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Trauma-focused therapies for posttraumatic stress in psychosis

Submission date	Recruitment status	[X] Prospectively registered
17/06/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
18/06/2019	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
28/05/2025	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

A substantial group of people with schizophrenia have experienced traumas in their lifetime and suffer from psychological complaints as a result of these traumas. Examples of these complaints are flashbacks, nightmares, avoidance of places and people related to the trauma, avoidance of thoughts and feelings related to the trauma, feeling strong negative emotions, and being more alert and vigilant than usual. This study investigates whether three trauma-focused treatments help to reduce these symptoms in people with schizophrenia. The treatments being investigated are Prolonged Exposure therapy (PE), Eye-movement Desensitization and Reprocessing (EMDR), and Cognitive Restructuring therapy (CR). PE and EMDR therapy aim to alleviate trauma-related complaints by encouraging the reprocessing of traumatic memories. In PE therapy, the therapist asks the participant to describe the traumas in a very detailed and vivid way while recording it. The participant listens to the recording at home. These exercises teach the participant that he or she can handle talking about the trauma and encourages the processing of the trauma. In EMDR therapy, the therapist asks the participant to talk about the trauma while the therapist moves his or her fingers from left to right in front of the eyes of the participant. The participant follows the fingers of the therapists with his or her eyes, thereby stimulating the processing of the trauma. CR works by changing negative trauma-related cognitions. In CR the therapist helps the participant to recognize negative trauma-related thoughts about the self, others and the world. Together, the participant and the therapist work to change these thoughts into more adaptive and tolerable thoughts. All three treatments consist of 16 sessions of 90 minutes over 10 weeks time.

Who can participate?

Adults with a psychotic disorder in the schizophrenia spectrum and post-traumatic stress disorder

What does the study involve?

Participants are randomly allocated into one of four groups: the PE group, the EMDR group, the CR group or the waiting-list group. Participants in the waiting list group receive a trauma-focused treatment of choice after 6 months. To measure if the treatments have an effect on the trauma-related complaints, participants participate in a set list of interviews and questionnaires before they start the treatment, after 8 sessions of treatment, after the last session of the

treatment, and 3, 9 and 21 months after the last session. These interviews are carried out at the clinic where the participants receive their treatment.

What are the possible benefits and risks of participating?
The aimed for benefit of the three treatments is a reduction of trauma-related complaints. The treatments have been investigated in people with PTSD and schizophrenia before and have been shown to be safe and effective in reducing trauma-related complaints. The medical ethical committee has judged the study as inducing "no increased risk" for participants.

Where is the study run from?
1. Parnassia, Den Haag, Netherlands
2. Arkin, Amsterdam, Netherlands
3. Antes, Rotterdam, Netherlands
4. GGz Noord-Holland Noord, Netherlands
5. GGz Centraal, Hilversum, Netherlands
6. PsyQ, Den Haag, Netherlands
7. GGz Eindhoven, Eindhoven, Netherlands
8. GGz Oost-Brabant, Boekol, Netherlands

When is the study starting and how long is it expected to run for?
January 2018 to December 2026

Who is funding the study?
Stichting tot Steun VCVGZ (Foundation for VCVGZ Support), Netherlands

Who is the main contact?
1. Dr David van den Berg (scientific contact)
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NL66431.029.19

Study information

Scientific Title
The effect of prolonged exposure, EMDR and cognitive restructuring on PTSD symptoms in patients with PTSD and psychosis: a multicenter randomised controlled trial

Acronym
RE.PROCESS

Study objectives
The primary objective is to determine the effects of a full treatment dose of PE, EMDR, cognitive restructuring (CR), and Waiting List (WL) on researcher-rated severity of PTSD symptoms. The secondary objective is to investigate the effects of these treatments on researcher-rated presence of PTSD diagnosis, self-rated severity of PTSD, severity of complex PTSD symptoms, post-traumatic cognitions, dissociation, depression, paranoia, auditory verbal hallucinations, social functioning, disruption of social functioning by PTSD symptoms, resilience, personal recovery, sexual functioning, adversities, and revictimization. Third, with the 24-month follow-up the aim is to test the long-term effects on all the outcomes for the first time. Fourth, the study aims to explore how post-traumatic stress and psychosis interact dynamically, how the experimental treatments influence these interactions, and what factors significantly predict treatment response. The fifth objective is to determine the cost-effectiveness of the interventions. Sixth, the researchers will conduct a process evaluation of the therapy process by conducting interviews to examine how participants experienced receiving trauma-focused treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/03/2019, Medical Ethics Committee of VU Medical Centre Amsterdam (METc VUmc: Van der Boechorstraat 7, room H-443, PO Box 7057, 1007 MB Amsterdam, the Netherlands; Tel: +31 (0)20 44 45 58 5; Email: metc@vumc.nl), ref: 2019.046 NL66431.029.19

Study design
Single-blind multicenter randomized controlled trial

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Post-traumatic stress symptoms in patients with chronic post-traumatic stress disorder and a comorbid psychotic disorder in the schizophrenia spectrum

Interventions
Participants are randomly assigned to one of four arms. Randomization is conducted by the independent randomisation bureau of Parnassia Psychiatric Institute with the use of block randomisation with the randomisation software from www.randomizer.org. Research Randomizer (Version 4.0). The three experimental arms consist of Prolonged Exposure therapy (PE), Eye Movement Desensitization and Reprocessing (EMDR), and Cognitive Restructuring (CR) therapy. The control arm is a waiting list group up to the 6-month follow-up, after which they may choose to receive a trauma-focused treatment of choice.

All therapists will deliver PE, EMDR and CR and will be trained in all the protocols. Participants in the three treatment arms will receive a maximum of 16 sessions. Sessions will be held two times a week and will last 90 minutes.

The PE therapy will be delivered conforming to the protocol of Foa, Hembree and Rothbaum (2007). This protocol consists of imaginal exposure (whereby each session is audio recorded and participants listen to these recordings five times per week) and in vivo exposure (based on a list of avoided trauma-related stimuli).

EMDR will be delivered according to the standard 8-phase protocol by Shapiro, using the Dutch translation of the EMDR protocol. Eye movements will be applied as the default dual attention stimulus.

The CR therapy will be delivered based on the treatment program developed by Mueser, Rosenberg, Jankowski, Hablen and Monica (2004). This adapted cognitive restructuring treatment is based on cognitive models of PTSD that posit that appraisals of traumatic events, and subsequent attempts to cope with the associated negative affect, are the key factors in the development and maintenance of PTSD. The most important adaptation of this CR protocol is the exclusion of direct memory processing since the developers expected that direct trauma memory processing would be too difficult to tolerate for patients with severe mental illnesses. The treatment methods and materials are also adapted to accommodate some of the unique challenges of people with severe mental illness, e.g. cognitive impairments.

Intervention Type
Behavioural

Primary outcome measure
Researcher-rated changes in severity of PTSD symptoms as measured by the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). This will be measured at baseline, at 7 weeks (mid-treatment), 13 weeks (post-treatment), 6-month follow-up, 12-month follow-up, and 24-month follow-up.

Secondary outcome measures
1. Changes in the number of participants fulfilling the diagnostic criteria of PTSD - CAPS-5
2. Self-rated severity of PTSD symptoms, measured using PTSD Checklist for the DSM-5 (PCL5)
3. Severity of complex PTSD symptoms, measured using International Trauma Questionnaire (ITQ)
4. Posttraumatic cognitions, measured using Brief version of the Posttraumatic Cognitions Inventory (PTCI-9)
5. Dissociation, measured using Trait State Dissociation Questionnaire short version (TSDQ-s)
5. Depression symptoms, measured usingBeck Depression Inventory II (BDI-II)
6. Paranoia, measured using Green et al. Paranoid Thought Scales (GPTS)
7. Auditory verbal hallucinations, measured using Psychotic symptoms rating scales (PSYRATS) & Voice Impact Scale (VIS)
8. Disruption of social functioning by PTSD symptoms, measured using ITQ
9. Resilience, measured using Brief Resilience Scale (BRS)
10. Personal recovery, measured using Questionnaire about the Process of Recovery (QPR)
11. Sexual functioning, measured using Arizona Sexual Experience Scale (ASEX) & Sexual Autonomy Scale (SAS)
12. Social functioning measured with 2 items adapted from the Time Use Survey
13. Adversities measured using the 7-item TTIP Adverse Events Questionnaire
14. Revictimization, measured using Trauma and Life Events Checklist (TALE)
Measures 1-11 will be measured at baseline, at 7 weeks (mid-treatment), 13 weeks (post-treatment), 6-month follow-up, 12-month follow-up, and 24-month follow-up.
Measures 12-14 will be measured weekly from baseline until 6-month follow-up.

Overall study start date
01/01/2018

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Age 16+ years
2. A lifetime diagnosis of a psychotic disorder in the schizophrenia spectrum, confirmed by the Structured Clinical Interview for DSM-5 (SCID-5)
3. Full DSM-5 diagnostic criteria for chronic PTSD on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) with a minimum score ≥23
4. Willingness to undergo randomisation and a trauma-focused therapy

Participant type(s)

Patient

Age group
Adult

Sex
Both

Target number of participants
200

Total final enrolment
162

Key exclusion criteria
1. Changes in antipsychotic or antidepressant medication regimen within 4 weeks before the inclusion interview assessment (to control for medication effects)
2. Insufficient competence in the Dutch language
3. Severe intellectual impairment, defined as an estimated IQ of 70 or less
4. Not being able to travel (or be accompanied) to the outpatient service
5. Not willing or able to learn to use a smartphone

Date of first enrolment
24/06/2019

Date of final enrolment
30/04/2024

Locations

Countries of recruitment
Netherlands

Study participating centre
Parnassia
Zoutkeetsingel 40
Den Haag
Netherlands
2512 HN

Study participating centre
Arkin
Tesselschadestraat 31
Amsterdam
Netherlands
1054 ET

Study participating centre
Antes
Prins Constantijnweg 48
Rotterdam
Netherlands
3066 TA

Study participating centre
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Stationsplein 138
Heerhugowaard
Netherlands
1703 WC

Study participating centre
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Hilversum
Netherlands
1211 MS

Study participating centre
PsyQ
Lijnbaan 4
Den Haag
Netherlands
2512 VA

Study participating centre
GGz Eindhoven
Doctor Poletlaan 40
Eindhoven
Netherlands
5626 ND

Study participating centre
GGz Oost Brabant
Kluisstraat 2
Boekol

Netherlands
5427 EM

Sponsor information

Organisation
Vrije Universiteit Amsterdam

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Sponsor type
University/education

Website
https://vu.nl/nl/index.aspx

ROR
https://ror.org/008xxew50

Funder(s)

Funder type
Charity

Funder Name
Stichting tot Steun VCVGZ (Foundation for VCVGZ Support), Netherlands

Results and Publications

Publication and dissemination plan
The researchers are planning to offer the protocol for publication soon. The results on all hypotheses - as described in the 'study hypothesis' section - will be published, unreservedly. The researchers aim to publish in high-impact peer-reviewed journals. The sponsor will have no influence on the publication of the results.

Intention to publish date

30/06/2024

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V2	15/02/2019	19/06/2019	No	No
Protocol article		05/10/2022	06/10/2022	Yes	No
Statistical Analysis Plan	version 1.0	28/05/2025	28/05/2025	No	No