigma etc.).

Cost-effectiveness: Given that t-CETA does not require local facilities and mental health professionals, it can be delivered more easily, more quickly and at lower cost than traditional mental health services which are centre based and delivered by professionals. This will also enable non-medical humanitarian organisations to offer t-CETA (in collaboration with medical organisations who are able to provide the required training and supervision).

6. TRIAL OBJECTIVES

The proposed study is an international collaboration between Queen Mary University of London (UK), Médecins du Monde (Lebanon), Johns Hopkins University (USA), American University of Beirut (Lebanon) and Medical School Hamburg (Germany) with the aim to adapt an existing effective transdiagnostic psychological intervention for children, **C**ommon **E**lements **T**reatment **A**pproach (CETA), to the delivery over phone to Syrian refugee children in Lebanon by trained and supervised lay counsellors. The project has two specific objectives:

1. Development of telephone-delivered CETA (t-CETA) by adapting the scientifically validated face-to face CETA programme (including manual and detailed training material). **This was completed during Phase I.**
2. Scientific evaluation of the effectiveness of t-CETA applying a randomised controlled clinical trial. **This will be completed during Phase II.**

7. METHODOLOGY

Inclusion Criteria

1. Age 8-17 years, male or female
2. Live with a parent or other legal guardian
3. Child and/or parent identifies that the child has mental health difficulties and requests services
4. High risk of having mental disorder as indexed by [A]
    a. Falling in the top 40% of the distribution in any one of the following child-report questionnaires:
        1. Screen for Child Anxiety Related Emotional Disorders (SCARED)
        2. Center for Epidemiological Studies Depression Scale for Children (CES-DC)
        3. Child PTSD Symptom Scale (CPSS)
    b. AND falling in the top 40% of the distribution in the following parent-report questionnaire:
        4. Strengths and Difficulties Questionnaire (SDQ) total difficulties
5. Confirmation of significant level of symptoms and functional impairment on clinical interview (MINI KID) as indicated by both of:
    a. Meeting full or probable diagnostic criteria for any category of mood disorder, any category of anxiety disorder, PTSD, conduct disorder, or oppositional defiant disorder
    b. Clinical Global Impression severity (CGI-s) score of >3
6. Parent/legal guardian gives informed consent and child gives assent to take part

[A] Criterion 4 only applicable to children for whom these data are available from participation in the BIOPATH study; Criterion 5 takes precedence over Criterion 4 where both are available

Exclusion Criteria

1. Problem for which t-CETA would not be appropriate, including psychiatric disorders for which CETA treatment is not recommended (e.g., bipolar disorder, psychosis), severe distress (e.g., acute suicidal ideation), or problems that would preclude delivery over telephone (e.g., selective mutism)
2. Parent or legal guardian is not able to provide consent
3. Child protection issues (e.g., acute maltreatment) that are judged by clinician to make trial inclusion inappropriate
4. Any inclusion criteria not met

Methodological Approach
In order to test telephone-administered psychological intervention using an adapted version of Common Elements Treatment Approach (CETA), we will apply a mixed methods approach throughout the project: Quantitative methods will be used in the form of a randomised controlled trial to investigate efficacy of the intervention and qualitative (in addition to quantitative) methods will be applied in order to explore implementation and acceptance of the phone-delivered treatment from the perspective of both patients and providers.

Study Design / Plan – Study Visits

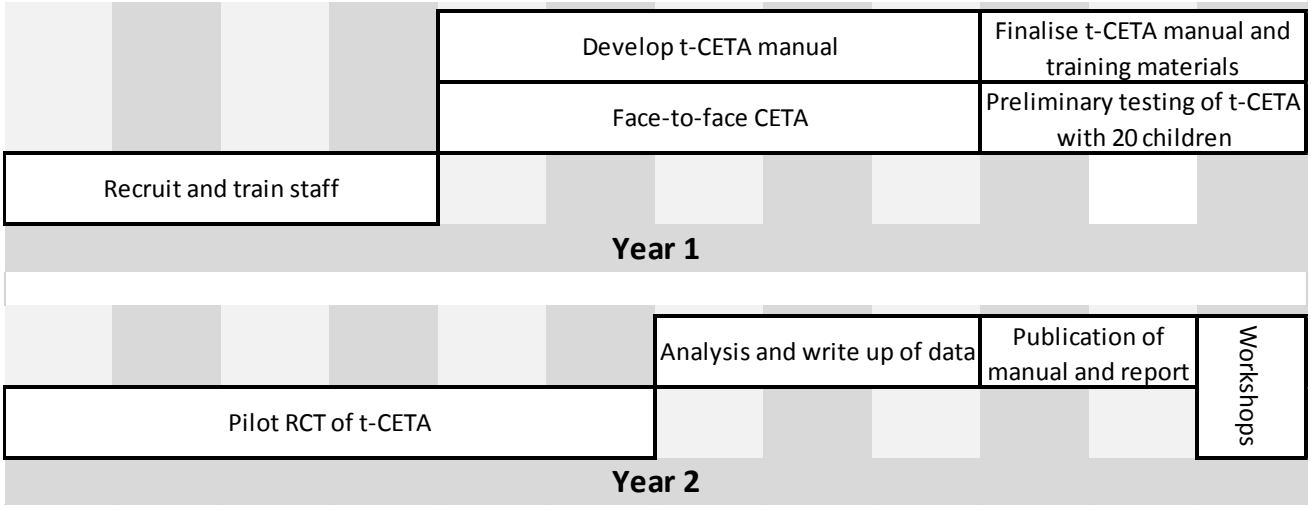
Design: The study will be conducted in Lebanon in two stages. In the first stage CETA was adapted for phone delivery (completed as Phase I). During Phase II the intervention will be tested in a randomised controlled trial.

Development Stage (Phase I; granted IRB approval on 8th November 2017, ref: FAS.TB.06/SBS-2017-0429): In order to adapt the existing CETA treatment for delivery over the phone, we first treated Syrian refugee children in the Beqaa valley with original face-to-face CETA. Local staff in Lebanon were trained and supervised by CETA expert Dr Murray and her team. Applying face-to-face CETA on an individual basis provides important insights regarding the mental health needs of these children and informed the team regarding which of the different CETA components are of particular relevance in this specific context. During this period, the local team and the CETA experts (Dr Murray and Ms Skavenski) regularly convened over skype to discuss which of the CETA components could be delivered in a culturally sensitive way without face-to-face contact and to develop a first written draft for each CETA component, in collaboration with our clinical experts Drs Bosqui, Hijazi and Weierstall. The complete draft of telephone administered CETA (t-CETA) is being tested over the phone with a small number of children (10-20 children) and continually adapted in close collaboration with all members of the local and international research team. As part of this developmental stage, qualitative data (i.e. individual interviews with treated Syrian refugee children, their primary caregivers as well as mental health staff) are being used to identify potential child protection, safety and privacy issues related to telephone-administered treatment. This is informing the development of detailed protocols to ensure children's safety at all times. These protocols form a crucial part of the t-CETA manual and training material. The end product is a detailed t-CETA manual and training material for non-specialist lay providers.

Piloting Stage (Phase II; for review by AUB IRB): The implementation and efficacy of t-CETA will be tested with a randomised controlled clinical trial. Up to 120 Syrian refugee children will be randomly allocated to either t-CETA or treatment as usual provided by Médecins du Monde in primary healthcare centres in the Beqaa valley.

When lack of access to a clinic would preclude inclusion in the study (i.e., randomisation is not possible in case the family are allocated to treatment as usual, which involves attending a Primary Healthcare Centre), families will be offered the option of receiving t-CETA only (non-randomised). Data from this non-randomised t-CETA group will not be included in the RCT but will provide additional, ecologically valid data about implementation and efficacy. Data from the original face-to-face delivery collected during the developmental stage may be used for comparison, providing that there have not been significant changes to the protocol from Phase I to Phase II that would make comparison illegitimate. In addition to questionnaires, clinical interviews with children and primary caregivers will be conducted before the intervention to determine suitability for inclusion. *Inclusion and exclusion criteria are identical to those used during Phase I, with the exception that questionnaire data will not be considered where children are recruited from sources other than the BIOPATH study (clinical interview data will take precedence in all cases)*. Assessments will be carried out before and after the intervention as well as during a 3-month follow-up assessment by independent trained enumerators blind to study condition. Implementation and acceptance of the intervention will be further assessed with a qualitative study based on interviews with a subset of involved Syrian refugee children, their caregivers as well as mental health staff.

Figure 1. Study Scheme Diagram



8. STUDY PROCEDURES

Sample: Children included in the proposed study will be selected from the large sample of a NICHD funded study on the biological pathways of risk and resilience in Syrian refugee children based in Lebanon headed by PI Prof Pluess and co-PI Dr Elie Karam (*Biological Pathways of Risk and Resilience in Syrian Refugee Children* [BIOPATH]; *Sponsor*: Queen Mary University of London [ReDA Ref: 011120]; *Ethical approval*: Institutional Review Board of the University of Balamand, Lebanon [Ref: IRB/O/024-16/1815] and Ministry of Public Health in Lebanon, in consultation with the Lebanese National Consultative Committee on Ethics). BIOPATH is a longitudinal study and includes 1,600 Syrian refugee families in the Beqaa valley. For each of these children we will already have data on a range of psychological outcomes (i.e., PTSD, depression, anxiety, behavioural problems; see Table 2 below). From the 1,600 children, we will select up to 60 based on various psychological symptoms

assessed routinely as part of the BIOPATH study at the first BIOPATH data collection (approximately October 2017-January 2018) and up to 120 children during the second BIOPATH data collection (approximately October 2018-January 2019).

If insufficient numbers of children from the BIOPATH study are recruited using the above approach, the following additional approaches will be used: (i) children from BIOPATH who take part in the linked VaST study (which involves completing the MINI KID clinical interview) will be approached if they meet inclusion criteria and are interested in accessing mental health services; (ii) other children in the families who took part in BIOPATH (e.g., siblings and cousins) and for whom families requested mental health services will be approached; (iii) referrals will be accepted from other agencies; (iv) information sessions will be conducted in the community (e.g., in ITS or PHCs) to inform families about the research and allow them to request mental health assessment for their child(ren); (v) families in contact with participating families will be able to contact the study for information and to request mental health assessment for their child (snowballing approach).

Primary caregivers will be contacted over the phone and offered clinical assessment for their child at no cost, ***as part of routine clinical care***. Families will be invited to attend an appointment at an MdM clinic for this assessment. During Phase II, families who attend the appointment will first undertake a brief interview to establish what the presenting problem is. Following this and providing children do not meet exclusion criteria, they will be offered inclusion in the t-CETA study. Those who ***do not*** want to participate in research, or who clearly meet exclusion criteria, will be offered a standard clinical intake assessment and treatment as usual provided by Médecins du Monde. Those who ***do*** want to participate in research will complete the informed consent process and a clinical interview (MINI KID) will then be used to determine whether children meet inclusion criteria; if the MINI KID has already been completed (e.g., as part of the VaST study) then it will not be repeated, but consent will be sought to use these data for the t-CETA study. Those who do not meet inclusion criteria or whose difficulties are not appropriate for CETA will be offered treatment as usual by Médecins du Monde or referral to another agency, as appropriate. Please see *t-CETA recruitment flowchart v2.1* for the routes into research or standard clinical care. Based on the most recent studies, it is expected that approximately 20-30% of the BIOPATH sample will suffer from clinical levels of psychological problems [5]. If insufficient numbers of children are recruited from the BIOPATH study then eligible children may be recruited through advertisement in the Primary Healthcare Centres that service refugee populations in the Bekaa Valley.

Recruitment: Children participating in BIOPATH will be screened and assessed to see if they meet inclusion criteria for this study. Evidence of high risk of mental disorder will be operationalized in the following way:

1. Child or parent reports during interview for the BIOPATH study that the child has a need for mental health services

   AND
2. Child exceeds a specified cut-off (highest 40% of the distribution) on any of the following child-report questionnaires completed during BIOPATH:
   a. Screen for Child Anxiety Related Emotional Disorders (SCARED)
   b. Center for Epidemiological Studies Depression Scale for Children (CES-DC)
   c. Child PTSD Symptom Scale (CPSS)

AND

3. Child exceeds a specified cut-off (highest 40% of the distribution) on the following parent-report questionnaire completed during BIOPATH:
    a. Strengths and Difficulties Questionnaire (SDQ) total difficulties

    AND
4. Child meets definite or probable diagnostic criteria for any mood or anxiety disorder, PTSD, conduct disorder, or oppositional defiant disorder (assessed using MINI KID 6.0; interviewers will gather additional information sufficient to assign diagnosis according to DSM-5)

    AND
5. Clinical Global Impression-severity (CGI-s) score >3

[see Table 2 for all measures]

Children who have not participated in BIOPATH will not have questionnaire data to review. In these cases, request for mental health services and meeting criteria 4 and 5 will be sufficient. In all cases, criteria 4 and 5 take precedence over questionnaire data.

Caregivers will be contacted over the phone by the t-CETA team to establish if they are interested in their child having an assessment, and an appointment with a t-CETA team member or other MdM case manager/psychotherapist at the MdM CETA centre or a Primary Healthcare Centre (PHC) (or in rare cases, in the family's home) will be arranged. This appointment will be offered as part of routine clinical care to ensure that all families can access an assessment, regardless of interest in research. At this appointment the child and parent will undergo a brief MdM intake interview. If the child has a problem that would make CETA inappropriate (e.g., acute suicidal ideation, acute child maltreatment) then an emergency procedure will be followed to arrange referral to an appropriate agency or hospital. If no such problems are disclosed, then inclusion in the t-CETA study will be offered. The study will be explained and the informed consent procedure followed. If they wish to take part, the parent will provide written consent and the child written assent for study participation. If any participant is unable to provide a signature then they will be given the option to provide oral consent in lieu of a signature (in the presence of a witness who is independent of the research team). If they do not wish to take part, then they will be offered standard MdM treatment.

For families who consent/assent to the study, a clinical interview (MINI KID) will then be conducted to establish if the child has difficulties that are suitable for treatment using CETA (definite or probable diagnosis of any mood disorder, any anxiety disorder, PTSD, conduct disorder, or oppositional defiant disorder). Following the MINI KID, if their child does not meet inclusion criteria, or meets exclusion criteria such as having difficulties that are not appropriate for CETA (e.g., bipolar disorder, schizophrenia) then they will be offered treatment as usual through Médecins du Monde or referral to another agency.

Families who agree to participate will be prepared for subsequent assessments at this or another appointment: they will be given a booklet that contains information about the assessments, visual aids to support the response format of questionnaires, and emergency contact numbers. The assessments will be explained in detail, both caregiver and child will complete practice questions, and there will be time for discussion to ensure that they understand and are able to complete assessments.

See Figure 2 and *t-CETA recruitment flowchart v2.1* for pathways from referral through treatment.

Procedure: Once informed consent and child assent have been gained, a trained assessor (not involved in providing treatment) blind to treatment condition (in Phase II) will conduct the baseline (pre-intervention) assessment, over the phone (or face-to-face if phone assessment is not possible), which will take approximately 30 minutes per child and 30 minutes per caregiver. The assessment includes standardized questionnaires and interview questions about the child's symptoms and adaptive functioning. Participants will use the visual aids in the booklet provided to help them respond to questions. Data will be collected with the help of tablet or laptop computers running Qualtrics and will be uploaded to a secure server. Participants will only be identified using an ID on Qualtrics; identifying details will not be entered. The assessment process will be supervised by a qualified clinical psychologist (Dr Tania Bosqui).

The schedule of assessments for different conditions is set out in Table 1.

Phase I (granted IRB approval on 8th November 2017, ref: FAS.TB.06/SBS-2017-0429): N=~60 children undergo face-to-face CETA over the course of approximately 8-12 weeks (approximately 1x30-60 minute session per week). At the first appointment, before CETA is started, the CETA therapist administers the PSYCHLOPS to allow the child to identify problems that are most salient to them and to rate the impact of those problems. This will form part of assessment, but will also help the therapist identify problems that the child wants help with. A Client Monitoring Form (CMF), a brief questionnaire that is integral to CETA and used to monitor problems throughout therapy, will be used at the beginning of each session.

CETA then proceeds for up to 12 weeks (the exact number of sessions will depend on the nature of the problems that each child has and which CETA components are selected by the therapist). At an appointment midway through CETA and at the last appointment, the PSYCHLOPS is used to measure the child's appraisal of the problem they first identified and any perceived change in the impact of that problem, as well as their experience of CETA. After the intervention and 3 months following the baseline assessment, children undergo a post-intervention assessment (questionnaires / interview). A final assessment is carried out 6 months after baseline (questionnaires / interview). Both assessments are conducted over the phone (or face-to-face if phone assessment is not possible) by trained assessors not involved in treatment provision.

Ten children will be selected at random from the ~60 that completed at least part of a course of CETA and will be invited to take part in a semi-structured interview for the **qualitative component** of the study. Caregiver and child will be asked to consent to this interview, including an audio recording of the interview. Caregiver and child will be interviewed separately about their experience of CETA. Responses will be transcribed and translated and used to guide the development of t-CETA.

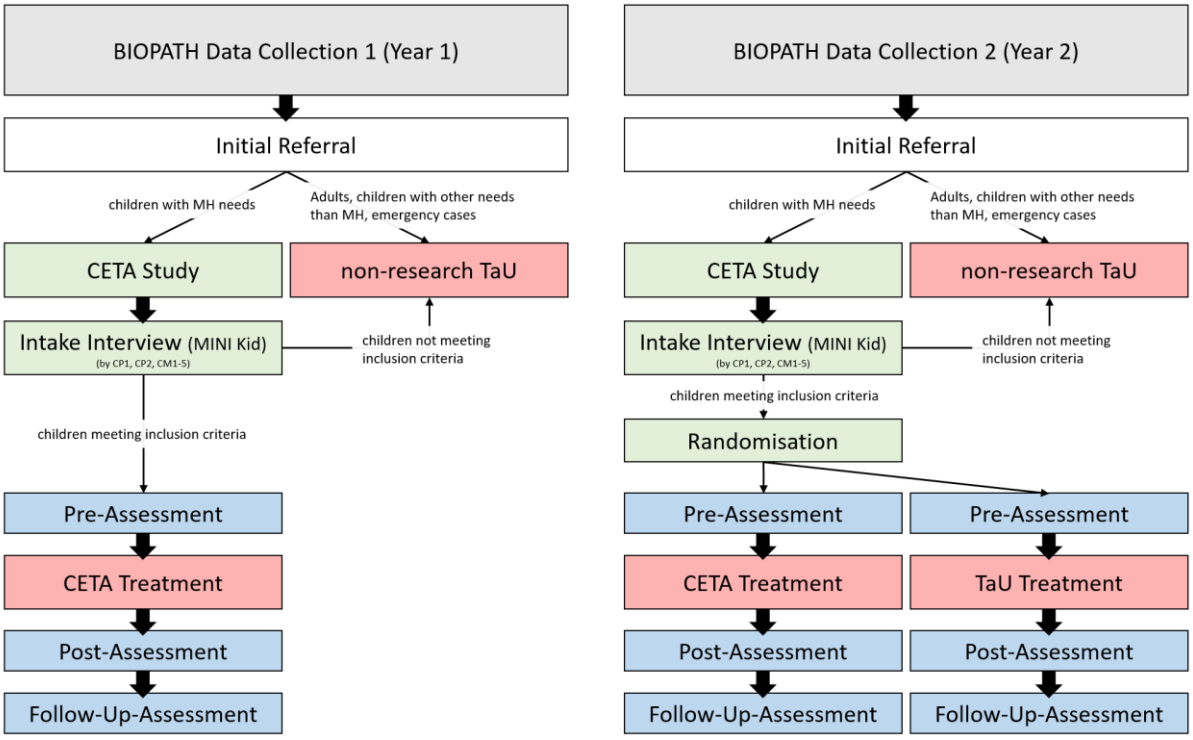
Once t-CETA has been developed approximately 10 children will be recruited from the BIOPATH study or via advertisement in the Primary Healthcare Centres that service refugee populations in the Bekaa Valley and invited to take part in **further development and testing of t-CETA**. These 10 children will undergo a course of telephone-delivered CETA over the course of up to 12 weeks (approximately 1x30-60 minute session per week). Testing over the phone will occur with the child in a private room at the clinic and the therapist in a nearby office. At the end of each session the therapist will conduct a short debrief to discuss any difficulties experienced with telephone delivery. Furthermore, if it is apparent during telephone delivery that the session is not working via phone, then the therapist can revert to face-to-face

treatment for the remainder of the session, thus ensuring that appropriate treatment has been provided to all children in this phase.

Phase II (for review by AUB IRB): N=~120 children will be recruited and will undergo baseline (pre-intervention) assessment over the phone (or face-to-face if phone assessment is not possible) by trained assessors that are not involved in treatment provision. They will then be randomized to two groups: t-CETA and Treatment-as-usual. Stratified randomisation will be used to ensure approximately equal numbers of males and females and younger (8-12 years) and older (13-17 years) children in each group. There will be an additional group of children who receive t-CETA but without randomization. The t-CETA groups will undergo telephone-delivered t-CETA over the course of up to 16 weeks (approximately 1 or 2 x 30 minute sessions per week). The Treatment-as-usual group will be assessed by a Médecins du Monde clinical case manager and further treatment (e.g., psychological treatment) or referral to other services will be offered in line with usual Médecins du Monde service provision. The PSYCHLOPS will be used as in Phase I at the beginning, middle, and end of the treatment period.

After the intervention and 3 months following the baseline assessment, children will undergo a post-intervention assessment (questionnaires / interview), again per phone (or face-to-face) by trained assessors not involved in treatment provision and blind to treatment condition. Ten children and caregiver dyads will be selected at random from the 60 that completed at least part of a course of t-CETA and will be invited to take part in a semi-structured interview for the **qualitative component** of the study. Caregiver and child will be asked to consent to this interview, including an audio recording of the interview. Caregiver and child will be interviewed separately about their experience of t-CETA. Staff who delivered t-CETA will also be interviewed as part of a Focus Group Discussion (FGD) to gain insight into their experience of delivering the intervention. Responses will be transcribed and translated for analysis. A final assessment will be carried out 6 months after baseline (questionnaires / interview). Assessors will be blind to group condition. The assessment process will be supervised by a qualified clinical psychologist (Dr Tania Bosqui).

Figure 2. Approach from BIOPATH referral to treatment



Key: CP Clinical Psychologist. CM Case Manager.
Note. In Year 2 referrals will be accepted from sources other than BIOPATH, but subsequent study involvement will be identical to those recruited from BIOPATH. Families unable to travel to the clinic will be given the option to choose t-CETA (without randomization) at recruitment; other than not being randomized, all other study procedures will be identical.

Table 1. Schedule of assessments

	Phase I **May – Dec 2018**			**Phase II** **Jan – July 2019**		
	Face-to-face CETA N=~60	***Interview*** N=10 (from CETA group)	***t-CETA development/ piloting*** N=10	***t-CETA***[C] N=~60	***Treatment-as-usual*** N=~60	***Interview*** N=10 (from t-CETA group)
Recruitment	Informed consent / assent (10-15 mins)	n/a	Informed consent / assent (10-15 mins)	Informed consent / assent (10-15 mins)	Informed consent / assent (10-15 mins)	n/a
Clinical assessment[B]	MINI-KID CGI-s score (30 mins child, 30 mins caregiver)	n/a	MINI-KID CGI-s score (30 mins child, 30 mins caregiver)	MINI-KID CGI-s score (30 mins child, 30 mins caregiver)	MINI-KID CGI-s score (30 mins child, 30 mins caregiver)	n/a
Baseline independent assessment (time=0)	Phone interview[A] (30 mins child, 30 mins caregiver)	n/a	Phone interview[A] (30 mins child, 30 mins caregiver)	Phone interview[A] (30 mins child, 30 mins caregiver)	Phone interview[A] (30 mins child, 30 mins caregiver)	n/a

TREATMENT (~ 8-12 weeks)	CETA x 8-12 sessions PSYCHLOPS at 1st session PSYCHLOPS at midway PSYCHLOPS at final session (each session up to 60 mins)	n/a	t-CETA x 8-16 sessions PSYCHLOPS at 1st session PSYCHLOPS at midway PSYCHLOPS at final session (each session up to 30 mins)	t-CETA x 8-16 sessions PSYCHLOPS at 1st session PSYCHLOPS at midway PSYCHLOPS at final session (each session up to 30 mins)	MdM standard treatment (number, type, and duration of sessions determined by therapist for each child) PSYCHLOPS at 1st session PSYCHLOPS at midway PSYCHLOPS at final session	n/a
Post-intervention independent assessment (time=3 months)	Phone interview[A] (30 mins child, 30 mins caregiver)	Informed consent / assent Qualitative interview (1 hour)	Phone interview[A] (30 mins child, 30 mins caregiver) Qualitative interview / debrief (1 hour)	Phone interview[A] (30 mins child, 30 mins caregiver)	Phone interview[A] (30 mins child, 30 mins caregiver)	Informed consent / assent Qualitative interview (1 hour)
Follow up independent assessment (time=6 months)	Phone interview[A] (30 mins child, 30 mins caregiver)	n/a	n/a	Phone interview[A] (30 mins child, 30 mins caregiver)	Phone interview[A] (30 mins child, 30 mins caregiver)	n/a

[A] Phone interview will consist of CPSS, CES-DC, SCARED, SDQ and externalizing behaviour problems, WHO-5, YLOT, WHODAS 2.0
[B] Clinical interview will not be repeated if it has already been completed, e.g., as part of the VaST study
[C] t-CETA cases include those randomized to t-CETA as part of RCT and the t-CETA only (non-randomized) group

Measures: Data collection will include questionnaires and standardized interviews on mental health disorder and mental well-being, and semi-structured interviews about the experience of receiving CETA or t-CETA. Caregivers and children will be interviewed.

Questionnaires. Most of the questionnaires/interviews have already been used in similar Middle Eastern populations or have been translated and pilot tested for the BIOPATH study.

Table 2. Constructs and Measures

Psychopathology			
Construct	***Measure***	***Informant***	***Assessment Point***
PTSD	Child PTSD Symptom Scale (CPSS) [12]	Child	Pre- and post-intervention and at 3 months follow up
Depression	Center for Epidemiological Studies Depression Scale for Children (CES-DC) [13]	Child	Pre- and post-intervention and at 3 months follow up
Anxiety	Screen for Child Anxiety Related Emotional Disorders (SCARED) [14]	Child	Pre- and post-intervention and at 3 months follow up
Externalising behaviour problems	Strengths and Difficulties Questionnaire (SDQ) [15] and Conduct Disorder / Oppositional Defiant Disorder items	Caregiver	Pre- and post-intervention and at 3 months follow up
Clinical Interview	MINI KID [16]	Child/ Caregiver	Pre-intervention
Clinical severity	Clinical Global Impression – severity (CGI-s) [17]	Therapist, reviewing MINI KID and information about impairment from caregiver and child	Pre-intervention
Well-Being			
Construct	***Measure***	***Informant***	
Well-Being	WHO-5 Well-Being Index (WHO-5) [18]	Child	Pre- and post-intervention and at 3 months follow up
Optimism	Youth Life Orientation Test (YLOT) [19]	Child	Pre- and post-intervention and at 3 months follow up
Adaptive functioning			

Disability	WHODAS 2.0 child and adolescent [20]	Child / caregiver	Pre- and post-intervention and at 3 months follow-up
Response to therapy	PSYCHLOPS [21]	Child / therapist	Pre-, during, and post-intervention
Personality			
High sensitive personality	High Sensitive Child (HSC) [22]	Child	Pre-intervention [BIOPATH data will be used where available; this will only be administered if children have not taken part in BIOPATH]

Covariates. In addition we will also assess a range of important demographic characteristics and covariates including Age, Puberty Status, Gender, Ethnicity, Self-Reported Global Health, Family Income, Parental Education, Family Structure and Size, Religious Affiliation, and Duration of Displacement. Relevant data collected during the BIOPATH study will be shared with this study, with the written consent of caregiver and child assent.

Intervention. The intervention that will be used and adapted to telephone delivery is the Common Elements Treatment Approach (CETA), a transdiagnostic intervention for children presenting with mood and/or anxiety problems, developed specifically for use in low and middle income countries (LMIC) [11]. CETA is not a "new" intervention, but rather a new approach to training lay counselors—one focused on common elements of evidence-based treatments and decision making for treatment focus, element selection, sequencing and dosing.

CETA is based on the fact that most evidence-based mental health treatments (EBTs) (most of which are cognitive behavioural) are made of similar elements or components. For example, most evidence-based treatments for a variety of disorders all contain psychoeducation, and cognitive coping. The idea is to train counselors in a range of different components that are similar across EBTs, and then teach them how to choose different orders and "dose" of components based on a client's presenting problems. Thus, rather than training on one packaged approach specifically for one disorder (e.g., IPT for Depression), CETA allows counselors to have the skills to treat at least the big mental health problems of trauma, depression and anxiety, and behavioral problems for youth. This approach is thought to be particularly helpful in low-resource countries where the ability to train counselors in multiple EBTs is not likely, and there are limited counselors available.

End of Study Definition
Study will end following the completion of the final follow-up assessment in Phase II and when all data have been received in the UK.

9. STATISTICAL CONSIDERATIONS

Power analysis: A-priori sample size calculation was performed using g*power 3.1. Based on an assumed effect size of d = .6 and a 1:1 ratio of intervention and control, a total sample of 90 (45 in each arm) is required to detect significant differences with

alpha = .05 and power = .80. However, we will aim to recruit 120 children (60 in each arm) to account for potential drop-outs.

Data Analysis: The main comparison is between the conditions t-CETA and Treatment-as-usual (Phase II of study). An intention-to-treat design (using imputation for missing data: multiple imputation and last observation carried forward approaches will be considered) will be used to compare t-CETA and Treatment-as-usual groups on primary and secondary outcomes measures (these measures have been shortened and modified for Syrian refugee children during pilot work). Face-to-face CETA in Phase I will be used as an additional condition in analyses, unless substantial adjustments have been made to the design and measures before the main trial begins in Phase II. Data from a further group of children who receive t-CETA, but who are not randomized, will be combined with those children who were randomized to t-CETA to explore efficacy (comparison of baseline, post-treatment, and 3-month follow up outcome scores) and implementation within the groups receiving t-CETA.

Primary outcome measures:

1. Emotional and behavioural problem composite score (derived from SCARED, CES-DC, CPSS, and SDQ externalising subscale plus additional externalising behaviour items)
2. Adaptive functioning score (WHODAS, adapted for low resource settings)

Secondary outcome measures:

1. PTSD symptom score (Child PTSD Symptom Scale (CPSS))
2. Depression symptom score (Center for Epidemiological Studies Depression Scale for Children (CES-DC))
3. Anxiety symptom score (Screen for Child Anxiety Related Emotional Disorders (SCARED))
4. Externalising behaviour problems (Strengths and Difficulties Questionnaire (SDQ) externalising subscale and Conduct Disorder / Oppositional Defiant Disorder items)
5. Response to intervention (PSYCHLOPS)
6. Well-Being score (WHO5)
7. Optimism (YLOT)

t-tests and repeated measures ANCOVA (including age and gender as covariates, as well as other variables identified at baseline that are associated with outcomes) will be used to compare outcome measures between interventions and over time.

10. ETHICS

The Principal Investigator ensures that the study will be carried out in accordance with the ethical principles in the Research Governance Framework for Health and Social Care, Second Edition, 2005 and its subsequent amendments as applicable and applicable legal and regulatory requirements.

Ethical approval for Phase I is from the IRB at the American University of Beirut, Lebanon (IRB ID: FAS.TB.06/SBS-2017-0429; 8th November 2017) and the Ministry of Public Health, Lebanon (10th January 2018). Caregivers have to provide written informed consent and children provide written assent for study participation (oral consent in the presence of a witness [independent of the research study] will be provided if participant cannot sign). Participants will be provided with oral and written

information about the study and will be given the opportunity to ask questions before deciding whether or not to participate. There will be approximately a week from being provided with information about the study over the phone and the first appointment, giving individuals time to consider research involvement before making a decision about participation. Furthermore, it will be made clear that participants can withdraw from the research at any point without penalty, including the option of continuing with treatment but without data collection.

There are no conflicts of interest.

11. SAFETY CONSIDERATIONS:

Potential Risks to Human Subjects

- The collection of psychosocial data may cause psychological distress for some participants. Study participants may be distressed at recalling war events or other traumatic events during therapy. In our pilot work for a related study, which included assessment of 19 war events and 23 items dealing with childhood maltreatment with a questionnaire/interview, all 726 participants were asked whether they found it difficult to share the things that happened to them. 19.8% of the participants stated that they found responding to the questionnaire/interview difficult. All research staff involved in the fieldwork (i.e. clinical psychologists, case managers (social workers), and assessors) will be trained to screen for acute psychological distress of study participants and administer psychological first aid. They will inform the clinical supervisor at Médecins du Monde immediately, and the local PI / clinical psychologist, Dr Tania Bosqui, within 24 hours. They will review the case, arrange further assessment as appropriate, and make a decision about whether participation in the trial should be discontinued. Discontinuation of the trial will be recommended if there has been a significant worsening of symptoms such that the child meets exclusion criteria (e.g., acute suicidal ideation, psychotic symptoms). In these cases an appropriate course of action will be determined by the clinical supervisor and Dr Bosqui, including referral to a higher level of psychological or psychiatric care, or other services as necessary. It is possible that participants will disclose information that indicates that someone is at immediate risk of harm (e.g., ongoing child maltreatment, suicidal ideation). Relevant information will be sought from the participant, where possible, including establishing whether this information has been shared with other agencies (e.g., child protection). The clinical supervisor will be informed immediately and the local PI will be informed within 24 hours and they will be responsible for determining the course of action. This is the only circumstance in which information may be shared with other agencies without consent, although all attempts will be made to gain consent from participating children and caregivers prior to sharing information, where this is appropriate and does not increase the risk of harm. The circumstances under which information will be shared will be explained at the beginning of therapy through the clinical agreement (verbal agreement between therapist and participant) and participants will be briefly reminded of this at the beginning of each therapy session and assessment. One CETA/t-CETA component, Safety Steps, covers safety related to the risk of suicidal thoughts and attempts and can be used during CETA/t-CETA when appropriate. Further detailed safety protocols have been developed specifically for this research study and are based on the extensive expertise of the research team, Médecins du Monde's extensive experience with Syrian

refugees in this region, and experience gained during Phase I of this study. These include information relating to referral to other specialised agencies (e.g., child protection, gender-based violence).

- Delivering therapy and conducting assessments over the phone may introduce additional risks. The following steps will be taken:
    - Emergency Referrals: For each community within which t-CETA is administered, relevant local services (i.e., primary healthcare clinics, child protection agencies) have been identified for potential emergency referrals before any child is treated, and in case risk issues arise during assessment, treatment, or follow-up. As an active provider of health services, Médecins du Monde has developed a strong network and professional working relationship with primary healthcare clinics and the main local and international child protection agencies operating in the field. For example, MdM arrange referrals to psychiatrists at FPSC (La Fundación Promoción Social de la Cultura), and to other agencies (e.g., child protection case management agencies such as IRC – International Rescue Committee and SCI - Save The Children International). Furthermore, we are using the Child Protection Working Group's (CPWG) most recent service mapping and GBV referral pathway, and will remain in regular contact with UNICEF and the CPWG, to ensure that the research team has the most up to date information to manage emergency referrals. In an emergency, MdM will be able to immediately and directly contact and coordinate help with these organisations. We will work with MdM to develop their child safeguarding policy to ensure that all children who receive services from MdM receive the same protection. Our safety protocols (CP/GBV) were reviewed by experts at UNICEF/CPWG.
    - Exclusion criteria: Given that we will select some children from the BIOPATH study and will conduct an intake interview prior to recruitment in all cases, children at severe risk of suicidal behaviour and acute maltreatment can be identified pre-enrolment (based on existing BIOPATH data and intake interview) and will be referred to the most appropriate services rather than included in the t-CETA trial.
    - Security/Privacy Checks for t-CETA: Only children whose primary caretaker provides informed consent will be included in the study. During the consent process, children and their primary caretaker will be informed about the confidentiality of the t-CETA sessions and research staff will inquire whether the parent and child will be able to find a safe, private and solitary place for the phone assessment +/- t-CETA sessions.
    - During the face-to-face intake assessment, the safety guidelines will be explained and agreed on between the case manager and the participants, to maximize the likelihood of ensuring safety and privacy for the participants. This in-depth discussion of safety guidelines will make it easier for assessors and t-CETA counsellors to review the safety steps with the caretaker and then the child when they are on the phone.
    - The types of places that would be considered a safe space to talk will be identified during the face-to-face intake assessment with the caretaker and child, while reviewing the steps of the treatment and research, the phone assessment and the safety guidelines. The case manager will follow the guidelines for safety that are also applied for phone assessments and reviewed with the child and the caretaker before participating in the study/treatment. The importance of only giving information over the phone to authorised study personnel will be emphasized; they will speak to the same

counsellor each time and will be instructed not to disclose any information if they do not recognise the person calling. In the rare event that it is necessary for a different counsellor to call, the family will be given full details of the alternative counsellor, and date and time of call, in advance. If, when the case manager calls, someone other than the participating caregiver answers the phone, no confidential information will be given regarding the treatment or research study.

- Case managers will ask at the beginning of each session whether the caregiver or child is in a safe and private place and free to talk. The call with the child will only be conducted after confirming over the phone with the caregiver that the child can find a safe and private place for the call, and the caregiver will be asked to help ensure this for the child (e.g., by asking others to leave the room).
- At the beginning of each t-CETA session, both the caregiver and child/adolescent will be asked to confirm their identity on the phone. This identity confirmation will be done through two main options:
    - First contact: we will make sure to review full name (+surname) and confirm that they had the intake assessment with (name of counsellor) while mentioning the period of time. We will also review what they agreed with the counsellor: that they will be contacted over the phone by a t-CETA counsellor
    - During t-CETA sessions:
        - With the caregiver: we will review the session we had with them, what we discussed regarding what the child did /would do in the sessions, the homework assigned to the child and the activities we asked the caregiver to do. We will also follow-up on how their week went regarding what we are working on with both them and their child.
        - With the child: we will review the activities done during the past session, the topic we discussed, we will ask about their week and we will review the homework assigned from the previous session.
- If, at any point, a participant seems uncomfortable and reluctant to answer questions (e.g., it's possible that there is someone else in the room but the participant does not want to say so) then the case manager will suggest stopping the interview and calling back at another time. Additionally, prior to starting t-CETA an agreement will be made with the caregiver as to how to proceed if the connection fails, such as calling back 3 times over 15 minutes, then postponing until the next day. In the case of the disclosure of risk issues over the phone, such as risk of suicidality or suspicion of child abuse, the case manager will pause the session in order to manage the risk, following pre-prepared protocols. All risk issues, or worry about risk, will be reported by the case manager immediately after the phone call to the responsible clinician who will follow up with the family, discuss with the clinical team and develop a risk management plan with appropriate actions. In cases of immediate risk, the case manager will try to keep the family on the phone until a senior clinician is contacted.
- It is important to highlight that steps regarding interruption, increased exposure to risk, not being able to talk because of external interruption, or pauses because of therapy resistance or not feeling comfortable to continue,

will be agreed upon and explain thoroughly to the caretaker and to the child. We will be closely monitoring safety and symptoms in every t-CETA session using the Client Monitoring Form (a standardised tool that was developed with this population of Syrian refugees).

- Security/Privacy Checks for independent phone assessments: Independent assessors will follow the same guidance for managing risk over the phone. They will establish a safe private place to talk, they will confirm the identity of the child/adolescent and caregiver, they will reiterate the rules of confidentiality, and they will follow the same protocols if disclosure of a risk issue occurs. The risks are likely to be lower for phone assessments as the phone assessments comprise of closed questions, requiring a response such as “Not at all”, “A little”, “Some”, or “A lot”. Anyone who overhears the phone call will only hear these responses, and not the questions, which reduces the risk that anyone will overhear sensitive information about the child’s mental state.
- Assessors will make the calls from a private room at the American University of Beirut so that it will not be possible for anyone to hear their end of the call. Assessors will have a CITI certificate (or equivalent) and training will be provided on the importance of confidentiality, practical ways to ensure this while conducting phone assessments, and how to deal with various scenarios that might threaten confidentiality (e.g., someone else walks into the room). Training has been developed and used successfully during Phase I of the study, and uses a combination of scripts and role play to ensure that assessors are prepared to deal with challenging situations. All assessors are graduate students of the MSc in Clinical Psychology (or related course in psychology or psychiatry) at the American University of Beirut and will already have received training in working with vulnerable populations, in addition to that which is provided by the study.
- Access to services for families who do not wish to take part in research: Children from the BIOPATH study, and those approached through other routes, who do not take part in the t-CETA study will be offered standard services through MdM. This will include children who requested referral following the BIOPATH study but who do not meet inclusion criteria for the t-CETA study, children who do meet inclusion criteria but exceed the number for recruitment to the t-CETA study, children who meet inclusion criteria but who do not wish to take part in the t-CETA study, and children whose problems are not suitable for t-CETA. Referral to MdM care as usual will be managed using a referral form which will provide name and contact details for the caregiver and child, details about the reason for referral, and steps taken by the t-CETA case manager prior to/ in addition to referral. Referral will occur with the knowledge and consent of the caregiver and child. Two additional MdM staff (a case manager and a psychotherapist) are being funded by the BIOPATH study to help meet the additional caseload. Mental health services provided by MdM are free of charge.
- The approach will follow the standard MdM approach: initial assessment by a case manager and then further assessment and treatment will be determined based on the child’s difficulties. This might include referral to an MdM psychotherapist, referral to a psychiatrist (FPSC La Fundación Promoción Social de la Cultura), or to other agencies (e.g., child protection case management agencies such as IRC – International Rescue Committee and SCI - Save The Children International). Please see t-CETA recruitment

flowchart v2.1 for full details of exit points from t-CETA processes to care as usual.

- Equality of benefits to research and non-research clients: We will also take steps to ensure that there is not undue pressure to agree to research involvement in order to secure an intake assessment, treatment, or transportation costs. Intake assessment following screening will be offered as part of routine clinical care, rather than only to families interested in research. Families who do not want to participate in the t-CETA study will then be offered standard treatment at MdM.
- Transportation coverage will be provided using MdM's standard approach to ensure that t-CETA study participants and those receiving standard MdM care receive the same benefits. MdM's standard approach is to offer transportation costs only if a client says that they will struggle to attend an appointment. The case manager discusses this with the client to establish whether the cost of transportation is a barrier to them accessing the service. Decisions are made on a case-by-case basis and there is no written protocol to follow, nor is written information provided to clients about transportation. We have decided to use the same approach so as not to create undue pressure for clients to participate in the research; if we create more favourable conditions for study participants – i.e., more generous transportation coverage – then more vulnerable clients may feel pressure to participate for this reason. We believe that it would not be ethical to highlight transportation coverage to MdM clients because this is likely to create an expectation that will not be possible to fulfil for many of those receiving standard care. It is also important that the research study does not place additional financial pressure on MdM's services by increasing demand for transportation costs. In the medium to longer term we will work with MdM to develop a more standardized approach to vulnerability assessment and decision-making about transportation costs so that it will be possible to put this in place for both research and care as usual clients.
- Furthermore, the study is embedded in the organizational structure of Médecins du Monde, including their stringent safeguards, and including training for all aspects of the study (research, therapy, referrals etc.) and regular supervision of the clinical staff. In addition:
    - Participants will be assured that participation and data collection is confidential
    - Participants will be assured that their participation or lack thereof in the study will not affect the benefits they receive from any Non-Governmental Organizations.
    - Participants will be given the contact information of the mental health team at Médecins du Monde so they can contact them in case they desire further psychosocial support or emergency care.
    - Senior members of the research team will monitor any adverse psychological events. In the case of such events, an appropriate course of action will be determined, and can range from stopping the treatment, to referral to a higher level of psychological care, etc.

Potential Problems and Risks Regarding the Execution of the Project

Given the fragility of the political context in which the research will be conducted, it is necessary to discuss potential risks that may threaten execution of the project.

Political risks are always looming in the background in Lebanon. Unexpected security events, sectarian street fights or external wars may all break out suddenly and may interfere with the execution of the project, delaying certain phases or making transportation unsafe to a degree where research activities may not be conducted as planned. However, the only foreseeable major risk regarding the planned research activities in Lebanon is a “force majeure” such as new onset war events or security conditions in Lebanon that would prevent field researchers from getting to their place of work, the team from holding activities such as meetings, or participants from attending the clinic. In that instance, these activities will be conducted at a later period when it is safe and secure to do so. Even if security events do occur in Lebanon, they tend to be restricted to narrow geographical regions. The areas in which data collection will take place are regions that have not recently had any major security events, and the research team does not expect the work to stop due to security conditions. Even in the worst case scenario where outbreaks of fighting occur, this is usually limited in time, and data collection can be expected to continue after cessation of hostilities. Importantly, the risk for spill-over of the Syrian conflict into Lebanon is unlikely according to current expert prognosis.

12. DATA HANDLING AND RECORD KEEPING:

- **Confidentiality:** The data will be used for clinical and research purposes only and collection, processing, use, and storage of the questionnaire and interview data will be treated with strict anonymity and confidentiality. Only the Lebanon-based research team will have access to identifiable private information about the participants during the study. The names and addresses of participants will be kept in locked filing cabinets and on secure password protected computers and/or servers. Identifying data will never be kept in the same electronic file as other data collected during the study. Personal data that could be used to identify participants will not be available to the international team members. Each subject will be assigned an internal study ID number. A key document linking names of study participants and internal study IDs will be stored separately in a secure location (locked cabinet and password protected system on password protected computers). When raw data is processed and final datasets for analysis are created, a second ID system will be used to further reduce the risk that data can be matched to individual participants. Only the London-based study coordinator will have access to the key to match both study ID systems.
- **Data Management and Sharing:** After data collection in Lebanon, all non-identifying data will be transferred to London where they will be processed for analysis. Most subsequent data preparation and analysis will be conducted at Queen Mary University of London where all data will be stored in the long term. All data will be processed centrally at Queen Mary University of London and stored in standard formats for use with statistical software (e.g., SPSS) after data cleaning and quality control and shared with the named co-investigators and collaborators for analysis.
- **Record Retention and Archiving:** After the funding period has ended, the data will be curated by the London based principal investigator. Once data has been collected and processed, it will be stored long-term on password-protected secure servers. Data generated will be stored for at least 20 years, in line with QMUL SOPs.

13. LABORATORIES

N/A

14. PRODUCTS, DEVICES, TECHNIQUES AND TOOLS

All psychological and psychosocial measures and interventions are described in section 8 (see Table 2. Constructs and Measures).

15. SAFETY REPORTING

AEs or SAEs are unlikely in this study as the procedures are low risk. However, any adverse events will be reported to and recorded by the Lebanon-based trial coordinator. SAEs will be immediately reported to the London-based study coordinator, who will report to the CI, sponsor, and American University of Beirut IRB when appropriate. The Lebanon-based trial coordinator will also report to the the local PI / clinical psychologist, Dr Tania Bosqui, within 24 hours so that appropriate clinical care (including referral to other services, if necessary) can be provided. AEs will be recorded and reported to the PI, London-based study coordinator, and DSMC monthly. Where necessary, they will be discussed with the PI and Study Coordinator during weekly skype meetings to agree on follow up or changes to treatment.

If the safety of the study participants or field work staff is believed to be at risk because of changes to the security situation in Lebanon then the CI, in discussion with the Lebanon-based PI, Co-I, and study coordinators, may make the decision to suspend or postpone data collection in some regions. In this event, the sponsor and American University of Beirut IRB will be informed by phone immediately and in writing within 3 days.

16. MONITORING & AUDITING

Development of SOPs for all aspects of the study will be carried out in consultation with relevant experts, and under the guidance of the JRMO, to ensure compliance with relevant UK and Lebanese laws.

A trial steering group (see section 17 for details) will review the protocol before each phase of data collection begins. Annual review by the steering group will also cover study milestones, difficulties and delays, and preliminary data analysis and results. They will suggest modifications to the protocol in light of review of the study progress and with changing ideas and emerging technologies in their fields of work.

Changes to the protocol will be reviewed by the sponsor and the IRB at the American University of Beirut. Where appropriate, advice will be sought from specific members of the trial steering group when changes to the protocol are being developed and prior to submission to the sponsor and IRB.

The Lebanon-based trial coordinator (Mr Chéhadé) will be responsible for monitoring recruitment and data collection. He will ensure that staff have entered all data into study databases and that these have been backed up. The Lebanon-based trial coordinator will report daily to the London-based study coordinator regarding recruitment and data collection. They will report on a weekly basis regarding whether recruitment and data collection targets are being met, and plans for future recruitment and data collection.

The London-based study coordinator (Dr. McEwen) will monitor data collection regularly by reviewing data uploaded to the Qualtrics server and will check that other databases have been backed up onto remote servers. She will identify any problems with meeting recruitment and data collection targets, as well as any other problems or breaches of protocol or SOPs and will report these to the CI (Prof. Pluess).

Clinical / technical supervision

Adequate clinical supervision is an important aspect of the study and will be provided separately for CETA/t-CETA and TaU staff. Supervision for the CETA/t-CETA will be provided by Laura Murray and Stephanie Skavenski, with Roland Weierstall acting in an advisory capacity. Staff delivering exclusively TaU will be integrated into the MdM Mental Health team structure and supervision will be provided by the dedicated clinician who supervises that team.

The clinical psychologist who leads the t-CETA study, Nicolas Chéhadé, will be supervised by Laura Murray (and/or Stephanie Skavenski). Case managers working on the t-CETA study will be supervised directly by Nicolas Chéhadé. CETA staff will receive the following clinical supervision per week (during treatment periods):

- Weekly one to two-hour skype supervision with Laura Murray (and/or Stephanie Skavenski) for Nicolas Chéhadé
- Weekly two-hour face-to-face supervision meetings with Nicolas Chéhadé for case managers delivering CETA or t-CETA
- Weekly one/two-hour skype or face-to-face supervision for Nicolas Chéhadé and case managers by Tania Bosqui on intake interviews, diagnostic decisions, and managing risk issues
- Ad-hoc supervision for Nicolas Chéhadé and case managers by Tania Bosqui on urgent/ emergency cases.

MdM Treatment as Usual:

- The psychotherapist and case manager will be integrated into the MdM Mental Health team and will receive weekly supervision from the MdM external clinical expert

Prof. Pluess will be responsible for overall monitoring of study progress and of submitting reports to the funder, sponsor, and IRB. Progress reports will be prepared by Prof. Pluess, Dr. McEwen, and Dr. Bosqui.

17. TRIAL COMMITTEES

Research Team:

The proposed study represents a strong collaboration between researchers from four leading research institutions in Europe, USA and the Middle East and an experienced international non-governmental medical humanitarian organisation:

- Queen Mary University of London (QMUL, UK): QMUL is ranked 9th in the UK for research quality and committed to achieving the highest quality research to tackle the most challenging and pressing research problems.
- Johns Hopkins Bloomberg School of Public Health (JHSPH, USA): JHSPH is the largest school of public health in the world with research ongoing in the USA and more than 90 countries worldwide.

- American University of Beirut (AUB, Lebanon): AUB is ranked as the number one university in Lebanon and is among the top 250 universities in the world.
- Medical School Hamburg (MSH, Germany): MSH is a new private state-approved university for health and medicine, founded in 2009.
- Médecins du Monde (MdM, Lebanon): For more than 35 years, MdM has been caring for the most vulnerable populations. MdM currently works in 44 countries across all continents. MdM has been working in Lebanon for nearly 30 years and specifically on the response to the Syrian crisis since 2012. The goal of MdM in Lebanon is to offer medical care to Syrian refugees and vulnerable Lebanese affected by this crisis. Currently, medical assistance, including mental health and psycho-social support, is provided through three partners in four primary healthcare centres in the Beqaa valley.

We will appoint a Trial Steering Group comprising at least two members of the study team and at least 2 independent members with expertise in clinical trials and/or psychological interventions. A similar advisory board is already in place for the BIOPATH study. Furthermore, we will work closely with the IASC Reference Group on Mental Health and Psychosocial Support in Emergency Settings. Importantly, the global IASC coordinator, the national mental health programme lead in Lebanon as well as all leading mental health stakeholders in Lebanon have already been consulted and informed in person by Prof. Pluess about the details of the proposed study.

Involvement in development of proposal

All partners actively contributed to the design of the study and have been involved in the write up of the proposal under the leadership of Prof. Pluess.

Commitment and ownership of local research partners: The local partners are involved in all questions and aspects regarding the research design and management of the study. MdM are highly committed to research as they have proven in the ongoing BIOPATH collaboration with Prof. Pluess over the last year. The current proposal reflects an equal and established collaboration with local partners, characterised by equity, transparency and mutual benefit.

History of Partnership: Prof. Pluess and his team have been collaborating with MdM and Dr Hijazi (AUB) over the last year in relation to a large ongoing NIH funded study on resilience of Syrian refugee children in Lebanon (BIOPATH). The collaboration with Drs Murray and Bolton from JHSPH, Dr Weierstall from MSH, and Dr Bosqui from AUB represents a new addition to the already established partnership between Prof. Pluess, Dr Hijazi, and MdM.

Quality of research consortium: The research consortium features an exceptionally strong team of world leading experts and is well positioned to conduct the planned work to the highest standard. Dr Murray is the original author of CETA and together with Ms Skavenski highly experienced in training and supervision of CETA providers in low and middle income countries. Drs Bolton and Murray have also extensive experience in conducting randomised controlled trials to test the efficacy and implementation of CETA. Further expertise in transcultural trauma research and treatment is provided by Dr Weierstall. MdM have a long history of providing

excellent health services in Lebanon and are perfectly suited to oversee the field work given their ongoing involvement in research.

PI: Prof. Pluess is currently heading a large study on resilience of Syrian refugees in Lebanon, supported by Dr McEwen. He and his team are familiar with the challenges and opportunities of cross-cultural international research as well as the specific refugee context in Lebanon. Over the last three years he established strong connections to the major mental health stakeholders in Lebanon, including the Ministry of Public Health, UNICEF, UNHCR and several NGO's.

Building capacity of local researchers: The study will build on and strengthen the research capacity already set up at MdM for the BIOPATH study and provide local researchers as well as students and lay providers with the opportunity to get involved in the study and acquire new skills (data collection, CETA training and delivery).

Steering Group

Membership

- Michael Pluess (chair)
- Fiona McEwen
- Representative for MdM (tbc)
- Representative for Clinical Team (tbc)
- Two independent experts (e.g., with expertise in clinical trials, mental health in refugee communities): Rabih El Chammay and Mary Deeb

Role

To set overall scientific direction of trial, develop and agree trial design, identify and suggest solutions to challenges, monitor trial progress.

Meeting schedule

1. Before trial begins
2. At conclusion of trial when preliminary data analysis has been conducted

Data Safety Monitoring Committee

Membership

- Michael Pluess (chair)
- Fiona McEwen
- Lead clinical psychologist on study
- Representative for MdM or clinical team (tbc)
- Two independent experts (e.g., with expertise in clinical trials, statistician): Rabih El Chammay and Mary Deeb

Role

To monitor data collection and management (including randomisation and blinding procedures), to monitor for adverse events and appropriate response to adverse events, to ensure that all data is managed to the standards expected of a randomised controlled clinical trial.

Meeting schedule

1. Before trial begins
2. Immediately after completion of t-CETA vs. TaU leg in Phase II

Ongoing monitoring

At the first meeting the committee shall agree on methods of monitoring data safety on an ongoing basis, decide on reporting procedures, and monitor according to these procedures for the duration of the trial.

18. FINANCE AND FUNDING

All costs will be covered with external grant money from R2HC.

19. INDEMNITY

The IRB at the American University of Beirut, QMUL, and Médecins du Monde have agreed that indemnity is not required during Phase I because participants will be provided with a treatment that is not novel and that does not pose any greater risk than the clinical care provided by Médecins du Monde.

For Phase II, the insurance that Queen Mary University of London has in place provides "No Fault Compensation" for participants which provides an indemnity to participants for non-negligent harm.

20. DISSEMINATION OF RESEARCH FINDINGS

Study results will be published in peer-reviewed journals and presented at scientific conferences. Additionally, summaries will be prepared for dissemination among NGOs and other agencies working with refugee populations.

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