1. STATISTICAL ANALYSIS PLAN (SAP)

1.1 TITLE OF THE PROJECT

Project Hope and Self-determination in everyday life
-Investigating the effectiveness of the co-created Paths to EvERyday (PEER) peer-support intervention

1.2 TRIAL REGISTRATION NUMBER

ClinicalTrials.gov NCT04639167

1.3 SAP VERSION NUMBER

This is a detailed version of the Statistical analysis plan (SAP) description in the protocol (Danish latest version 4 sent approved by the Regional Ethics Committee) and protocol paper (Poulsen et al., 2022). This detailed SAP is version 1, Oct 2022. The headings in this SAP are in many instances aligned with the structure recommended by Gamble et al., 2017 (1).

1.4 NAMES, AFFILIATIONS, AND ROLES OF SAP CONTRIBUTORS

This SAP has been drafted by Chalotte Heinsvig Poulsen (MSc, PhD) guided by senior researcher and statistical supervisor Carsten Hjorthøj (MSc, PhD) and principal investigator for Project 'Hope and Self-determination in everyday life' Lene Falgaard Eplov (MD, PhD). Chalotte Heinsvig Poulsen, Carsten Hjorthøj (CH) and Lene Falgaard Eplov are all employed at Copenhagen Research Center for Mental Health (CORE). CH is also an associate professor at the University of Copenhagen.

2. INTRODUCTION

2.1 TRIAL BACKGROUND AND RATIONALE

The background and rationale are described detailed in the protocol paper (Poulsen et al., 2022).

2.2 OBJECTIVES OR HYPOTHESES

From the protocol paper (Poulsen et al., 2022):

The primary aim of the Paths to EvERyday life (PEER) trial is to compare the effect on self-assessed personal recovery of the following interventions: 1) PEER intervention added to service as usual (SAU) and 2) SAU. An additional component of the PEER intervention is that the participants have if needed an opportunity of individual companionship to e.g., the group course, local communities, volunteer work, education, mental health services etc. by a volunteer peer for up to 6 months. A secondary aim of this study is therefore, to investigate whether the individual companionship increased participation in local communities, activities etc. through a self-assessed questionnaire given to the participants in the intervention-arm.

The primary hypothesis is that participants allocated to the PEER intervention added to SAU gain a significantly increased experience of self-assessed personal recovery compared to participants who are allocated to SAU alone. Additionally, we hypothesize, that the superiority of the PEER intervention will be applicable for secondary outcomes and exploratory measures at postintervention so that improvement in empowerment, hope, self-efficacy, self-advocacy, social network, quality of life, work and social functioning will be significantly increased among participants allocated to the PEER intervention.

3. STUDY METHODS

3.1 TRIAL DESIGN

From the protocol paper (Poulsen et al., 2022):

The PEER trial is designed as a randomized, two-arm, investigator initiated, multi municipal, parallel-group superiority trial. The primary outcome is self-assessed personal recovery collected at baseline and end of intervention. Secondary outcomes include self-assessed empowerment, quality of life and work and social functioning collected at baseline and end of intervention. Potential participants are informed about their opportunity to participate by social workers and local coordinators from the participating municipalities of Copenhagen, Rødovre, Gladsaxe, Helsingør and Fredericia, as well as through information meetings in the municipalities, mental health organizations or advertisements. It is an obligation that potential participants on their own initiative participate in an introductory meeting about the group course and the PEER trial.

Included participants were allocated with a 1:1 ration to either Paths to EvERyday life (PEER) a peer-designed co-created group-based peer-support intervention in addition to SAU, or SAU alone. The enrolment started at December 2020 and lasted to October 2022.

The PEER intervention consists of voluntary 10 group sessions (N_{max}=10) and the opportunity of individual companionship by a matched volunteer peer for up to 6 months. The group sessions are delivered by two volunteer peers in collaboration aged 18 years or older with their own experiential skills with mental vulnerability and mental health difficulties, and in case of absence by local coordinators. The group-course is held in civil society locations other than the municipal social service and the mental health centres. The volunteer peers and the local coordinators must complete a specific peer education to facilitate the PEER group course. Peers entering individual companionship must complete additional specific peer training. PEER is a manualized intervention, with a manual for the peers and material developed for the participants to support learning and personal exploration. The content of the group sessions is developed from themes identified in the CHIME (Connectedness; Hope; Identity; Meaning; Empowerment) framework as promoting the personal recovery process (19), as well as knowledge from systematic reviews and meta-analyses in the field focusing on the effect of peer support (5,6,9). Additionally, the method of life story telling (20) and the mindset of acceptance and commitment therapy (ACT) (21) has formed the basis of specific group sessions.

3.2 RANDOMIZATION

From the protocol paper (Poulsen et al., 2022):

Participants gave informed consent (verbal and written) and filled out the baseline questionnaire. After baseline data are obtained, the participants are randomly assigned to either the control (service as usual) or experimental group (PEER + service as usual) with a 1:1 allocation using the randomization module in REDCap (Research Electronic Data Capture). To ensure concealment, the randomization schedule is stored away from the research team and the block sizes are not disclosed. The allocation is performed by a not-blinded research coordinator, who informs the participants allocated to the control group through a central telephone. Moreover, the research coordinator informs the local coordinators in each municipality about participants allocated to the intervention group through submitting the record id via secure email. The local coordinators will be able to identify the participants through their access to REDCap. The allocation sequence will be stratified by municipality study site.

3.3 SAMPLE SIZE CALCULATION

Below numbers are retrieved from the protocol paper (Poulsen et.al 2022).

- Type 1 error set at: 0.05 (α)
- Power: 0.80 (β)
- Difference in mean: 5 points
- within group standard deviation (SD): 15

The sample size calculation is based on tracking a minimal but clinically significant difference between the intervention group and the control group on the continuous scale QPR-15. The RCT by Johnson et al. (2018) recruited a broad target group of individuals who approached psychiatric crisis centres. The response to QPR-22 was normally distributed and with a standard deviation (SD) of 16 in intervention and control group at end of intervention at 4 months (15). In the present RCT, we plan to measure QPR-15 at end of intervention at 3 months and therefore choose a SD of 15 based on the hypothesis that the SD increases over time. A minimum clinically relevant difference between intervention and control group between 4-5 points is recommended (25,33). With an allocation ratio of 1:1 and a minimum clinically relevant difference of 5, a power of 80% and a significance level of 0.05%, we need 284 participants, i.e., 142 in the intervention group and 142 in the control group (Figure 1) to reject the null hypothesis that self-assessed personal recovery is equal in the control group and the PEER group. The sample size and power calculations is conducted using PS Power and Sample Size Calculations software (34). Power calculations (Table 1) indicate that a sample size of 142 participants per group will be adequate to detect relevant significant differences in the secondary outcome measures with a minimum power of 80%.

Table 1: Power calculations for secondary outcomes

Outcome	δ-value for clinically relevant difference in means	σ-value for expected SD	α	Power	Test	Reference
Empowerment Scale, Rogers (ESR)	0.2	0.35	0.05	0.998	t test	(26,35)
Manchester Short Assessment of Quality of life (MANSA)	6	1	0.05	1.0	t test	(28,36)
The Work and Social adjustment scale (WSAS)	4	10	0.05	0.920	t test	(27,37)

No interim analyses were planned.

There were no guidelines for stopping the trials early.

3.5 TIMING OF OUTCOME MEASUREMENTS

Post interventions, about 3 months: Questionnaires were sent out approximately 1-2 weeks after the last group session. There is no definite upper limit for when the follow-up data is not relevant anymore; however, the contact procedure included 6 contact attempts for 3-8 weeks.

4. TRIAL POPULATION

4.1 ELIGIBILITY CRITERIA

Eligibility is assessed by local coordinators and social workers according to the following inclusion criteria:

1) Individuals using the municipal social service in the participating municipalities for support and assistance due to mental vulnerability and mental health difficulties, corresponding to the target group for §82 in the law of social service – i.e., individuals diagnosed with a mental illness and/or who is affected by mental dissatisfaction to a degree that limits the unfolding of their life. Additionally, individuals who self-refer to the trial with similar mental health challenges
2) Are residents of the participating municipalities at baseline
3) Can understand, speak, and read Danish
4) Are aged 18 years or older
5) Have given verbal and written consent to participate in the trial.

The PEER intervention is not designed to accommodate individuals in need of acute or highly specialized care, why individuals who cannot participate in the group on an equal footing as the other group participants will be advised to contact professional mental health care or counselling.

4.2 INFORMATION TO BE INCLUDED IN THE CONSORT FLOW DIAGRAM

Participants attending introductory meeting; People not enrolled; Enrolment – informed consent signed; Excluded after enrolment; Randomization; Allocated to PEER + SAU; Allocated to control group (SAU); Follow up at 3 months (answered questionnaires); Loss to follow-up (did not want to answer questionnaire, never answered questionnaire); Retracted consent; Analyzed according to intention to treat (ITT) analyses.

4.3 WITHDRAWAL

4.3.1 WITHDRAWAL FROM TREATMENT

It was always possible to drop out of the PEER intervention. Hereafter one could choose to participate in follow-up (answer questionnaire etc.) or not. If a person in the intervention group dropped out this was registered by the local coordinators (+ preferably reason if possible). If the participant was in the control group drop out of treatment as usual was not registered as it was not possible to get this information.

4.3.2 WITHDRAWAL FROM RESEARCH

It was always possible to drop out from research and thus not answer questionnaires at follow up. This was registered as e.g., did not want to answer questionnaire/loss to follow-up if the participant explicitly communicated this to the project, otherwise unspecified reason to dropout (e.g., not possible to get in touch with participant/loss to follow-up) was registered. According to Danish law it is possible for participants to withdraw their consent and have all person sensitive data deleted. In these cases, data cannot be used in the statistical analyses. In these instances, we will keep the randomization result and projects specific ID (not identifiable CPR number) in the database. Dropout from research (loss to follow-up and withdrawn consent) is summarized at 3 months follow-up.

4.4 BASELINE CHARACTERISTICS

Register-based data will be summarized e.g., sex, age, civil status, psychiatric diagnosis, educational level, and work status. Additionally, number of contacts to general practitioner, psychologists, and psychiatrists, respectively, will be

calculated in a 5-year period before inclusion in the PEER trial. Also, number of outpatient visits and inpatient bed-days in psychiatric and somatic departments, respectively, will be calculated in a 5-year period before inclusion in the PEER trial. Moreover, number of weeks in ordinary employment, as well as number of weeks on sickness or disability pension benefits, respectively, will be calculated in a 5-year period before inclusion in the PEER trial. Also, allocation of specific municipality social service benefits will be summarized in a 2-year period before inclusion in the PEER trial. Lastly, self-reported baseline outcome measures will be summarized e.g., outcomes of personal recovery (empowerment, hope, self-efficacy, and self-advocacy), social network, quality of life and functioning.

5. STATISTICAL PRINCIPLES AND ANALYSIS

5.1. CONFIDENCE INTERVALS AND P-VALUES

The primary outcome is personal recovery measured on QPR-15 at post intervention. Primary and secondary outcomes are continuous. Differences between the intervention group and the control group will be analyzed using analysis of covariance (ANCOVA) adjusted for municipality study-site. The two-sided significance level for statistical tests will be 5 %. Differences in means and proportions will be presented with a 95% confidence interval (CI) and a p-value. All primary, secondary and exploratory measures will be presented.

5.2 ADHERENCE

Participant adherence to the PEER is not defined as a minimum number of sessions that the participants have participated in. PEER combines group sessions and an opportunity of individual companionship for up to 6 months after group allocation if the need is there.

Participation in group sessions will be reported separately for the type of session and totally for the sessions together. Number of participants receiving the individual companionship will be reported.

Fidelity to the PEER intervention and its principles is evaluated through fidelity reports. Fidelity to PEER will be described as a result of one or more fidelity reports (i.e., poor, good or excellent fidelity to the model).

Major deviations (i.e. outcome changes etc.) from this SAP will be presented/summarized in the reporting of results.

5.3 SPECIFICATION OF OUTCOMES AND TIMING

See appendix 1 for an overview over outcomes and timing.

➢ Personal recovery (measured by QPR-15) at 3 months follow up is the primary outcome (end point comparison).

➢ Empowerment (measured by the Empowerment scale), quality of life (measured by Manchester Short Assessment of Quality of Life (MANSA), and levels of functioning (measured by Work and Social Adjustment Scale (WSAS)) at 3 months follow up are secondary outcomes (end point comparisons).

➢ Self-efficacy (measured by the General Self-Efficacy Scale (GSE), hope (measured by the State Hope Scale (SHS), self-advocacy (measured by the self-advocacy scale (SAS), and social network (measured by the Copenhagen Social Relations Questionnaire (CSRQ) at 3 months follow up are exploratory outcomes (end point comparison).

5.4 ANALYSIS METHODS

The trial is analyzed according to the statistical principle “intention-to-treat”. This means that analyses are based on all included participants as opposed to “per protocol” analyses.

For the primary outcomes in both trials, the null hypothesis tested is that there is no difference in personal recovery (QPR-15) between the two groups (intervention group and control group) at 3 months' follow-up. The null hypotheses are similar in the other analyses assuming no differences between groups.

5.4.1 BASELINE VARIABLES

The chi^2 test is used to test for differences in nominal baseline variables (sex, civil status, psychiatric diagnosis, educational level, work status and allocation of specific municipality social benefits) and the t-test is used to test for differences in continuous baseline variables (age, personal recovery, empowerment, functioning, quality of life, self-efficacy, hope, self-advocacy, and social network). If the test assumptions in the latter are not met i.e., if the data is not normally distributed at all, a non-parametric test will be performed instead (e.g., Kruskal Wallis or Mann Whitney U test). The associations between intervention groups, number of contacts to primary and secondary health care, as well as number of weeks in ordinary employment, and number of weeks on sickness or disability pension benefits will be assessed using Poisson regression models to estimate incidence rates and incidence rate ratios (IRRs) with 95% confidence intervals.

5.4.2 SELF-REPORTED OUTCOMES

Primary, secondary, and exploratory outcomes are calculated and presented in means of scores at 3 months follow-up.

The primary outcome is personal recovery measured on QPR-15 at post intervention. Primary and secondary outcomes are continuous. Differences between the intervention group and the control group will be analyzed using analysis of covariance (ANCOVA) adjusted for municipality study-site. Effect sizes to judge clinical relevance will be calculated by Cohen's d.

Data analyses will be based on the intention-to-treat principle i.e., that data from all participants will be included corresponding to the group to which the participants have been allocated. The prerequisite for using the ANCOVA analysis is that it is a general linear model that tests whether the average of a dependent variable is similar across levels of a categorically independent variable, in this case the PEER intervention, while statistically controlling for the effects of other continuous variables i.e., co-variates are not of primary interest.

5.5 SENSITIVITY ANALYSES

No adjustments will be made in the primary analyses other than for stratification variables.

Sensitivity analyses are made with:

● Adjustment for baseline differences for those baseline characteristics with unequal/skewed baseline means and that can thus be associated with the outcome. Baseline characteristics in this case include (in addition to stratification variables) psychiatric diagnosis, age, and functioning) and self-reported outcome measures at baseline. Baseline tests will not be used exclusively in judging whether to include in the sensitivity analysis. Inclusion will be based on whether the groups are different to the extent that it could affect the analyses. The selection will be guided by CH.

● Imputations of missing values representing "worst" and "best" case of imputations. We will make two analyses: one where we in both groups replace imputations with "worst" case defined as the 90 percentiles from the imputed value and one where we in both groups replace imputations with "best" case defined as the 90 percentiles from the imputed value.

● The observed data.

Sensitivity analyses will be made for the primary outcome.

5.6 SUBGROUP ANALYSES

Inclusion in the PEER trial was initiated during the COVID-19 pandemic in Dec. 2020. Therefore, we plan to perform a subgroup analysis accounting for national restrictions due to the COVID-19 pandemic because the varying degrees of restrictions might have had an impact on intervention adherence and outcome during the PEER trial. We plan to perform this subgroup analysis despite a small sample size and thereby a probably lack of statistical power.

5.9 MISSING DATA

In case of missing data, multiple multivariate imputations will be used and all co-variates of supposed prognostic significance will be used to impute a distribution of missing data. If possible, multiple multivariate normal regression imputations (Markov Chain Monte Carlo (MCMC)) will be used. This is possible if all imputed data follow the same distribution (e.g. are scale variables). A table of auxiliary variables are made based on the list of variables used in the PEER project. These are chosen for being theoretically associated with the specific outcome. Also, variables that are predictive for missing data are included. This selection will be based on whether there is skewed dropout for the specific outcome variable. In the cases of extreme distributions i.e., if the data are not normally distributed at all, predictive mean matching will be used instead of multivariate normal imputations. All variables in the model will also be included in the imputation model. We will perform at least 100 imputations for each analysis.

5.10 ADDITIONAL STATISTICAL ANALYSES

Additional to the planned analyses in the protocol we will:

- Calculate the effect size (based on Cohen's d) of the primary outcome QPR-15 at 3 months follow up.

5.11 SAFETY DATA

The following variables will be summarized for each randomization group at 3 months follow-up.

- Number of bed days and admissions (somatic indication)
- Number of bed days and admissions (psychiatric indication)
- Number of deaths from suicide and other causes
- Number of probably self-harm

5.12 STATISTICAL PACKAGES TO BE USED TO CARRY OUT ANALYSES

We will primarily use the statistics program SPSS. Other statistical packages SAS or STATA might be used for some analyses.