Clinical Effectiveness of Training for Awareness Resilience and Action Online Compared to Standard Treatment for Adolescents and Young Adults With Depression: Study Protocol and Analysis Plan for a Pragmatic, Multi-Center Randomized Controlled Superiority Trial

NCT registration identifier: NCT04747340

Study protocol revision, amendment 1.0

Date: 2022-10-14

Eva Henje

Eva Henje, PI, on behalf of the TARA study-group

Introduction

As outlined in the study protocol (1): “We strive for full transparency throughout the study and any changes made to and/or deviations made from the protocol will be reported. Any modifications of the protocol including changes of study objectives, study design, participant population, sample size, study procedures, or significant administrative aspects will require a formal amendment to the protocol. The same applies to any changes of the protocol that may be a potential benefit, disadvantage or safety concern for the participants. Such amendments will be agreed upon by the study group, approved by the national ethical review board prior to implementation and notified to all study personnel involved.”

Based on that intention and due to circumstances, that were not anticipated at the time of protocol publication we now officially make several changes to the study protocol. All changes have been agreed upon by the study group, reviewed and approved by the national ethical review board in Sweden (D.nr 2020-05734, D.nr. 2021-06418-02) and notified to all study personnel involved.

Purpose

The purpose of this amendment is to describe the revisions made to the study protocol for the clinical trial specified above.

Implementation

The changes outlined in the amendment will be implemented immediately from the time this document is published on clinicaltrials.gov. As the changes are considered minor and as only three groups (n=18) have been randomized thus far, we will not perform any separate analyses on the participants based on their inclusion before/after the implementation of the amendment.

Revision history

Revision to previous protocol version 1.0, published 11 October 2021 (1).
Amendment 1.0, 8 October 2022:

Change	Rationale	Affected protocol section
Patients will be eligible for recruitment from the year they turn 15, not from the date they turn 15 as previously specified.	To increase recruitment rates	Eligibility
Child and Adolescent psychiatry units and Youth Clinic units that belong to the same administrative Region will recruit and randomize and treat patients	The units within the same administrative Region share staff and management personnel. Region-wide recruitment facilitates the recruitment process.	Center and Participant Recruitment Procedure

Region-wide and not locally as previously specified. In the analysis these Region-wide centers (N=3-4) will be treated as one center each and not as several centers as previously specified. New randomization lists have been created using the same procedure as outlined previously. In the analysis, groups that have already been randomised will be treated as belonging to the larger center from within which they were recruited.		
A new data collection timepoint is introduced at 12 months follow-up. Only self-rating will be performed at that timepoint using the scales Reynolds Adolescent Depression Scale 2nd edition, and Multidimensional Anxiety Scale for Children.	More data will be collected for subsequent analysis of "other outcome measures", and contact is maintained with the participants to reduce participant dropout at the 24-months follow up.	Outcome Measures Analysis Plan
The timepoint from which the calculated time to follow up (3-months, 6 months follow-up etc.) starts will be the time of treatment initiation in the TARA-arm and from randomization in the Standard Treatment arm.	This was not previously defined.	Assessments
The cut-off at which participants may be recruited on CDRS-R-score only will be reduced from 40 to 35.	To increase recruitment rates.	Eligibility
Youth clinics will also post flyers with information about the study on their social media platforms.	To increase recruitment rates from these centers specifically.	Center and participant recruitment procedure.
We will allow for the possibility of randomizing up to eight eligible individuals if eight have been recruited (instead of six as previously specified).	To enable a reduction in waiting-times from recruitment to randomization.	Randomization

Consent from parents/legal guardians is no longer needed for individuals below 18 years of age.	For participation not to be contingent upon cooperating caregivers.	Eligibility
Two new exploratory outcomes have been added and both are self-rated by the participant. The scales include: 1.) A self-made questionnaire with questions related to community-aspects of TARA (administered at 3-, 6-, and 24-months follow-up to TARA-arm participants only), and 2.) A checklist with questions regarding bullying and harassment in school, during leisure-time or on-line (administered at 3-, 6-, and 24-months follow-up).	Qualitative interviews with previous TARA-participants have highlighted community-aspects as important parts of the intervention. Previous questionnaires assessed trauma in a narrow way.	Other outcome measures.

References

1. Ekbäck E, Granåsen G, Svärling R, Blomqvist I, Henje E. Clinical Effectiveness of Training for Awareness Resilience and Action Online Compared to Standard Treatment for Adolescents and Young Adults With Depression: Study Protocol and Analysis Plan for a Pragmatic, Multi-Center Randomized Controlled Superiority Trial. Front Psychiatry. 2021;12:674583.

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NCT registration identifier: NCT04747340

Study protocol revision, amendment 2.0

Date: 2024-04-09

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Introduction

As outlined in the study protocol (1): “We strive for full transparency throughout the study and any changes made to and/or deviations made from the protocol will be reported. Any modifications of the protocol including changes of study objectives, study design, participant population, sample size, study procedures, or significant administrative aspects will require a formal amendment to the protocol. The same applies to any changes of the protocol that may be a potential benefit, disadvantage or safety concern for the participants. Such amendments will be agreed upon by the study group, approved by the national ethical review board prior to implementation and notified to all study personnel involved.”

Based on this intention and due to circumstances, that were not anticipated at the time of the protocol publication, we now officially make an amendment with some new changes to the study protocol. All changes have been agreed upon by the study group, reviewed and approved by the national ethical review board in Sweden (D.nr 2020-05734, D.nr. 2021-06418-02, 2022-04979-02) and notified to all study personnel involved.

Purpose

The purpose of this amendment is to describe the revisions made to the study protocol for the clinical trial specified above.

Implementation

The changes outlined in the amendment will be implemented immediately from the time this document is published on clinicaltrials.gov. As the changes are considered minor, we will not perform any separate analyses on the participants based on their inclusion before/after the implementation of the amendment.

Revision history

Revision to previous protocol version 1.0, published 11 October 2021 (1).
Amendment 1.0, 8 October 2022.

Amendment 2.0, 9 April 2024:

Change	Rationale	Affected protocol section
Participants will be recruited to the primary care center in Region Västerbotten also from primary care units that are not youth clinics specifically. No additional pilot trial will be performed before their inclusion in the RCT.	To increase recruitment rates and to recruit with a more even distribution across the age-range. The pilot trial step is not performed as all the implementation infrastructure is already in place.	Center and participant recruitment procedure.

No MRI-scanning is performed	A large neuroimaging study of TARA has been launched at University of California San Francisco (NCT05267340)	Assessments.
The main mixed effects model will include fixed effects for treatment allocation, RADS-2-score at T0, age, study center and sex.	To avoid potential problems related to analyzing age as a dichotomous variable as previously suggested. The cut-off at 18 years of age is arbitrary and does not match cognitive and brain maturation processes.	Analysis plan
Additional professions are included as TARA-facilitators: such as pharmacist, students of clinical psychology, public health scientist	To widen the recruitment base for TARA facilitators, and to evaluate the feasibility of a broader facilitator population.	TARA intervention protocol.

References

1. Ekbäck E, Granåsen G, Svärling R, Blomqvist I, Henje E. Clinical Effectiveness of Training for Awareness Resilience and Action Online Compared to Standard Treatment for Adolescents and Young Adults With Depression: Study Protocol and Analysis Plan for a Pragmatic, Multi-Center Randomized Controlled Superiority Trial. Front Psychiatry. 2021;12:674583.