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Brief imagery rescripting vs. usual care and treatment advice in refugees with posttraumatic stress disorder: study protocol for a multi-center randomized-controlled trial

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ABSTRACT

Background: Many refugees have experienced multiple traumatic events in their country of origin and/or during flight. Trauma-related disorders such as posttraumatic stress disorder (PTSD) or complex PTSD (CPTSD) are prevalent in this population, which highlights the need for accessible and effective treatment. Imagery Rescripting (ImRs), an imagery-based treatment that does not use formal exposure and that has received growing interest as an innovative treatment for PTSD, appears to be a promising approach.

Objective: This randomized-controlled trial aims to investigate the efficacy of ImRs for refugees compared to Usual Care and Treatment Advice (UC+TA) on (C)PTSD remission and reduction in other related symptoms.

Method: Subjects are 90 refugees to Germany with a diagnosis of PTSD according to DSM-5. They will be randomly allocated to receive either UC+TA ($n = 45$) or 10 sessions of ImRs ($n = 45$). Assessments will be conducted at baseline, post-intervention, three-month follow-up, and 12-month follow-up. Primary outcome is the (C)PTSD remission rate. Secondary outcomes are severity of PTSD and CPTSD symptoms, psychiatric symptoms, dissociative symptoms, quality of sleep, and treatment satisfaction. Economic analyses will investigate health-related quality of life and costs. Additional measures will assess migration and stress-related factors, predictors of dropout, therapeutic alliance and session-by-session changes in trauma-related symptoms.

Results and Conclusions: Emerging evidence suggests the suitability of ImRs in the treatment of refugees with PTSD. After positive evaluation, this short and culturally adaptable treatment can contribute to close the treatment gap for refugees in high-income countries such as Germany.

Trial registration: German Clinical Trials Register under trial number DRKS00019876, registered prospectively on 28 April 2020.

HIGHLIGHTS
• Many refugees have experienced traumatic events.
• This trial investigates the efficacy of imagery rescripting, a short and culturally adaptable treatment that can contribute to close the treatment gap for refugees with posttraumatic stress disorder in high-income countries.

Breve Reescritura de imágenes vs. Cuidado habitual y consejería de tratamiento en refugiados con trastorno de estrés postraumático: Protocolo de estudio para un ensayo multicéntrico controlado y aleatorizado

Antecedentes: Muchos refugiados han experimentado múltiples eventos traumáticos en su país de origen y/o durante la huida. Los trastornos relacionados con el trauma, como el trastorno de estrés postraumático (TEPT) o el trastorno de estrés postraumático complejo (TEPTC), son frecuentes en esta población, lo que pone de relieve la necesidad de un tratamiento accesible y eficaz. La reescritura de imágenes (ImRs, en sus siglas en inglés), un tratamiento basado en imágenes que no utiliza la exposición formal y que ha recibido un creciente interés como tratamiento innovador para el TEPT, parece ser un enfoque prometedor.

Objetivo: Este ensayo controlado aleatorizado tiene como objetivo investigar la eficacia de la ImRs para los refugiados en comparación con cuidado habitual y consejería de tratamiento (UC+TA) en la remisión del TEPT(C) y la reducción de otros síntomas relacionados.

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Método: Los sujetos son 90 refugiados en Alemania con un diagnóstico de TEPT según el DSM-5. Serán asignados aleatoriamente para recibir UC+TA (*n* = 45) o diez sesiones de ImRs (*n* = 45). Las evaluaciones se llevarán a cabo al inicio, post-intervención, con un seguimiento de tres meses y un seguimiento de 12 meses. El resultado primario es la tasa de remisión del TEPT(C). Los resultados secundarios son la gravedad de los síntomas del TEPT y del TEPTC, los síntomas psiquiátricos, los síntomas disociativos, la calidad del sueño y la satisfacción del tratamiento. Los análisis económicos investigarán la calidad de vida y los costos relacionados con la salud. Medidas adicionales evaluarán los factores relacionados con la migración y el estrés, los predictores de la deserción, la alianza terapéutica y los cambios sesión por sesión en los síntomas relacionados con el trauma.
Resultados y conclusiones: Las evidencias emergentes sugieren la idoneidad de la ImRs en el tratamiento de los refugiados con TEPT. Después de una evaluación positiva, este tratamiento corto y culturalmente adaptable puede contribuir a reducir la brecha de tratamiento para los refugiados en países de altos ingresos como Alemania.

患有创伤后应激障碍的难民中简短意向重构与常规护理和治疗建议的对比：一项多中心随机对照试验的研究方案

背景: 许多难民在其原籍国和/或在逃亡过程中经历了多次创伤事件。例如创伤后应激障碍 (PTSD) 或复杂性PTSD (CPTSD) 的创伤相关疾病, 在此人群中普遍存在, 这凸显了对于可用且有效治疗方法的需求。意向重构 (ImRs) 是一种基于影像, 不使用正式暴露方法的治疗方法, 作为一种治疗PTSD的创新方法受到越来越多的关注, 似乎是一种有前途的方法。
目的: 此项随机对照试验旨在考查相较于常规护理和治疗建议 (UC + TA), ImRs对难民 (C) PTSD的缓解和其他相关症状的减轻上的疗效。
方法: 被试为90名具有DSM-5 PTSD诊断的德国难民。他们将被随机分配至接受UC + TA组 (n = 45) 或10疗程ImR组 (n = 45) 。在基线, 干预后, 3个月随访和12个月随访时进行评估。主要结果是(C)PTSD的缓解率。次要结果是PTSD和CPTSD症状, 精神病症状, 分离症状的严重程度, 睡眠质量和治疗满意度。经济分析将考查健康相关生活质量和费用。其他测量将评估移民和压力相关因素, 辍学的预测因素, 治疗联盟以及创伤相关症状的疗程性治疗变化。
结果与结论: 新兴证据表明ImRs在治疗PTSD难民中的适用性。经过积极评估后, 这个短期, 具有文化适应性的治疗方法可以缩小德国等高收入国家对难民的治疗差距。

1. Background

Currently, 79.5 million people have been forcibly displaced worldwide and 26 million of them have fled to another country (United Nations High Commissioner for Refugees, 2020). More people have therefore been forced to leave their home country than ever before and the majority has experienced multiple traumatic events (Nesterko, Jäckle, Friedrich, Holzapfel, & Glaesmer, 2019). Accordingly, posttraumatic stress disorder (PTSD) was the most prevalent mental disorder in a survey of refugees recently arrived in Germany (35%; Nesterko et al., 2019). High prevalence rates (e.g. 21% in a sample of refugees living in Switzerland; Hecker, Huber, Maier, & Maercker, 2018) have also been found for Complex PTSD (CPTSD), a new diagnosis in ICD-11 that is conceptualized as a reaction to chronic or repeated traumatic events from which escape is difficult or impossible (e.g. torture) and that is characterized by additional symptoms related to disturbances in self-organization (DSO; World Health Organization, 2019). Treatment of trauma-related disorders in refugees therefore presents an urgent clinical problem Figure 1.

1.1. Psychological treatment for PTSD in refugees

Several clinical trials have investigated the efficacy of psychological interventions for refugees with PTSD (RWP). Most trials have studied trauma-focused cognitive-behavioural therapy (CBT), including narrative exposure therapy. Meta-analyses and systematic reviews summarizing the current evidence have shown trauma-focused psychotherapy to be effective with medium to large effects (Kip, Priebe, Holling, & Morina, 2020; Lambert & Alhassoon, 2015; Morina, Malek, Nickerson, & Bryant, 2017; Nosè et al., 2017; Thompson, Vidgen, & Roberts, 2018; Tribe, Sendt, & Tracy, 2019; Turrini et al., 2019). However, results are heterogeneous across meta-analyses and reviews, and considerable challenges remain. First, the number of published randomized-controlled trials (RCTs) is still limited [e.g. the most recent meta-analysis by Kip et al. (2020) included a total of 14 RCTs], and their methodological quality is considered rather low (Kip et al., 2020; Nosè et al., 2017; Thompson et al., 2018). With few exceptions, sample sizes are modest at most. Second, although existing trials have typically shown large uncontrolled effect sizes (ESs) on the reduction of PTSD symptoms from pre- to post-treatment, controlled ESs are mostly in the moderate range, leaving room for improvement. For example, Kip et al. (2020) reported that active interventions yielded a pooled ES of 0.77 when experimental treatments were compared to passive and active control conditions. This effect size is lower than effect sizes resulting from trials including all populations with PTSD (Lewis, Roberts, Andrew, Starling, & Bisson, 2020). Third, it remains unclear whether the observed short-term effects are sustainable in the long term. Finally, most evidence-
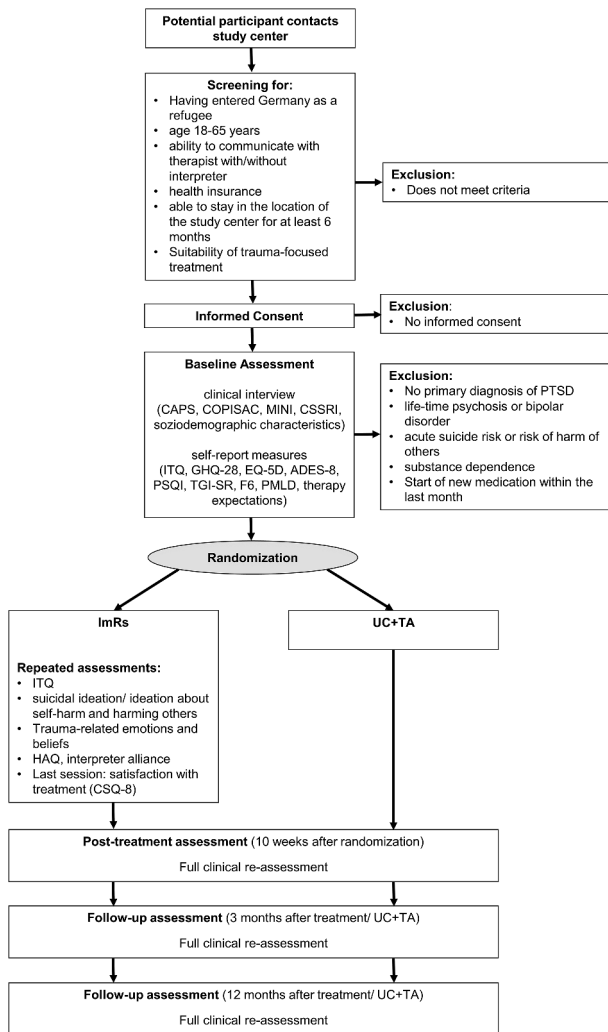
Figure 1. Flowchart.

based treatments for RWP include repeated exposure to the trauma memory. The dissemination of exposure-based treatment for PTSD is, however, notoriously challenging as therapists and patients are often reluctant to use this type of intervention in populations suffering from more complex symptomatology (Becker, Zayfert, & Anderson, 2004). A possible alternative is Imagery Rescripting (ImRs), an imagery-based treatment that does not use formal exposure and that has received growing interest as an innovative treatment for PTSD.

1.2. Imagery rescripting

ImRs is designed to directly modify the content of distressing memories using imagery (Arntz, 2012; Holmes, Arntz, & Smucker, 2007). Patients are first guided to imagine the beginning of a traumatic event, including all sensory impressions, emotions, bodily sensations, and cognitions. When the memory of the traumatic event is fully and vividly activated, they are asked to imagine changing the course of events in a helpful way until their needs in this situation are

fully met. This typically involves disempowering the perpetrator(s) and then establishing feelings of safety, comfort, assurance, self-efficacy, and social inclusion. It is hypothesized that ImRs works through changing the meaning of the memory (Arntz, 2012) and entails transformations in core belief systems (Arntz & Weertman, 1999; Holmes et al., 2007).

A meta-analysis on the efficacy of ImRs has shown large treatment effects for psychological complaints associated with aversive memories, such as PTSD but also other disorders (Morina, Lancee, & Arntz, 2017). Clinical trials evaluating imagery-based interventions for patients with PTSD symptoms have typically found large to very large pre-post effects (e.g. Jung & Steil, 2013; Müller-Engelmann & Steil, 2017; Raabe, Ehring, Marquenie, Olff, & Kindt, 2015). However, to date, there is only one study investigating the efficacy of ImRs in RWP (Arntz, Sofi, & van Breukelen, 2013). In this multiple-baseline study, 10 sessions of ImRs were administered to 10 RWP. Participants were highly burdened in terms of PTSD severity as well as poor social integration, resettlement distress, or the need of interpreters in treatment. However, results of this pilot study were highly promising showing significant and substantial reductions in PTSD symptoms and all patients but one had remitted from PTSD at the end of treatment (Arntz et al., 2013).

1.3. Rationale for the present study

Given the current evidence and the potential advantage over traditional exposure-based interventions when treating PTSD (Arntz et al., 2013; Morina et al., 2017), ImRs appears to be a highly promising intervention for RWP. This study, therefore, aims to compare the efficacy of ImRs as an innovative intervention for refugees suffering from PTSD with usual care and treatment advice (UC+TA). ImRs comprises individually tailored outpatient culturally adapted techniques to alter trauma memories. It is based on patients' idiosyncratic needs and preferred course of action and thus can easily be tailored to each patient's individual situation as well as cultural and religious background.

The principal research objectives are 1) to test the efficacy of ImRs on PTSD and CPTSD remission and symptom reduction in refugees comparing the short- and long-term outcome with UC+TA, 2) to investigate gender as a potential moderator of treatment effects, and 3) to test the effects of treatment on secondary outcome measures including improvement of general psychiatric symptoms and functioning, dissociation, and sleep.

2. Methods

The present study is part of the ReCAP consortium (Federal Ministry of Education and Research, 2020) investigating interventions for refugees at different

levels of specificity and treatment intensity. ReScript is conducted as a multi-centre RCT at four sites in Germany (Frankfurt, Munich, Muenster & Marburg). Patients will be treated at four university outpatient centres for psychological treatment.

2.1. Sample

Patients can be included in the study if they have a primary diagnosis of PTSD according to DSM-5, have entered Germany as a refugee, are between 18 and 65 years old, are able to communicate with the therapist with or without the help of an interpreter, are motivated to undergo trauma-focused treatment, have health insurance that covers psychological treatment costs,[1] are able to stay in the location of the study centre for at least another six months, and have signed an informed consent form. Exclusion criteria are a lifetime diagnosis of psychosis, bipolar disorder or substance dependence, acute suicide risk or risk of harm of others, and start of new medication for mental health problems within one month prior to the study.

Recruitment of patients will be conducted via established collaborations with local service providers for refugees, health-care providers, cultural brokers, and via a project website and (social) media.

2.2. Procedure

When a potential participant contacts the study centre, an initial screening will be conducted (see Figure 1). If a patient seems eligible for the study, written informed consent will be obtained and they will be invited for the baseline assessment. A trained assessor will perform a clinical interview to determine whether inclusion and exclusion criteria are met. The patient will then complete self-report instruments assessing symptoms of PTSD and CPTSD and further outcomes. Patients meeting all inclusion and none of the exclusion criteria will then be randomly assigned to receive either ImRs or UC+TA. Randomization will be stratified by gender and centre and performed centrally by the Coordinating Center for Clinical Studies in Marburg, Germany. The chance for allocation to the intervention group and the control group is 1:1. If a patient is randomized to the ImRs group, treatment will begin within eight weeks after randomization.

2.3. Use of interpreters

If a patient does not have sufficient German language skills, an interpreter will be present during interactions with study personnel, including interviewers and therapists. Interpreters are fluent speakers of the patient's language. It is their task to provide verbatim interpretation of what is being said by study personnel and the patient.

All interpreters will complete a web-based training that covers study procedures including aims and techniques of ImRs and appropriate translation in the psychotherapy context. Interpreters will receive regular supervision by the supervisors at the study site (i.e. a principal investigator or a supervisor with extensive experience in trauma-focused psychotherapy and imagery rescripting) or supervisors at collaborating institutions that provide therapy and counselling for refugees. Accuracy of interpretation will be confirmed using videotapes of therapy sessions and clinical interviews. Videotapes will be randomly selected and the accuracy of the interpretation will be evaluated by a trained independent interpreter.

2.4. Treatment

2.4.1. Imagery rescripting

ImRs consists of ten 100-min sessions of manualized treatment within 10 weeks. The first two sessions are dedicated to psychoeducation about PTSD, providing a rationale for ImRs, and constructing a list of traumatic events and intrusive memories. In Session 2, ImRs is practised with an unpleasant but non-traumatic memory. After that, each session is dedicated to rescripting at least one traumatic memory according to a previously established order. This order is based on the age when the event occurred and the (decreasing) amount of distress caused by the traumatic event and memory.

If a patient suffers from severe dissociative symptoms, frequent and/or severe suicidal ideation, or frequent ideas of harming others, a maximum of two additional sessions can be scheduled. A training in skills for distress tolerance and emotion regulation as used in Dialectical Behaviour Therapy (Linehan, 1993) is provided in these sessions. Similarly, if the patient experiences a crisis caused by external factors (e.g. issues related to the asylum-seeking process, court hearings, or housing) the additional sessions can be used for formal problem-solving interventions. In the case of imminent suicidality, the usual measures as required in the German Healthcare System will be taken, including initiating inpatient crisis intervention if necessary. After such crisis intervention, the type and dosage of crisis intervention are assessed and the study treatment can continue. Additional sessions can be scheduled in case it would not be ethically acceptable or irresponsible to stop treatment. The decision to continue treatment is made by the principal investigators and documented in the study database as a protocol violation.

The majority of sessions are dedicated to rescripting procedures. The trauma memory is first reactivated by asking the patient to vividly imagine and describe the traumatic experience from the first-person perspective and in present tense, including

sensory impressions, thoughts, feelings, bodily sensations, and needs. When the trauma memory and the associated meanings and emotions are vividly activated, the rescripting starts. The patient is asked to imagine an intervention changing the course of events in a helpful way, e.g. disempowering the attacker, getting saved or freeing themselves from the situation, and being comforted, cared for, reassured, and/or socially reconnected. Patients are explicitly encouraged to use anything needed to achieve the alternative outcomes, including helpers (e.g. the therapist, the now grown-up or older patient, or another person), superpowers, or fantasy figures. The rescripting always ends with the patient feeling safe. To train the patient in this procedure, the therapists takes the lead in the first rescriptings, i.e. enters the scene and intervenes according to the patient's needs. The lead is then gradually handed over to the patient. In case of childhood trauma, the grown-up patient then enters the scene to help the child and provide comfort and support to the past self.

The procedure is different from imaginal exposure because the focus is on meeting the patient's personal needs and being safe instead of on habituation. In addition, rescripting starts before the worst moment of the traumatic memory is activated, making the treatment potentially more tolerable for patients than exposure-based treatment (Morina et al., 2017). The last session focuses on the evaluation of treatment and relapse prevention.

ImRs will be administered by fully licenced psychotherapists or psychotherapists in advanced training. All therapists will attend a two-day workshop and then treat a pilot case under close supervision.

Regular supervision twice a month at the four centres as well as telephone-based case consultation for all therapists twice a month will ensure treatment adherence. Therapists' adherence to the treatment manual and general competence, PTSD-specific competence, and ImRs-specific competence will be evaluated with rating scales that will be developed based on existing instruments (Dittmann et al., 2017; Gutermann et al., 2015). All therapy sessions will be videotaped and two randomly selected videos per patient will be rated by trained independent raters.

2.4.2. Usual care and treatment advice (UC+TA)

Patients in the UC+TA condition will be referred to institutions of public mental health-care and psychological support for refugees. Referral will be made through a standardized information leaflet that is adapted to the local situation at the respective trial site and includes information about the German mental health-care systems as well as local services. If patients are dissatisfied with the support or treatment they receive, they will be offered ImRs after Follow-up 2 that is carried out 15 months after study intake.

2.5. Assessments

Assessments will be conducted at four time points: Baseline, after the end of the intervention period (i.e. 10 weeks after randomization), three months after the end of treatment (Follow-up 1), and 12 months after the end of treatment (Follow-up 2). Patients will receive a compensation of 8 Euro/hour for their participation in the follow-up assessments. Table 1 gives

Table 1. Schedule of assessments.

	Baseline (before randomization)	Session[1] 1	2	3	4	5	6	7	8	9	10	Post-Intervention (10 weeks after randomization)	Follow-Up 1 (3 months after ImRs/UC+TA)	Follow-Up 2 (12 months after ImRs/UC+TA)
Socio-demografic information	x													
CAPS & COPISAC	x											x		x
MINI	x											x		x
LEC	x													
CSSRI	x											x (social and health services only)	x	x
ITQ	x	x	x	x	x	x	x	x	x	x	x	x	x	x
GHQ-28	x											x	x	x
ADES-8	x											x	x	x
PSQI	x											x	x	x
EQ-5D	x											x	x	x
FS6	x													
TGI-SR	x											x	x	x
PMLD	x													
therapy expectations	x													
HAQ[1]				x		x				x				
Interpreter alliance[2]		x												
suicidal ideation, and ideation about self-harm and harming others	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Emotions and beliefs[1]		x	x	x	x	x	x	x	x	x	x			
CSQ-8[1]											x			

CAPS = Clinician Administered PTSD Scale, COPISAC = Complex PTSD Item Set additional to the CAPS, MINI = Mini International Neuropsychiatric Interview for DSM-5, LEC = Life Events Checklist, CSSRI = Client Sociodemographic and Service Receipt Inventory, ITQ = International Trauma Questionnaire, GHQ-28 = General Health Questionnaire, A-DES = Adolescent Dissociative Experiences Scale, PSQI = Pittsburgh Sleep Quality Inventory, EQ-5D = Euroqol-5D, FS6 = Forcedness Scale, TGI-SR = Traumatic Grief Inventory–Self Report, PMLD = Post-Migration Living Difficulties Questionnaire, HAQ = Helping Alliance Questionnaire, CSQ-8 = Client Satisfaction Questionnaire. [1]ImRs group only, [2]therapists and interpreters only.

an overview of all collected measures at each measurement point.

If needed, clinical interviews will be conducted with the help of an interpreter. Self-report instruments are available in German, English, Arabic, and Farsi. If available, instruments with validated Farsi and Arabic versions were selected. Instruments without validated translations were translated into Farsi and Arabic and back-translated by native speakers with a background in psychology. Patients unable to complete self-report questionnaires on their own will receive assistance from the interviewer and the interpreter.

2.5.1. Primary outcome

Primary outcome is the remission rate, i.e., the percentage of patients going into remission after the baseline assessment. Remission is defined as not meeting DSM-5 criteria for PTSD or ICD-11 criteria für CPTSD. Diagnosis of PTSD will be established using the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2013), a structured clinical interview for the assessment of PTSD criteria according to DSM-5. PTSD symptom severity, as well as the onset and duration of symptoms, subjective distress, and functional impairment, can also be evaluated. The CAPS has very good psychometric properties and is widely considered as the gold standard in assessing PTSD (Weathers et al., 2018). To enable a diagnosis of CPTSD according to ICD-11, the Complex PTSD Item Set additional to the CAPS (COPISAC; Lechner-Meichsner & Steil, under review) will be used. COPISAC consists of three items pertaining to DSO. One item each assesses persistent and pervasive difficulties with affect regulation, self-concept, and relationships. Two additional items assess impairment regarding social, occupational or other areas of functioning. Structure and scoring closely follow the CAPS-5.

Clinical interviews will be videotaped. To assess interviewer reliability, two interviews per interviewer will be randomly selected. Independent ratings of these videos will be made by a clinician rater who is very experienced in administering the CAPS but not involved as an interviewer in the study.

2.5.2. Secondary outcomes

Severity of PTSD and CPTSD will be rated by trained interviewers using the CAPS-5 and COPISAC. The International Trauma Questionnaire (ITQ; Cloitre et al., 2018) will be used to measure self-reported symptoms of PTSD and CPTSD according to ICD-11. The ITQ measures PTSD and CPTSD symptom clusters with two items each; six additional items measure functional impairment. The measure has good psychometric properties (Cloitre et al., 2018). The ITQ will be administered at the four measurement points as well as in every therapy session to assess trajectories of change over treatment duration in the ImRs group.

General psychiatric symptoms will be assessed using the General Health Questionnaire (GHQ-28; Goldberg, 1978). Its 28 items form four subscales measuring somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression.

Dissociative symptoms will be assessed with the eight-item version of the Adolescent Dissociative Experiences Scale (ADES-8; Martínez-Taboas et al., 2004). The scale focuses on both problematic dissociative experiences as well as normal dissociative experiences. Its items correspond in content to items from the short version of the Dissociative Experiences Scale for adults (Bernstein & Putnam, 1986), but both items and instructions are simpler and briefer. The ADES-8, therefore, seemed suitable for our sample.

Sleep quality will be measured with the Pittsburgh Sleep Quality Inventory (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Its 19 items focus on different sleep-related characteristics (e.g. quality, latency, duration, efficiency, and disturbances).

Satisfaction with treatment will be assessed with the Client Satisfaction Questionnaire (CSQ-8) at post-treatment in the ImRs group (Hasler et al., 2004; Larsen, Attkisson, Hargreaves, & Nguyen, 1979). It comprises eight items.

2.5.3. Health economics

For economic analysis of ImRs vs. UC+TA, costs will be measured by a modified Client Sociodemographic and Service Receipt Inventory (CSSRI; Roick et al., 2001). The section of the CSSRI that allows to assess the use of social and health services (i.e. inpatient hospital services, outpatient hospital services, primary and community care contacts, non-medical support) is used to assess amount and type of treatment received by UC+TA participants at all points of measurement. Utilities will be assessed by the EuroQol (EQ-5D; EuroQol Group, 2019). Good psychometric properties of the EQ-5D have been reported in different languages (e.g. Aburuz, Bulatova, Twalbeh, & Gazawi, 2009).

2.5.4. Additional measures

2.5.4.1. Migration and stress-related measures.

We will assess perceived forcedness to flee the home country using the six-item Forcedness Scale (FS6; Echterhoff et al., 2020). This newly developed scale is based on a recent model of refugee integration that emphasizes perceived forcedness and ensuing perils as distinctive factors of refugee migration.

Recent studies have shown a high comorbidity between PTSD and Prolonged Grief Disorder (PGD) in refugees (e.g. Comtesse & Rosner, 2019). PGD symptoms will therefore be assessed using the Traumatic Grief Inventory-Self Report (TGI-SR; Boelen, Djelantik, de Keijser, Lenferink, & Smid,

2019) at all time points. At baseline, a history of loss experiences and information regarding the most distressing loss will be collected.

2.5.4.2. Predictors of dropout. The Post-Migration Living Difficulties Questionnaire (PMLD; Silove, Steel, McGorry, & Mohan, 1998) and three items assessing therapy expectations from the COMPASS feedback system (Lutz, Neu, & Rubel, 2019) are included as potential predictors of dropout. These measures are part of a collaboration with the PrevDrop study (*Predicting and preventing Dropout in Research, Assessment, and Treatment with Refugees*) funded by the Federal Ministry of Education and Research under grant number 01EF1901 (Federal Ministry of Education and Research, 2020).

2.5.4.3. Process measures. A number of measures will be collected in the ImRs condition during therapy in addition to the above mentioned ITQ. Before every session, a brief measure of trauma-related emotions (i.e. shame, loneliness, anger) and core beliefs (e.g. 'The world is a dangerous place.') will be administered. Four beliefs and six emotions are assessed using visual analogue scales ranging from 0 (not at all) to 10 (very much). Suicidal ideation and ideation about self-harm and harming others will be assessed by the therapist in each session.

Ratings of therapeutic alliance will be collected from patients and therapists using the Helping Alliance Questionnaire (HAQ; Bassler, Potratz, & Krauthauser, 1995) at three times during treatment (sessions 3, 6, and 10). If an interpreter is used, therapists and interpreters will complete an extended assessment of working alliance with special respect to the co-working alliance between therapist and interpreter in Session 3. Interpreters will also make a rating of barriers experienced while translating.

2.6. Safety

The study will be conducted in line with standards of good clinical practice and the applicable national laws and regulations to assure that the rights, safety, and well-being of participants are protected consistent with the ethical principles according to the Declaration of Helsinki. The ethics committee of the German Psychological Association has approved the study (transaction numbers SteilRegina2019-10-18-VA, SteilRegina2020-02-26AM).

Adverse events (AE) and serious adverse events (SAE) are documented at each assessment and after each therapy session. (S)AE cover any sign, symptom, syndrome, or illness that appear in a participant during the study period and that may impair the well-being of the subject whether or not it is related to the treatment. AEs comprise occurrence of new symptoms

of a severe mental disorder, clinically significant worsening of clinical symptoms such as exacerbation of PTSD symptoms, and unforeseen or prolonged hospitalization due to psychiatric problems. SAEs comprise suicide or other cause of death, suicide attempt, self-harm, harm of others, and any other life-threatening event or event that led to physical disability. If an (S)AE has occurred, it will be entered into the electronic patient file and reported to the Data Safety and Monitoring Board and followed through until resolved.

2.7. Sample size and power calculations

The sample size calculation is based on the primary endpoint remission from PTSD, remission rate estimates for ImRs taken from the refugee pilot trial (Arntz et al., 2013), and remission rate estimates for UC+TA taken from Stenmark, Catani, Neuner, Elbert, and Holen (2013). To be on the safe side, smaller remission rates are expected for ImRs in this multi-site trial than for the pilot study carried out by experts on ImRs. Remission from PTSD is assumed to take on higher values in women than in men (Stenmark, Guzey, Elbert, & Holen, 2014; Wade et al., 2016). The gender ratio in the participants is estimated as 67% men vs. 33% women. Estimates for percent of patients with remission are as follows: a) women: ImRs = 70%, UC+TA = 28%; b) men: ImRs = 60.9%, UC+TA = 20.6%. In order to detect an odds ratio of six in each stratum between groups given a Type I error rate of 0.05 and power of 80%, 54 persons (27 per group) are required (Cochran Mantel-Haenszel test, software PASS 14, version 14.0.4, NCSS, LLC). Compensating for 40% dropouts, 90 patients will be randomized.

3. Analysis

Cochran-Mantel-Haenszel statistics will be applied to test for a difference (two-tailed) in the PTSD and CPTSD remission rates between the ImRs and UC+TA group stratified for gender. Estimated remission rates in each group and corresponding 95% confidence intervals will be presented. In addition, multivariable binary logistic regression analyses will be performed to analyse the influence of baseline covariates. As sensitivity analysis, the analysis will also be performed for the per-protocol population. The Reliable Change Index (Jacobson & Truax, 1991) will also be reported as an evaluation of clinically significant change.

Secondary endpoints include both absolute changes in continuous scores as well as categorical assessments of CAPS and COPISAC severity scores, and longitudinal data on scores on the self-report measures which will each be analysed by appropriate

hierarchical regression models adjusting for baseline covariates. All efficacy analyses will be performed for the intention-to-treat population. Statistical results reported for secondary and exploratory endpoints will not be corrected for multiple testing. Since secondary and exploratory analyses are considered expressing supportive evidence for the predefined primary endpoint, p-values therein will not be corrected for multiple testing and confidence intervals and statistical tests are of descriptive nature.

If a participant drops out of the study, multiple imputation of missing values will be applied in all efficacy analyses according to Rubin's concept (i.e., data missing completely at random, missing at random, missing not at random). Multiple imputation is a regression-based imputation procedure replacing each missing value with a set of plausible values that represent the uncertainty about the right value to impute. Thus, multiple imputation is performed with the purpose of reducing bias, but not increasing precision. Sensitivity analyses will be performed to investigate the effect of different modelling strategies for the imputation of missing values on the primary endpoint. Patients in the interventional arm who have completed less than seven sessions of ImRs are considered as dropout.

For analysis of health economics, health-care utilization will be monetarily valued by unit costs. By synthesizing costs and (clinical) outcomes, the cost analyses will be extended to a cost-effectiveness analysis or/and a cost-utility analysis depending on data quality. Economic outcomes include the incremental cost-effectiveness ratio (ICER) and cost-effectiveness acceptability curves (CEACs) based on net-benefit regression to adjust for potential confounding.

4. Discussion

Emerging evidence suggests that ImRs is at least as effective as state-of-the-art treatment for PTSD and particularly suitable in the treatment of RWP (Arntz et al., 2013). This study compares the efficacy of ImRs with UC+TA for RWP. As refugees face many barriers to receiving appropriate mental health-care, the study's objectives are of particular importance.

Compared to other psychological treatments for PTSD, ImRs is tailored idiosyncratically to each single patient instead of following the same rigid manual. The treatment is therefore adaptable to the cultural background and individual needs of each patient. This is especially important against the background of research that has shown that culturally adapted interventions are more effective than non-adapted versions of the same intervention (Hall, Ibaraki, Huang, Marti, & Stice, 2016), and that it is essential to adjust interventions developed with populations from the Global North in order to meet the needs of refugees (Naseh et al., 2019).

ImRs is also shorter than many other treatments. It, therefore, has the potential to lead to quick recovery and enable refugees to take better advantage of occupational and social opportunities. Regarding clinical practice, a short treatment may use available therapist resources in the best way, thus making trauma-focused psychotherapy available to many refugees in need. ImRs is also innovative in abstaining from formal exposure to traumatic memories. Given the known difficulties of disseminating exposure-based treatments, this is an important advantage of ImRs.

UC+TA was chosen as a comparator to provide a strong control condition for which very few data exist so far. This condition will provide important information on the quality of routine mental health-care for RWP in Germany. Results can shed light on the suitability and effects of different routine mental health-care services and identify directions for future development.

Two scheduled follow-ups will allow to study long-term effects of treatment. With a sample size based on a-priori power analysis, the trial is also adequately powered. The inclusion of additional measures to be collected over the course of therapy will provide insights into the therapeutic process including the interpreting process. To our knowledge, this is the first RCT to collect this kind of data in trauma-focused treatment with refugees. The trial will furthermore investigate the health economics of PTSD and its treatment in refugees in a Western country, which has not been assessed before.

Considering the high number of refugees who have been arriving in Europe suffering from mental health problems (Nesterko et al., 2019), suitable and efficacious treatment programmes are urgently needed. With this trial, we hope to contribute to overcoming the treatment gap for refugees in Germany and to the evidence for ImRs as a suitable treatment for trauma-related disorders.

Note

1. Health-care is compulsory in Germany and covers costs for psychotherapy. Refugees receive health insurance after a waiting time of 15 months. Before that, urgent medical needs that may also include psychotherapy are covered through social welfare services.

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