Development and Feasibility of Augmented Depression Therapy for Complex Depression: A randomised, controlled feasibility trial. (ADepT+ Feasibility Trial)

Trial Steering Committee Charter and Terms of Reference

The role of the Trial Steering Committee (TSC)

The Trial Steering Committee (TSC) will provide guidance and supervision for the project on behalf of the project's sponsor (University of Exeter) and funder (Department of Health) and to ensure that it is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice.

The day-to-day running of the project is the responsibility of the Chief Investigator.

Team Definitions

TMG – Trial Management Group: This is a group made up of the Chief Investigator, statistician and research associates. It will meet approximately monthly and oversee the running of the project.

TAG – Trial Advisory Group: This is a group of individuals with lived experience, facilitated by the Chief Investigator, which meets frequently to co-develop, consult or advise on all aspects of the project.

The general roles of the TSC are as follows:

- To provide advice, through its Chair, to the project's funder, sponsor, Chief Investigator, and TMG.
- To concentrate on the project's progress, adherence to the protocol, and patient safety.
- To consider new information of relevance to the research question.
- The rights, safety and well-being of the participants are the most important considerations and should prevail over the interests of science and society.
- To ensure appropriate ethical and other approvals are obtained in line with the project plan.
- To agree proposals for substantial protocol amendments and provide advice to the sponsor and funder regarding approvals of such amendments.
- To provide advice to the investigators on all aspects of the project.

Specific role of TSC:

Regular review of the project's progress including recruitment figures, data completeness, adherence to protocol treatment and follow-up, and safety data.

As a relatively small feasibility trial, the project does not require a separate Data Monitoring and Ethics Committee (DMEC). Some functions normally carried out by a DMEC, however, will be performed by the TSC. This will include reviewing some data and reports of serious adverse events.

Specifically, the TSC will be asked to:

- Review reports on the following data:
    - Participants' baseline characteristics
    - Data relating to key feasibility outcomes (e.g. rates of participant recruitment and retention, levels of data completeness)

    - Summaries of adverse events and serious adverse events, and more detailed case reports if deemed necessary.
- Monitor recruitment and loss-to-follow-up rates and advise on measures to increase recruitment if required.
- Make recommendations regarding the continuation or termination of the trial and any substantial amendments to the Protocol proposed by Investigators or Sponsor (e.g. eligibility criteria, sample size, or trial endpoints).
- Monitor evidence for participant safety and treatment harm (e.g., adverse events and serious adverse events) at regular intervals or in the event of concerns.
- Assess data completeness (and so encourage the collection of high-quality data).
- Consider the ethical, practical, statistical, and financial implications of any recommendations made by the TMG.
- Review and approve the Statistical Analysis Plan (SAP).
- Assess the impact and relevance of external or newly-available evidence on the trial.
- Provide advice and guidance to the CI and TMG to increase the scientific integrity of the work, the scientific validity of the protocol, and the scientific quality of the final reports.
- Be informed of any abstract submissions or presentation of any results during the running of the case series or trial.
- Maintain confidentiality of all trial information that is not in the public domain.

Blinding status of the TSC

With respect to the ADepT+ Feasibility trial the TSC will be:

- Blinded in any consideration of aggregated study data (e.g. when comparing the trial arms in terms of rates of adverse events).
- Unblinded as necessary when reviewing potential SAEs or related AEs, or other participant events: this will apply only to those members reviewing the event and only in relation to the allocation status of the participant concerned.
- The blinded status of certain non-independent TSC members and observers (research associates and assistants, trial statistician and health economist) will be respected in any decisions to unblind at TSC level.

Constitution of the TSC

- Independent members must make up a minimum of 75% of the Committee membership.
- The minimum quoracy for any TSC meeting to conduct business is 67% (two thirds) of the appointed membership.
- Only appointed members will be entitled to vote (irrespective of their level of independence) and the Chair will have a casting vote.
- The Chair and members must sign and maintain a log of potential conflicts and/or interests.
- Attendance at TSC meetings by non-members is at the discretion of the Chair.
- The primary TSC reporting line is via the Chair to the relevant NIHR Programme Director; however, communication is likely to be between the Chair and the NIHR Research Manager who has day to day responsibility for the project.

- The TSC will also have an advisory non-member who will provide mentorship to the independent statistician. The advisory non-member will not be entitled to vote and will not attend TSC meetings.

Independent TSC members:

Dr. Peter Taylor (Chair)

Prof. Jaime Delgadillo

Dr. Rosemary Greenwood

Julie Cooper (Public contributor)

Non-Independent TSC members:

Prof. Stephen Kellett

Trial Steering Committee meetings

- Meetings will take place at least every 6 months (approximately) over the course of the project, although there may be periods when more frequent meetings are necessary.
- Meetings will be called for and organised by the Chief Investigator (CI) in collaboration with the TSC Chair.
- Papers for meetings will be circulated at least one week in advance of the meeting.
- Accurate minutes of the meeting will be prepared by the CI and agreed by all members.
- Copies of minutes will be circulated amongst all TSC and TMG members, and a copy retained in the Trial Master File.
- Should the need arise, the independent members of the TSC have the option to meet without members of the research team being present.
- TSC meetings will adopt the following standing agenda items:
    - Disclosure of new competing interests
    - Relevant new information
    - Trial update
    - Recruitment and retention update
    - Adverse Events
    - PPI
    - AOB

Communication

- Communication between the TSC and the TMG will usually be between the TSC Chair and the Chief Investigator.
- All significant communications outside of formal TSC meetings should be in writing or backed up with a written record where these have taken place orally.

Procedure for Reviewing Adverse Events Trial Steering Committee (TSC).

The CI or her delegate will make an initial determination of whether the event is an SAE, and whether the event may be related to the study procedures (relatedness) as well as expectedness. SAEs will be reported to the sponsor as well as the SAE TSC subgroup by the CI or her delegate within 24 hours of notification. The SAE TSC subgroup will provide an initial judgement on seriousness and relatedness based on the available data, and communicate this to the study team who will share this with the sponsor, who will make the final decision. Further input from the TSC subgroup may be requested at a later point if more information is available about the event.

In order to facilitate the timely review of Serious Adverse Events (SAEs) identified during the trial, a subgroup of the TSC will be formed with the function of reviewing the SAE.

SAEs deemed by the sponsor to be related to the study (i.e. resulting from the administration of research procedures) and unexpected (i.e. not listed in the protocol as an expected outcome) will be emailed to HRA using the "Non-CTIMP safety report to HRA" form. This process will need to be completed as soon as possible, but definitely within 15 days of becoming aware of these as per HRA guidance.

Adverse events (that are not SAEs) that are viewed to be potentially related to study procedures (and this is not expected) by the CI will be reported to the TSC subgroup within 24 hours of notification, who will advise on relatedness and course of action. This judgment will be communicated to the sponsor by the CI.

Role of the Chair of the Trial Steering Committee

- Liaising with the Chief Investigator to set up a schedule of meetings to align with the project plan.
- Establishing clear reporting lines to the Funder, Sponsor, and TMG.
- Providing an independent, experienced opinion if conflicts arise between the needs of the research team, the funder, the sponsor, the participating organisations and/or any other agencies.
- Leading the TSC to provide regular, impartial oversight of the study, especially to identify and pre-empt problems.
- Ensuring that changes to the protocol are debated and endorsed by the TSC; letters of endorsement should be made available to the project team when requesting approval from the funder and sponsor for matters such as changes to protocol.
- Being available to provide independent advice as required, not just when TSC meetings are scheduled.
- Commenting on any extension requests and, where appropriate, providing a letter to the funder commenting on whether the extension request is supported or otherwise by the independent members of the TSC.
- Commenting in detail (when appropriate) regarding the continuation, extension, or termination of the project.
- To contribute to the evaluation of AEs and SAEs as noted above.